2(58) `2017
ISSN 1813 1905

ЯКУТСКИЙ МЕДИЦИНСКИЙ ЖУРНАЛ

YAKUT MEDICAL JOURNAL

SCIENTIFIC - PRACTICAL JOURNAL
OF THE YAKUT SCIENCE CENTRE
OF COMPLEX MEDICAL PROBLEMS

The founder
The Yakut Science Centre
of Complex Medical Problems

ISSN 1813 1905
2(58) '2017

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Quarterly

Registered by the Office of the Federal Service on supervision in the field of communications, information technologies and mass communications in the Republic Sakha (Yakutia) December 13/2016

Registration number PI No.TU 14-00475

Subscription index: 78781
Free price

"Yakut Medical Journal" is included in the approved by the Higher Attestation Commission of the Russian Federation List of leading peer-reviewed scientific journals and publications, in which the main scientific results of dissertations for the acquisition of scientific degrees of Doctor and Candidate of science on biological sciences and medicine should be published.

The journal is included in the international directory system under periodic and proceeding editions "Ulrich's International Periodicals Directory"

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FACTORS OF THE ENVIRONMENT AND MORBIDITY OF THE POPULATION OF THE SOUTHERN INDUSTRIAL TERRITORY OF YAKUTIA WITH MALIGNANT NEOPLASMS

ABSTRACT

The authors present analysis of the degree of influence of anthropogenic and technogenic load on the state of the environment of the territory and the incidence of malignant neoplasms in the population of the districts of the Southern industrial zone of Yakutia.

Keywords: Southern industrial zone of Yakutia, neoplasms, environmental factors, morbidity.

INTRODUCTION

The territory of the industrial zone of South Yakutia (486.8 thousand km2), which includes Aldan, Neryungri, Tomponsky, Ust-Maysky districts, for many decades is experiencing a huge burden from the industrial-urban human activities. In these areas, the average annual temperature ranges from - 6 ° C (Lensky) to - 1.7 ° C (Tomponsky). By the level of the average annual temperature, the Aldan district is relatively moderate, Neryungri, Ust-Maysky is relatively extreme, and the Tomponsky region is to extremes. The level of heat supply in the Ust-Maysky region is more favorable for the development of agriculture, the sum of the average daily temperatures here ranges from 1647.0 to 1764.5 °C. In Aldan, Neryungri, and Tomponsky districts, heat supply is estimated as «inadequate» (Σ T> o5 is from 1365 to 1577°C), and the average January temperature is often lowered to -30°C. The level of supply with precipitation is estimated as «relatively low» in Ust-Maysky (260.0 mm), and «moderate» in Neryungri (520.3 mm) areas. The capacity of permafrost soils ranges from 120 to 250 m.

In Southern Yakutia the mining industry is developed: in Neryungri district - coal mining, in Aldansky - gold mining, mica, in addition, there are rail and road transport. From traditional industries - reindeer husbandry, hunting, there is some development of agriculture, herd horse breeding. In the Tomponsky region, coal and gold mining are developed, from traditional industries - reindeer herding, meat and milk cattle breeding, herd horse breeding. In the Ust-May district there is the Dzhugdzhursky knot for the extraction of gold and antimony.

The purpose of the study is to analyze the degree of influence of anthropogenic, technogenic factors caused by industrial-urban human activity on the incidence of malignant neoplasms (MN) in the population of Southern Yakutia.

MATERIALS AND METHODS

The materials of reporting of the Yakut republican oncological dispensary for the period of 1989 - 2010 are analyzed. The materials of the State report of the Ministry of Nature Protection of the Republic of Sakha (Yakutia) for the period 2010 - 2014 were used. [9,10], statistical data of the Territorial authorityof the Federal State Statistics Service for the RS (Y) [4,5], the results of their own research [1, 2, 6, 7]. Assessment of the impact of anthropogenic and man-made loads on the state of the environment (OS) is carried out using the methods developed by EI. Burtseva [3]. The statistical data were processed according to the standard method using the «Statistical» software package.

RESULTS AND DISCUSSION

The environment of the territories of the industrial regions of South Yakutia is experiencing tremendous anthropogenic and technogenic stresses from the industrial and urban human activities.

Medico-demographic indicators and anthropogenic load on the state of the regions. The population of the regions of South Yakutia increased by 154.4 thousand (67.3%) by 1990 compared to 1959, which is connected with the development of the mining industry and led to an increase in the intensity of anthropogenic and technogenic loads on the OS of the districts . By 2012, the population as compared with 1990 decreased by 54.0 thousand people. On 6,1%.

In the industrial regions of South Yakutia, the predominant nationalities are Russian and other newcomers, attracted to work in extractive industries (Table 1).

After 1990, in connection with the collapse of the mining industry from the industrial regions of South Yakutia, by 2012, 121,400 people left the RS (Y) area, mostly young people of working age. According to the calculation, the density of the population in the Neryungri district is high, in the Aldan - middle, Tomponsky and Ust-May districts - low.

According to the Republican statistic data, the indigenous population in the zone of South Yakutia ranges from 3.5% in the Neryungri district to 25.4% in the Tomponsky region, and relatively low birth rates for children are recorded in the Aldan and

Earlier, we found that the maximum incidence of MN of women's reproductive organs in the republic is registered in industrial regions, where the majority of the population are visitors who work at mining enterprises [8-10]. It was found that with the decline in the birth rate of children is associated with an increase in the incidence of women with MN of the reproductive organs (r = -0.68), primarily of the breast (r = -0.62).

Economic and technogenic stress on the environment of the districts. The environment of the territory of industrial regions is experiencing a high man-caused strain on the part of mining enterprises, emissions of pollutants into the atmosphere, discharges of polluted sewage, an increase in the areas of disturbed land and transport load (table 2).

Agriculture load of a surrounding medium of territories slight as in these areas the livestock production and reindeer breeding (tab. 3) is developed.

Evaluation of the influence of district-forming factors on the state of the environment. In industrial regions of South Yakutia, the main area-forming factor is the industrial-urban type of nature use.

Table 1

Medico-demographic indicators of the population in industrial regions of South Yakutia per 1000 population, Stat. Yearbook of the RS (Ya), 2009, 2012; Demographic Yearbook of the RS (Ya)

Content	Years	Districts			
		Aldan	Neryungri	Tom-ponsky	Ust-May
Fertility of children	1990	15,7	15,9	19,9	17,5
	2000	10,6	11,1	13,4	10,3
	2005	12,0	11,5	11,6	10,5
	2011	13,0	13,0	15,4	14,3
Mortality of the population	1990	8,1	3,6	6,0	6,0
	2000	13,7	6,7	10,7	13,6
	2005	14,8	8,7	11,2	13,2
	2011	14,6	9,6	12,1	15,7
Population increase	1990	7,6	12,3	13,9	11,5
	2000	-3,0	4,3	2,7	-3,3
	2005	-2,8	2,9	0,5	-2,8
	2011	-1,6	3,4	3,3	-1,4
Yakuts and indigenous peoples,%	1990	7,3	3,5	25,4	16,6
	2011	9,2	3,9	45,6	33,2
Russian and other visiting nationalities , %	1990	92,7	96,5	75,6	83,4
	2011	90,8	96,1	54,4	66,8
Population density, people. per 1 km2	1990	0,41	1,21	0,17	0,22
	2011	0,27	0,82	0,10	0,08
Scale of ranking	1990	3	4	2	3
	2011	3	4	1	1
Load on the environment	1990	Me	Mi	Mu	Me
	2011	Me	Mi	L	L

Note. In Table. 1-4: H- high, Mu - moderately the under, Mi- moderately increased; I - intense, Rs - relatively satisfactory, Rt - relatively tense; Me - medium, L – low

Table 2

Technogenic loads in industrial regions of South Yakutia

Indicator	Total for Southern Yakutia	Districts			
		Aldan	Neryungri	Tomponsky	Ust-May
The mountain weight taken from an earth subsoil till 2002, million m3	1693,4	1096,6	439,0	36,7	121,1
Emissions of air pollutants for 2011-2014, thousand tons	270,7	60,6	150,7	38,3	21,1
% Captured and purified	139,4	23,0	92,6	5,3	18,5
Including sulfur dioxide, thousand tons	24,2	4,1	16,8	2,1	1,2
Carbon monoxide, thousand tons	84,9	32,0	19,8	20,9	12,2
Nitrogen oxides, thousand tons	60,4	6,2	50,6	2,0	1,6
Volatile organic compounds + hydrocarbons, thousand tons	3,5	0,4	2,3	0,6	0,2
Solids, thousand tons	96,8	17,2	60,6	12,8	6,2
Effluent discharge into surface water, million m3	255,9	62,9	157,4	7,4	28,2
Including the share of polluted water, %	262,6	81,1	39,2	98,5	43,8
Disturbed lands, hectar	17985	8861	8296	515	313
Load on the environment	Mi	H	H	Mu	Mi
State of the environment	Rt	I	I	Rs	Rt

Note. In Table. 1-4: H- high, Mu - moderately the under, Mi- moderately increased; I - intense, Rs - relatively satisfactory, Rt - relatively tense; Me - medium, L – low

Based on a comprehensive assessment of the environmental conditions of the industrial areas of South Yakutia, the environmental conditions of the Aldan and Neryungri areas are estimated as tense, Ust-Maysky as relatively tense, and Tomponsky as relatively satisfactory.

The results of the assessment of the effects of regional environmental factors on individual territories should be taken into account when developing scientifically based prevention measures aimed at improving the quality of environmental protection measures.

Morbidity of the population with malignant neoplasms. Throughout the analyzed period (1989-2010), almost everywhere in the territories included in the industrial zone of South Yakutia, there was an increase in the incidence of heart failure (table 4). Thus, by the 2001-2010 period, In comparison with 1989-1998, the incidence of malignant neoplasms per 100,000 population increased significantly - in Aldansky by 93.1 (with an average annual growth rate of 4.20%), in Neryungri district 118.4 (7.50) , In the Tomponsky region 68.7 (3.90), in Ust-Mayskiy 66.5 (4.35).

In the areas of the industrial zone, the growth of general indicators of the oncological morbidity of the population was due to the high average annual growth rates of indicators for malignant neoplasms of the digestive tract, the indices for individual regions range from 1.35 (Tomponsky) to 6.20% (Neryungrinsky).

The same situation develops when analyzing the dynamics of the incidence of malignant neoplasms of the respiratory system (from 0.96 - Ust-May to 4.00% - Tomponsky), the female breast (from 2.15 - Ust-May to 9.95% - Neryungrinsky) and urinary organs (5.55 - Aldan to 16.6% - Neryungri district).

In conclusion, we note that the presented materials suggest that in the zone of industrial regions of South Yakutia, one of the main reasons for the increase in the incidence of malignant diseases may be environmental contamination of the territories of the districts as a consequence of the industrial-urban nature use.

As a result of human economic activity, the state of the environment of the Aldan and Neryungri areas is estimated as tense, Ust-Maysky is relatively tense, the Tomponsky region is relatively satisfactory. Consequently, as the degree of environmental contamination increases, the incidence rates of malignant neoplasms significantly increase, which is confirmed by the results of the analysis of the dynamics of the morbidity of the population of the zone of South Yakutia, calculated for 100 thousand, for the periods from 1989-1998 and 2001-2010.

According to the analysis, the incidence rates of malignant neoplasms in the population of the Neryungri district increased by more than 2 times, Ust-Maysky by 1.8 times, Tamponsky and Aldansky by 1.5 times, at the expense of the growth of tumors considered Indicators that indirectly determine the level of environmental pollutants.

REFERENCES:

1. Abramov A.F., Abramova T.A. Vliyanie social'no-ehkonomicheskih faktorov, obraza zhizni, antropogennyh,

Table 3

Load of agriculture in the industrial regions of South Yakutia

District	Yaers	Cattle		Horses		Reindeer		Arable land			Assessment of the load of agriculture
		Total head of livestock	Load on the environment	Total head of livestock	Load on the environment	Total head of livestock	Load on the environment	Yaers	total head of livestock	Load on the environment	
Aldan	1995	1847	L	435	Mu	13757	Mi	1990	2312	Me	Mu
	2008	567	L	598	L	2207	L	2008	1859	Me	L
	± cattle	-280		+163		-11550		±hectare	-453		
Neryungri	1995	512	L	24	L	11886	Mi	1990	518	L	L
	2008	180	L	4	L	6922	Me	2008	65	L	L
	± cattle	-332		-18		-4964		±hectare	-453		
Tomponsky	1995	5952	Mu	2058	Mu	20730	H	1990	2325	Me	Me
	2008	3090	L	1582	Mu	20545	H	2008	2318	Me	Me
	± cattle	-2862		-476		-185		±hectare	-7		
Ust-May *											

Note: * There is no statistical data

Table 4

Morbidity of the population of Southern Yakutia by malignant neoplasms and its average annual growth rate from 1989 to 1998 and from 2001 to 2010, per 100 thousand people

Localization	Years	District			
		Aldan	Neryungri	Tomponsky	Ust-May
Malignant neoplasms - total (C00-97)	1989-1998	183,7	111,7	144,7	124,5
	2001-2010	276,8	230,1	213,4	191,0
	growth rate	4,20	7,50	3,90	4,35
Head and neck (C00-14)	1989-1998	10,6	5,6	13,0	7,4
	2001-2010	6,8	4,5	6,9	4,5
	growth rate	4,35	-2,02	-6,20	-4,85
Organs of digestion - total (C15-25)	1989-1998	71,9	32,1	50,4	41,8
	2001-2010	94,4	61,8	57,6	57,8
	growth rate	2,75	6,70	1,35	3,30
Respiratory organs - total (C32-34)	1989-1998	36,5	23,6	29,9	30,7
	2001-2010	50,3	33,5	42,6	33,7
	growth rate	3,60	3,55	4,00	0,95
Bones and articular cartilages (C40-41)	1989-1998	1,4	1,0	2,6	1,4
	2001-2010	2,2	2,1	2,6	3,5
	growth rate	4,65	8,60	0,05	9,60
Soft tissues (C46-49)	1989-1998	0,0	0,0	0,9	0,7
	2001-2010	0,8	0,9	2,0	1,7
	growth rate	*	*	8,30	9,25
Skin (including melanoma) (C43-46)	1989-1998	6,7	5,8	4,4	3,9
	2001-2010	14,6	13,4	9,2	6,9
	growth rate	8,10	9,75	7,65	5,85
Female breast (C50)	1989-1998	31,3	23,7	25,4	23,3
	2001-2010	40,3	61,2	37,7	28,8
	growth rate	2,55	9,95	4,55	2,15
Female reproductive organs - total (C53-56)	1989-1998	66,5	43,3	52,6	41,6
	2001-2010	96,1	109,1	78,0	68,4
	growth rate	4,20	9,70	4,50	5,65
Male genital organs - total (C61-63)	1989-1998	7,0	3,1	1,8	0,0
	2001-2010	7,7	14,4	1,3	6,6
	growth rate	1,05	16,60	-2,55	*
Urinary organs - total (C64-67)	1989-1998	9,8	6,3	4,8	3,3
	2001-2010	16,8	14,6	15,7	14,7
	growth rate	5,55	8,75	12,60	16,15
Central nervous system (C70-72)	1989-1998	2,5	3,4	2,2	2,3
	2001-2010	2,8	6,1	3,9	6,1
	growth rate	1,15	6,00	5,90	10,25
Thyroid gland (C73)	1989-1998	1,9	1,6	2,6	2,5
	2001-2010	3,4	3,2	5,2	7,8
	growth rate	5,95	8,05	8,05	12,05
Hemoblastoses (C81-96)	1989-1998	8,3	6,4	7,4	4,3
	2001-2010	12,6	11,6	13,1	8,6
	growth rate	4,75	6,15	5,90	8,05

tekhnogennyh nagruzok na demografiyu i zdorov'e naseleniya Yakutii [Influence of socio-economic factors, lifestyle, anthropogenic, technogenic pressures on the demography and health of the population of Yakutia], Yakutsk [Yakutsk] 2014. 400 p.

2. Abramov A.F., Ivanov P.M., Tomskij M.I. Sreda i zlokachestvennye novoobrazovaniya v Yakutii [Environment and malignant neoplasms in Yakutia] Yakutsk: Sfera [Yakutsk: Sphere], 2016. 210 p.

3. Burtseva E.I. Geoehkologicheskie aspekty razvitiya Yakutii [Geoecological aspects of the development of Yakutia], Novosibirsk: Nauka [Novosibirsk: Science] 2006. 269 p.

4. Gosudarstvennyj doklad o sostoyanii i ob ohrane okruzhayushchej sredy Respubliki Saha (YAkutiya) v 2014 godu [State report on the state and protection of the environment of the Republic of Sakha (Yakutia) in 2014], – Yakutsk [Yakutsk] 2015. 304 p.

5. Demograficheskij ezhegodnik Respubliki Saha (YAkutiya): statisticheskij sb. – YAkutsk: Territorial'nyj organ Federal'noj sluzhby gosudarstvennoj statistiki po RS (YA) [Demographic Yearbook of the Republic of Sakha (Yakutia): statistical collection] Yakutsk: Territorial authorityof the Federal State Statistics Service for the RS (Y) [Territorial authority of Federal State Statistics Service in RS (Ya)], 2012. 186 p.

6. Ivanov P.M., Tomsky M.I., Karataev P.D. Zlokachestvennye novoobrazovaniya v Yakutii na rubezhe vekov [Malignant neoplasms in Yakutia at the turn of the century] Yakutsk: Sfera [Yakutsk: Sphere], 2008. 272 p.

7. Ivanov P.M., Tomskij M.I., Kipriyanova N.S. Statistika zlokachestvennyh novoobrazovanij v nachale tret'ego tysyacheletiya [Malignant neoplasm statistics at the beginning of the third millennium] Yakutsk: OOO «Smik-Master. Poligrafiya» [Yakutsk: Smik-Master LLC. Polygraphy «], 2012. 166 p.

8. Makarova N.N., Ivanov P.M., Pisareva L.F. Ehpidemiologiya raka shejki matki na Severe [Epidemiology of cervical cancer in the North] Yakutsk: Sfera [Yakutsk: Sphere], 2008. 128 p.

9. Myreeva S.A., Makarova N.N., Ivanov P.M. Ehpidemiologiya zlokachestvennyh opuholej zhenskih polovyh organov v Yakutii (rasprostranennost', faktory riska, profilaktika, rannyaya diagnostika) [Epidemiology of malignant tumors of female genital organs in Yakutia

Table 5

The annual incidence of malignant neoplasms in Southern Yakutia in 2006-2015, (per 100 000 population)

Localization	RS(YA)	Zone of southern Yakutia	District			
			Aldan	Neryungri	Tomponsky	Ust-May
Men						
All malignant neoplasms(C00-97)	149,9±0,18	307,8±0,66*	398,5±1,37**	264,6±0,83**	258,8±1,94**	328,4±2,84**
Including: Lip (00)	0,7±0,01	1,6±0,05*	1,9±0,09**	1,3±0,06**	1,5±0,15	2,5±0,25**
Tongue and oral cavity (C01-09)	3,1±0,03	7,2±0,10*	8,9±0,20**	7,0±0,13	2,9±0,21**	7,4±0,43
Pharynx (C10-14)	2,0±0,02	3,1±0,07*	5,2±0,16**	1,6±0,06**	4,4±0,25**	4,9±0,35**
Esophagus (C15)	7,1±0,04	9,9±0,12*	13,7±0,25**	6,5±0,13**	13,1±0,44**	17,2±0,65**
Stomach (C16)	15,8±0,06	30,2±0,21*	46,2±0,47**	23±0,24**	21,8±0,56**	29,4±0,85**
Colon (C18)	5,4±0,03	13,0±0,14*	15,5±0,27**	11,6±0,17**	10,2±0,39**	17,2±0,65**
Rectum (C19-21)	6,5±0,04	16,9±0,15*	17,9±0,29	19,9±0,23**	5,8±0,29**	2,5±0,25**
Liver (C22)	11,0±0,05	8,2±0,11*	9,9±0,22**	5,4±0,12**	13,1±0,44**	17,2±0,65**
Pancreas (C25)	5,4±0,03	10,6±0,12*	10,8±0,23	9,6±0,16**	11,6±0,41	17,2±0,65**
Larynx (C32)	3,5±0,03	9,0±0,11*	8,9±0,20	8,8±0,15	11,6±0,41**	7,4±0,43**
Lung (C33,34)	32,0±0,08	63,9±0,30*	84,8±0,63**	51,5±0,36**	71,3±1,02**	61,3±1,23
Bone and cartilages (C40-41)	1,3±0,02	2,0±0,05*	1,4±0,08**	2,1±0,07**	1,5±0,15**	4,9±0,35**
Skin melanoma (C43)	1,4±0,02	2,1±0,05*	2,4±0,11*	1,8±0,07**	1,5±0,15**	4,9±0,35**
Skin (C44-46)	3,1±0,03	6,6±0,10*	4,7±0,15**	7,2±0,14**	5,8±0,29**	12,3±0,55**
Soft tissue (C46-49)	5,0±0,03	12,1±0,13*	8,5±0,20**	14±0,19**	10,2±0,39**	17,2±0,65**
Prostate gland (C61)	7,1±,04	14,0±0,14*	17,4±0,29**	14±0,19	5,8±0,29**	9,8±0,49**
Testicle (C62)	1,3±0,02	2,3±0,06*	1,9±0,09**	2,8±0,09	0,0±0,00	2,5±0,25
Kidney (C64)	5,9±0,04	12,4±0,13*	12,7±0,24	12,4±0,18	8,7±0,36**	17,2±0,65**
Bladder (C67)	6,3±0,04	15,0±0,15*	16±0,27	15,3±0,20	10,2±0,39**	14,7±0,60
Central nervous system (C70-72)	3,4±0,03	7,1±0,10*	5,7±0,16**	9,1±0,15**	0,0±0,00	7,4±0,43
Thyroid gland (C73)	1,1±0,02	2,0±0,05*	2,8±0,11**	1,3±0,06**	4,4±0,25**	0,0±0,00
Hemoblastoses (C81-96)	8,2±0,04	18,8±0,1*	17,4±0,29	17,6±0,21	21,8±0,56**	31,9±0,88**
Women						
All malignant neoplasms(C00-97)	225,4±0,21	302,5±0,64*	341,0±1,27**	293,5±0,84**	250,3±1,90**	283,8±2,67**
Including: Lip (00)	0,2±0,01	0,3±0,02	0,9±0,07**	0,0±0,00	0,0±0,00	0,0±0,00
Tongue and oral cavity (C01-09)	2,6±0,02	2,8±0,06*	4,7±0,15**	1,4±0,06**	1,4±0,14**	10,0±0,50**
Pharynx (C10-14)	0,8±0,01	0,9±0,03	0,9±0,07	1,0±0,05	1,4±0,14	0,0±0,00
Esophagus (C15)	4,3±0,03	3,6±0,07*	6,1±0,17**	1,9±0,07**	4,3±0,25**	7,5±0,43**
Stomach (C16)	13,9±0,05	18,5±0,16*	25,0±0,34**	16,6±0,20**	11,5±0,41**	15,1±0,62**
Colon (C18)	13,7±0,05	22,0±0,17*	27,4±0,36**	20,0±0,22**	17,3±0,50**	22,6±0,75
Rectum (C19-21)	10,0±0,05	15,6±0,14*	22,6±0,33**	12,8±0,17**	8,6±0,35**	20,1±0,71**
Liver (C22)	12,8±0,05	6,5±0,09*	12,3±0,24**	3,1±0,09**	8,6±0,35**	7,5±0,43
Pancreas (C25)	7,3±0,04	9,0±0,11*	9,0±0,21	9,3±0,15	5,8±0,29**	12,6±0,56**
Larynx (C32)	0,6±0,01	0,7±0,03	0,9±0,07	0,7±0,04	0,0±0,00	0,0±0,00
Lung (C33,34)	19,0±0,06	18,1±0,16	23,6±0,33**	15,0±0,19**	15,8±0,48**	25,1±0,79**
Bone and cartilages (C40-41)	1,2±0,02	1,1±0,04	0,9±0,07**	1,4±0,06	0,0±0,00	0,0±0,00
Skin melanoma (C43)	1,9±0,02	5,4±0,0*	12,3±0,24**	3,1±0,09**	0,0±0,00	2,5±0,25**
Skin (C44-46)	4,1±0,03	9,0±0,11*	8,0±0,19	10,5±0,16**	5,8±0,29**	5,0±0,35**
Soft tissue (C46-49)	6,2±0,04	13,7±0,14*	11,3±0,23**	16,4±0,20**	8,6±0,35**	7,5±0,43**
Mammary gland (C50)	40,2±0,09	58,6±0,28*	41,0±0,44**	67,5±0,40**	74,8±1,04**	30,1±0,87
Uteral cervix (53)	19,9±0,06	27,6±0,19*	30,2±0,38**	25,0±0,24**	27,3±0,63	42,7±1,04
Body of the womb (54)	10,2±0,05	18,6±0,16*	21,7±0,32**	18,3±0,21	12,9±0,43**	15,1±0,62
Ovari (56)	11,0±0,05	12,0±0,13	9,0±0,21**	13,3±0,18**	14,4±0,46**	10,0±0,50**
Kidney (C64)	5,8±0,03	4,2±0,08*	5,7±0,16**	4,0±0,10	1,4±0,14**	2,5±0,25**
Bladder (C67)	5,6±0,03	8,8±0,11*	9,9±0,22**	9,0±0,15	2,9±0,20**	10,0±0,50**
Central nervous system (C70-72)	3,9±0,03	4,6±0,08*	2,4±0,11**	5,7±0,12**	4,3±0,25	5,0±0,35
Thyroid gland (C73)	6,5±0,04	8,9±0,11*	7,5±0,19**	9,3±0,15	5,8±0,29**	17,6±0,66**
Hemoblastoses (C81-96)	9,8±0,04	11,0±0,12*	9,9±0,22**	12,6±0,17**	7,2±0,32**	7,5±0,43**

Note. The difference of indexes statistically is significant ($p < 0.05$) – in relation to national average (*) and srednezonalny (**) to indexes.

(prevalence, risk factors, prevention, early diagnosis)] Yakutsk: Sfera [Yakutsk: Sphere] 2011. 173 p.

10. Nikolaeva T.I., Ivanov P.M., Pisareva L.F. Rak molochnoj zhelezy v regione Krajnego Severa [Breast cancer in the Far North region] Yakutsk: Sfera [Yakutsk: Sphere], 2009. 127 p.

11. Statisticheskij ezhegodnik Respubliki Saha (Yakutiya): statist. sb. [Statistical Yearbook of the Republic of Sakha (Yakutia): Statistical collection]. Yakutsk [Yakutsk], 2009. 691 p.

12. Statisticheskij ezhegodnik Respubliki Saha (Yakutiya): statist. sb. [Statistical Yearbook of the Republic of Sakha (Yakutia): statistical collection]. Yakutsk [Yakutsk], 2012. 737 p.

Information about authors:

Yakutsk, Republic Sakha (Yakutia), Russia:

IVANOV Peter Mikhaylovich. – D. Med. Sc, Professor of Medical University of NEFU, senior researcher YSC CMP, petr_ ivanov_38@mail.ru;

ABRAMOV Alexey Fedorovich - D. Biol. Sc, Professor., Yakut research institute of agriculture of the Russian academy of agricultural sciences;

TOMSKY Mikhail Innokentievich - D. Med. Sc, Director of YSC CMP;
GOLDEROVA Aitalina Semenovna - D. Med. Sc, chief researcher of YSC CMP; ROMANOVA Anna Nikolaevna. - D. Med. Sc,, chief researcher of YSC CMP;
NIKOLAEV Vyacheslav Mikhailovich - Cand of Biol. Sc, senior researcher of YSC CMP;
KIPRIYANOVA Nadezhda Sidorovna - D. Med. Sc, Professor Medical University of NEFU:
NIKOLAEVA Tatiana Ivanovna – Cand. Med. Sc., deputy chief doctor of Yakut Republican Oncology Center (YROC),
ZHARNIKOVA Tatyana Nikolaevna - Cand of Med. Sc., head of the surgical department of YROC,
MAKAROVA Natalia Nikolaevna - Cand of Med. Sc., head of the gynecology department YROC,
MYREEVA Svetlana Anatolievna - Cand of Med. Sc, surgeon-oncologist of YROC.

ORIGINAL RESEARCHES

E.P. Borisova, E.S. Kylbanova

VALUE OF ENVIRONMENTAL FACTORS IN THE YAKUTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND CHRONIC BRONCHITIS IN COMBINATION WITH METABOLIC SYNDROME

ABSTRACT

Objective. To assess the influence of environmental factors in the Yakuts with the combination of chronic obstructive pulmonary disease and chronic bronchitis with metabolic syndrome.

Materials and methods. A comprehensive examination of 148 patients was performed on the basis of the emergency department of the Republican Hospital No. 2 - the Center for Emergency Medical Care in Yakutsk. The main group consisted of 88 patients with metabolic syndrome in combination with chronic obstructive pulmonary disease (COPD) and chronic bronchitis (CB) of Yakutia. The average age was 50.9 ± 0.91 years, for gender: women 69.3%, men 30.7%. The comparison group consisted of 60 patients of Yakut nationality with COPD and chronic bronchitis without metabolic syndrome. The average age of 48.9 ± 1.35 years was consistent with the age of the main group, the gender composition of women was 80%, men 20%. Patient survey was carried out taking into account the developed questionnaire, approved by the ethical committee, which contained questions on the blocks: socio-demographic characteristics, anamnestic data, heredity research, behavior and health.

Results. In the course of the study, it was revealed that for such environmental risk factors as physical activity, smoking, alcohol consumption, the frequency of occurrence in the groups does not differ. At the same time, a higher index of a smoker and fewer hours spent on physical activity a week are more common in Yakuts with chronic obstructive pulmonary disease and chronic bronchitis with a metabolic syndrome, which negatively affects the risk of cardiovascular complications in this category of patients.

Conclusion. Thus, we have identified a significant contribution of environmental factors, in particular low physical activity, to the development of MS and a negative characteristic for a greater number of pack-years in individuals with CK / COPD in combination with MS.

Keywords: metabolic syndrome, chronic obstructive pulmonary disease, chronic bronchitis, environmental factors.

Diseases of the respiratory system in the Republic Sakha (Yakutia) occupy one of the leading places in the structure of morbidity and determine to a large extent the level of temporary disability, disability and mortality of the population.

According to WHO, chronic obstructive pulmonary disease (COPD) is one of the most common diseases, it is expected to become the third leading cause of death in 2020. Over the past decade, the concept of COPD has been recognized as a disease with systemic manifestations including cardiovascular pathology, cachexia, muscle dysfunction, osteoporosis, anemia, clinical depression, metabolic disturbances and endothelial dysfunction [7].

Currently, the metabolic syndrome (MS) is seen as a «21st century pandemic» by the WHO experts. Its prevalence among the adult population of Russia according to the data of the VNOK, 2009, is 20-40% and more often it occurs in middle-aged and older people. The prevalence of MS according to the criteria of the International Diabetes Federation among the aboriginal population of Yakutia is 8.8% [5].

However, currently the peculiarities of the combined course of the pathology of the respiratory tract with MS in the domestic science are devoted to single studies and there is no data on this combined pathology in the Yakut ethnic group.

The aim of the study was to assess the influence of environmental factors in the Yakuts with the combination of chronic obstructive pulmonary disease and chronic bronchitis with metabolic syndrome.

MATERIALS AND METHODS OF RESEARCH

A comprehensive examination of 148 patients was performed on the basis of the emergency department of the Republican Hospital No. 2 - Center for Emergency Medical Care in Yakutsk. All patients signed informed consent to participate in the survey. The research was carried out within the framework of the research project «Metabolic syndrome and chronic non-infectious diseases among the inhabitants of Yakutia». The approval of the local ethical committee of the Yakutsk Scientific Center of Complex Medical Problems of the Siberian Branch of the Russian Academy of Medical Sciences was obtained.

The main group consisted of 88 patients with metabolic syndrome in combination with chronic obstructive pulmonary disease (COPD) and chronic bronchitis (CB) of Yakutia. The average age was 50.9 ± 0.91 years, for gender:

women 69.3%, men 30.7%. The study included: patients with a diagnosis of COPD 44.3%, with a diagnosis of chronic bronchitis 55.7%.

The comparison group consisted of 60 patients of Yakut nationality with COPD and chronic bronchitis without metabolic syndrome. The average age of 48.9 ± 1.35 years was consistent with the age of the main group, the gender composition of women was 80%, men 20%, patients diagnosed with COPD 41.7%, diagnosed with chronic bronchitis 58.3%. During the statistical analysis, it was established that the study groups did not differ significantly in age, sex composition, and the correlation of diagnoses of COPD and CB.

The diagnosis of COPD and chronic bronchitis was established on the basis of complaints, a history of the disease, an objective examination, spirometry data, in accordance with international conciliation documents: The Global Strategy for the Diagnosis, Treatment and Prevention of Chronic Obstructive Pulmonary Disease 2011 revision (Global Initiative For Chronic Obstructive Lung Disease), the definition of experts from the World Health Organization, the international classification of diseases X revision. Metabolic syndrome was established on the basis of the recommendations of the All-Russian Scientific Society of Cardiology of 2009.

The patients were questioned according to the developed questionnaire, approved by the ethical committee. The status of married (married) included married (married) or living with a partner outside of marriage; In the «lonely» group included single (unmarried), widowers, widows, divorced or living separately. By the level of education, groups with average general, secondary vocational and higher education were selected, by type of employment: mental work, manual labor, pensioners and unemployed.

When studying the history of smoking, the index of the smoking person (ICC) was used in units of «pack / years», which was calculated by the formula: total number of packs / years = number of cigarettes smoked per day × number of years / 20. Index of smoking person> 10 packs / years - a reliable risk factor for COPD.

The assessment of the level of activity was conducted by questioning and is based on one's own assessment of the level of activity by patients, taking into account the number of hours spent on household physical activity per week, physical education and sports.

Statistical processing and analysis of data was carried out using the statistical software package SPSS for Windows. The quantitative indices in the study groups were described by mean values (M) and standard error (m). The verification of the laws of distribution of quantitative indicators was carried out using the Kolmogorov-Smirnov test. The results of the audit showed that the distribution of many quantitative indicators does not obey the normal law. Therefore, for a comparative analysis of quantitative indicators, a nonparametric Mann-Whitney test was used. Investigation of the interrelations of qualitative features was carried out using the classical criterion of Chi-square Pearson. The threshold value of all statistical criteria used was p <0.05.

RESULTS AND DISCUSSION

Due to the fact that social factors undoubtedly influence the incidence of chronic non-infectious diseases, we analyzed groups of patients depending on the marital status, educational level and nature of work.

The data of the comparative social characteristics are presented in Table 1. According to the social status of the main group (COPD / HB + MS, Yakuts), married people prevailed - 77.3%, with secondary vocational education - 48.9%, pensioners - 34.1%. In the comparison group, the share of married people was 66.7%, the level of education was dominated by patients with secondary general education - 35.0%, by employment - mental workers - 38.3%. In analyzing the social status, no statistically significant differences between the groups were found.

In the development of COPD / CB and MS components, heredity is of particular importance. From the unmodified risk factors, the presence of weighed heredity for the development of hypertension, coronary artery disease, cerebral circulatory disorders, diabetes mellitus, oncological pathology, bronchial and pulmonary diseases was assessed. Both in the main and in the comparison group, the aggravated heredity for development of hypertension (56.3% and 51.7%), bronchial and pulmonary diseases (36.4% and 28.3%) was detected quite often (Table 2), however Significant differences in the ratio of AH, IHD, cerebral circulation disorders, diabetes mellitus, oncological pathology, bronchial and pulmonary diseases among the groups studied, we were not identified.

It is known that patients with COPD had a sedentary lifestyle, which contributes to the development of obesity: a study conducted by F. Pitta et al. (2005) showed that patients with COPD go on average 44 minutes a day, while healthy ones 81 minutes a day (p <0.001) [6]. A number of studies have shown that patients with COPD have one or more components of the metabolic syndrome, and a coexisting metabolic syndrome is associated with systemic inflammatory response and lack of physical activity [1, 8]. It is known that the lack of physical activity is one of the most important factors determining the accumulation of visceral fat, which is observed in patients with COPD and MS [3, 4].

In the group with the combined course of COPD / CB and MS, the share of people engaged in physical training was 6.8%, which did not differ from that in the COPD / CB group without MS (13.4%). While the number of hours spent on physical activity per week in the main group was significantly lower than in the comparison group without MS: 23.7 ± 1.98 hours compared to 27.9 ± 2.34 hours, p = 0.000, respectively (Table 3).

The reason for the frequent association of COPD and cardiovascular disease may be a common risk factor - smoking [2]. When assessing a risk factor such as smoking, it was found that 28.4% and 28.3% of the patients we examined were regular smokers in the respective groups, p = 0.644 (Table 3). However, the analysis of the index of a

Table 1

Social status of the surveyed individuals of the Yakut nationality with COPD / CB in the association and without MS, %

Sign		COPD / CB + MS (n=88)	COPD / CB (n=60)	p
Family status	Married	77,3	66,7	0,154
	Lonely	22,7	33,3	
Education	Higher education	20,5	31,7	0,134
	Secondary vocational	48,9	33,3	
	Average total	30,7	35,0	
Employment	Employment Retired	34,1	28,3	0,729
	Brainwork	29,5	38,3	
	Physical work	30,7	28,3	
	Unemployed	5,7	5,0	

Note: In the Tables 1-2 p - significance of differences on x2 Pearson criterion

Table 2

Hereditary burden in Yakut people with COPD / CB in association and without MS, %

Sign	COPD / CB + MS (n=88)	COPD / CB (n=60)	p
Heart diseases	21,6	26,7	0,476
Stroke	17,0	11,7	0,366
Diabetes	9,1	5,0	0,352
Oncological pathology	18,2	10,0	0,170
Arterial hypertension	56,3	51,7	0,578
Diseases of the bronchi and lungs	36,4	28,3	0,216

Table 3

Influence of external factors in persons of Yakut nationality on COPD / CB in association and without MS, %

Sign		COPD / CB + MS (n=88)	COPD / CB (n=60)	p1,2	
Physical training	6,8	13,4	0,3391	0,339[1]	
Physical activity per week (hours), M±m	23,7±1,98	27,9±2,34	0,0002	0,000[2]	
Smoking	Да, регулярно	28,4	28,3	0,644[1]	
	Yes, regularly	28,4	28,3	0,6441	
	YES, PERIODICALLY	4,5	1,7		
	NO, THREW	15,9	11,7		
	No, never smoked	51,1	58,3		
IKS, M±m	8,9±1,51	4,5±1,01	0,0032	0,266[1]	
	Alcohol consumption	Yes, regularly	10,2	3,3	0,2661
	YES, PERIODICALLY	14,8	13,3		
	No	75,0	83,3		

Notes: p1 - significance of differences on x2 Pearson criterion, p2 - significance of differences on Mann-Whitney test

smoking person showed that the value of this indicator in the group of patients with combined pathology was statistically significantly higher - 8.9 ± 1.51 pack-years, than in the comparison group I - 4.5 ± 1.01 pack-years, p = 0.003. Thus, there is a negative characteristic for a greater number of pack-years in COPD / CB patients in combination with MS.

According to alcohol consumption, no statistically significant differences between the groups studied were obtained.

CONCLUSION

Thus, we found that the social status, hereditary burden does not differ in the groups we surveyed. On the risk factors of the external environment in the surveyed, such as physical activity, smoking, alcohol consumption, the frequency of occurrence in groups does not differ. At the same time, a higher index of a smoker and fewer hours spent on physical activity a week are more common in Yakuts with COPD / CB and MS, which negatively affects the risk of cardiovascular complications in this category of patients.

REFERENCES

1. Osakovskiy V.L., Gol'dfarb L.G., Klimova T.M., Sambuugin N., Odgerel Z., Yakovleva M.N., Ignat'ev P.M., Alekseeva L.L., Baltakhinova M.E., Timofeev G.A., Krivoshapkin V.G., Platonov F.A. Metabolicheskiy sindrom u aborigennogo naseleniya Yakutii [Metabolic syndrome in aboriginal population of Yakutia]. Yakutskiy meditsinskiy zhurnal [Yakut Medical Journal]. 2010; 2:98-102.

2. Molenaar E.A., Massaro J.M, Jacques P.F., Pou K.M., Ellison R.C., Hoffmann Udo, Pencina Karol, Shadwick S.D., Vasan R.S., O'Donnell C.J., Fox C.S. Association of lifestyle factors with abdominal subcutaneous and visceral adiposity: the Framingham Heart Study. Diabetes Care. 2009; 32 (3):505-510.

3. Pitta F., Troosters T., Spruit M.A., Probst V.S., Decramer M., Gosselink R. Characteristics of physical activities in daily life in chronic obstructive pulmonary disease. Am. J. Respir. Crit. Care Med. 2005;171 (9):972-977.

4. Anthonisen N.R., Connett J.E., Kiley J.P., Altose M.D., Bailey W.C., Buist A.S., Conway W.A. Jr., Enright P.L., Kanner R.E., O'Hara P. et al. Effects of smoking intervention and the use of an inhaled anticholinergic bronchodilator on the rate of decline of FEV1: the Lung Health Study. JAMA. 1994; 272 (19):1497-1505.

5. Cecere L.M., Littman A.J., Slatore C.G., Udris E.M., Bryson C.L., Boyko E.J., Pierson D.J., Au D.H. Obesity and COPD: Associated Symptoms, Health-related Quality of Life, and Medication Use. COPD. 2011; Vol. 8 (4):275-284.

6. Akpınar E.E., Akpınar S., Ertek S., Sayın E., Gülhan M. Systemic inflammation and metabolic syndrome in stable COPD patients. Tuberk. Toraks. 2012; 60 (3):230-237.

7. Watz H., Waschki B., Kirsten A., Müller K.C., Kretschmar G., Meyer T., Holz O., Magnussen H. The metabolic syndrome in patients with chronic bronchitis and COPD: frequency and associated consequences for systemic inflammation and physical inactivity. Chest. 2009; 136 (4):1039-1046.

8. Tkacova R. Systemic Inflammation in Chronic Obstructive Pulmonary Disease: May Adipose Tissue Play a Role? Review of the Literature and Future Perspectives. Tkacova R. Mediators Inflamm. 2010; 5:859-889.

Information about authors:

Borisova E.P. (Borisova E.P.) - senior lecturer of the Department «Internal Diseases and General Practice (Family Medicine)» of the Faculty of Postgraduate Education of Physicians of the Medical Institute of the Federal State Educational Establishment of Higher Professional Education «North-Eastern Federal University named after M.K. Ammosov «, borisovaep75@mail.ru Yakutsk, Republic Sakha (Yakutia), Russia;

Kylbanova Elena Semenovna (Kylbanova E.S.) - Doctor of Medicine, Head. Department of Internal Medicine and General Practice (Family Medicine), Faculty of Postgraduate Training of Doctors of the Medical Institute of the Federal State Educational Institution of Higher Professional Education «North-Eastern Federal University. M.K. Ammosov «, kyles@list.ru Yakutsk, Republic Sakha (Yakutia), Russia.

Contact information: Borisova Ekaterina Petrovna address: 677005, Yakutsk, ul. Petra Alexeeva 73 sq. M. 24. Telephone 8914 220 67 69.

L.P. Malezhik, M.S. Malezhik, D.T. Nimaeva,
V.B. Tsentendorzhieva

CHANGES OF CYTOKINE PRODUCTION IN CHILDREN AFFECTED WITH ACUTE RESPIRATORY VIRAL INFECTIONS AT POLYMORPHISM OF TOLL-4 (ASP299GLY) AND TOLL-6 (SER249PRO) GENES RECEPTORS

ABSTRACT

The article analyzes the role of polymorphism of Toll-4 (Asp299Gly) and Toll-6 (Ser249Pro) receptor genes in the development of low antiviral protection in children with frequent episodes of acute respiratory infections. It is shown that the synthesis of cytokines IL-1-β, TNF-α decrease in the blood of patients with Toll-4 receptor gene polymorphism and IL-1RA content is increased in comparison with the group of diseased children without abnormal disturbances in signal receptors. Polymorphism in the Toll-6 receptor genes decreases the concentration of cytokines IL-1β, IL-8, TNF-α and IL-10. The concentration of IL-1RA is increased in Pro / Pro and Gly / Gly genotypes compared to the group of patients without polymorphic changes in the corresponding receptors. Genetic disorders in the synthesis of cytokines in the polymorphism of the Toll-4 (Asp299Gly) and Toll-6 (Ser249Pro) receptors are one of the reasons for the failure of antiviral protection in children who often have ARI.

Keywords: acute respiratory viral infection, TLR, polymorphism, cytokines.

INTRODUCTION

"Often ill children (OIC)" is a term for a group of children with a higher incidence of acute respiratory viral infection (ARVI) than among peers. The maximum incidence of acute respiratory viral infection among children is from 6 months to 6 years old and is more than 6 episodes a year [3,8]. According to modern ideas, the main reason for the high susceptibility of children to a viral infection is immaturity of the immune system [1,2,9] and a hereditary predisposition to infectious diseases [4,5]. Genetic changes in the immune system can occur at different stages of the immune response. First of all, this concerns receptors that come into contact with the pathogen. The main role in the recognition of the pathogen is played by Toll-like receptors (TLR). They are part of the cell membranes of all immunocompetent cells [6]. Polymorphism of Toll-receptor genes is associated with a number of diseases. From the literature it is known that SNP (Asp299Gly) of the Toll-4 gene is associated with septic shock [11], with the development of atherosclerosis and coronary heart disease [10], diabetes mellitus [7]. SNP Ser249Pro in the Toll-6 receptor gene was noted in patients with bronchial asthma [12]. In earlier works [4], we found that 55.6% of children with a chronic respiratory viral infection had genetic mutations in Toll-4 (Asp299Gly) and 75% in the gene (Ser249Pro) of the Toll-6 receptor.

Ligands for Toll-4 receptors are double-stranded DNA viruses, and for Toll-6 receptors - Gram-negative bacteria. The contact of pathogen-recognizing receptors with the ligand triggers the synthesis of cytokines, which regulate the degree of immune reactions. We believe that genetic disorders in Toll-receptors affect the level of intracellular signaling and the amount of cytokines produced.

The aim of the study was to study the effect of Toll-4 (Asp299Gly) and Toll-6 (Ser249Pro) receptor polymorphism on the production of cytokines in children who often suffer from acute respiratory viral infection.

MATERIALS AND METHODS

The clinical group consisted of 190 children of both sexes aged 1 to 3 years, often with acute respiratory viral infections. Of the children surveyed, 49% had influenza, 26% had parainfluenza, 5% had an adenovirus infection, and 4% had a syncytial virus. The criteria for inclusion in the studies were: in the history of at least 6 episodes of acute respiratory viral infection, the age of patients from 1 to 3 years, the first 3 days of the disease.

The study did not include children with chronic bronchopulmonary diseases (bronchial asthma, recurrent bronchitis, malformations of the respiratory system, allergic diseases). The work was carried out on the basis of the Scientific Research Institute of Medical Ecology. The studied material was venous blood.

As a population control was used a sample of 76 conditionally healthy children (30 boys and 46 girls) aged 1 to 10 years. DNA extraction was carried out with the help of «DNA Express Blood» kits (NPF «Litech», Russia, Moscow). Synthesis of oligonucleotide primers used in the work was carried out by NP «Litehs», Moscow. The detection of mutations was carried out by PCR. The concentration of cytokines was determined by the method of solid-phase ELISA using reagents LLP «Vector-Best» Novosibirsk.

Studies were carried out on 90 patients with ARVI children with Toll-4 gene polymorphism (Asp299Gly) and 100 patients with polymorphism carriers Toll-6 (Ser249Pro) receptors. All subjects were divided into 7 groups: 1 group - healthy children, control (n = 76); 2 group - patients with ARVI children with the genotype Asp / Asp (n = 40); Group 3 - sick children with the Asp / Gly genotype (n = 18); Group 4 - sick children with genotype Gly / Gly (n = 32); Group 5 - sick children with genotype Ser / Ser (n = 25); 6 group - children having genotype Ser / Pro (n = 50); Group 7 - children with genotype Pro / Pro (n = 25).

The statistical processing of the material was carried out by the method of variational statistics with the help of the Microsoft Excel 2007 software packages, STATISTICA 6.0. Before the analysis, the variational series were tested for normality using the Shapiro-Wilk test. Under normal distribution was used the Student's test (t-test). The indicators are presented as mean values with a standard deviation (M ± SD). With an abnormal distribution of the trait was

applied the Mann-Whitney test (U-test).

RESULTS AND DISCUSSION

Our research has shown that with the polymorphism of the genes (Asp299Gly) of Toll-4 receptors, the synthesis of IL-1ß is reduced compared to the group of patients with the Asp / Asp genotype who do not have polymorphic changes (Table 1).

Synthesis of the second anti-inflammatory cytokine TNF-α in polymorphism of the Toll-4 receptor gene in frequently ill children is increased in comparison with the control, but in the case of the Asp / Gly genotype to a lesser extent (9.9 pkg / ml) than in the Gly / Gly genotype 12.34 pkg / ml).

The concentration of chemokine IL-8 in ARVI is high regardless of the presence or absence of mutations in the gene.

Synthesis of anti-inflammatory cytokine IL-4 in the first days of the disease does not change and the polymorphic variants of the Toll-4 gene do not affect it.

The concentration of IL-10 increases in patients with ARVI - the carriers of all studied genotypes.

The level of IL-1RA is significantly elevated in the blood of patients with Gly / Gly genotype carriers. The concentration of IL-1RA in them is very high and amounts to (1984.3 pkg / ml).

Trying to relate the genetic anomalies of Toll-4 to the synthesis of inflammatory mediators, we were able to note a unidirectional decrease in the concentration of IL-1β in the Asp / Gly and Gly / Gly genotypes compared to the Asp / Asp genotype.

More precise results were obtained in the analysis of cytokine reactions in patients - carriers of polymorphism of the Toll-6 receptor gene.

In patients with all polymorphic variants in the Toll-6 gene, the level of the pro-inflammatory cytokine IL-1ß was significantly increased in comparison with the control group. Carriers of the normal homozygous genotype Ser / Ser exhibited the highest cytokine values, in comparison with the rest of the groups (Table 2).

The concentration of TNF-α in the group of patients with the Pro / Pro genotype increased by 11.7 pkg / ml in comparison with the control group (2.3 pkg / ml), but was lower than for carriers of the normal Ser / Ser genotype - 14.3 pkg / Ml. When assessing the level of IL-8, it was found that the concentration of chemokine in children with the Pro / Pro genotype was the lowest (16.8 pkg / ml). In Ser / Ser genotype carriers -22.6 pkg / ml, in carriers of the Ser / Pro genotype - 17.7 pkg / ml.

IL-4 had no distinct differences depending on the polymorphic variants. In children bearing the homozygous Pro / Pro genotype, the concentration of IL-4 was 1.3 pkg / ml, in children with the Ser / Ser genotype - 1.2 pkg / ml, in the control group - 1.9 pkg / ml.

The IL-10 content was highest in children with a normal homozygous genotype Ser / Ser of 3.7 pkg / ml, in heterozygotes somewhat lower - 3.2 pkg / ml. With the replacement of alleles (genotype Pro / Pro) the concentration of IL-10 decreased to 2.2 pkg / ml.

The concentration of IL-1RA is very high in all polymorphic variants of the Toll-6 gene and, especially, in the genomes Pro / Pro-1404 pkg / ml.

Conclusion. Thus, our studies showed that the functional insufficiency of antiviral protection arises at the level of synthesis of cytokines that are regulators of inflammatory reactions in children often sick with acute respiratory viral infection carriers of gene polymorphisms (Asp299Gly) Toll-4 and (Ser249Pro) Toll-6. Although the total number of pro- and anti-inflammatory cytokines in the first days of infection increases, it does not reach the values of diseased children without abnormal impairments in signaling receptors.

The defect of signaling reactions is

Table 1

The content of cytokines in patients with carriers of polymorphic alleles of Asp299Gly in the gene Toll-4 receptors (median, 25-75 percentile) (pkg / ml)

Cytokines	Здоровые дети (n=76) (1)	Asp/Asp (n=40) (2)	Asp/Gly (n=18) (3)	Gly/Gly (n=32) (4)
IL-1β	5,4 [3,6-6,5]	17,6* [12,9-22,1]	14,6* [9,9-20,5]	13,9* [11,2-17,5]
IL-8	7,9 [6,9-9,1]	21,8* [12,3-22,2]	20,3* [13,1-21,9]	27,7* [11-29,2]
ФНОα	2,3 [1,5-2,5]	11,3* [8,25-14,3]	9,9*# [8,0-12,1]	12,4* [11,4-15,4]
IL-4	1,9 [1,2-2,5]	1,5 [0,85-2,02]	1,4 [0,9-2,09]	1,7 [1,3-2,09]
IL-10	1,2 [0,7-1,8]	2,6* [1,7-3,9]	2,9* [1,5-2,8]	2,4* [1,9-4,2]
IL-1RA	342,9 [263,8-465,4]	1571* [1179-1649]	1139,2*# [1050-1578]	1984,3*# [1214-2033]

Note: U is Mann Whitney's criterion; * - the significance of differences in comparison with the control. # - significance of differences in comparison with the group of carriers of the homozygous Asp / Asp genotype.

Table 2

The content of cytokines in patients with ARVI - carriers of polymorphic alleles Ser249Pro In the Toll-6 receptor gene (median, 25-75 percentile) (pkg / ml)

Cytokines	Здоровые дети (n=76) (1)	Ser/Ser (n=25) (5)	Ser/Pro (n=50) (6)	Pro/Pro IL-1β (n=25) (7)
IL-1β	5,4 [3,6-6,5]	21,9* [20,6-23,3]	18,2*# [13,4-25,2]	15,4*# [10,3-21,9]
IL-8	7,9 [6,9-9,1]	22,6* [19,5-27,2]	17,7*# [12,9-19,8]	16,8*# [14,4-19,9]
ФНОα	2,3 [1,5-2,5]	14,3* [11,9-16,5]	12,3*# [8,8-14,5]	11,7*# [10-14,7]
IL-4	1,9 [1,2-2,5]	1,2 [0,8-1,6]	1,6 [1,4-1,9]	1,3 [0,9-1,7]
IL-10	1,2 [0,7-1,8]	3,7* [2,4-4,7]	3,2*# [2,1-4,1]	2,2*# [1,1-4]
IL-1RA	342,9 [263,8-465,4]	1391* [1207-1536]	1249,2*# [1053-1577]	1404,3*# [1193-1817]

Note: U is Mann Whitney's criterion; * - the significance of differences in comparison with the control. # - significance of differences in comparison with the group of carriers of the homozygous Ser / Ser genotype.

exacerbated by a high IL-1 receptor antagonist (IL-1RA), which inhibits the Th-1 cellular pathway of immunity. In addition, IL-10 and IL-1RA are suppressive factors. Their high concentration limits the development of protective antiviral reactions, which complicates the course of the inflammatory process.

CONCLUSIONS

1. In ARVI, the dynamics of cytokines has its own variations depending on the presence or absence of genetic defects in Toll-receptors that perceive the action of the pathogen.

2. Point polymorphism in the genes of Toll-4 and Toll-6 receptors is one of the reasons for the failure of antiviral infection in children who often have ARV.

3. The presence of polymorphism of the signal receptor genes will make it possible to single out a special group of dispensary patients for the organization of personal prophylaxis for routine recurrences of acute respiratory viral infection.

REFERENCES

1. Borisova V.N. Bulgakova V.A. Sostoyaniye sistemy immuniteta u chasto boleyushchikh detey [The state of the immunity system in often ill children] Immunomodulyatory i vaktsinatsiya [Immunomodulators and vaccination]. Moscow: 4 Mpress, 2013, 272 p.

2. Zheleznikova G.F. Tsitokiny kak prediktory techeniya i iskhody infektsiy [Cytokines as predictors of the course and outcomes of infections] Tsitokiny i vospaleniye [Cytokines and inflammation]. Saint-Petersburg, 2009, № 8 (1), P. 10-17.

3. Kazyukova T.V. Koval' G.S. Samsygina G.A. Chasto boleyushchiye deti: sovremennyye vozmozhnosti snizheniyarespiratornoyzabolevayemosti [Often ill children: modern opportunities to reduce respiratory disease] Pediatriya [Pediatrics]. Moscow, 2012, 91(5), P.42-48.

4. Karpova N.I. Malezhik L.P. Malezhik M.S. Geneticheskiye osnovy nizkoy protivoinfektsionnoy zashchity u chasto boleyushchikh detey v Zabaykal'ye [Genetic bases of low anti-infectious protection in often ill children in Transbaikalia] IY Mezhd.Konf. «Meditsinskiye i psikho-pedagogicheskiye aspekty» [IY Mezhd. Konf. «Medical and psycho-pedagogical aspects»]. Slavyansk, 2012, P.135-139.

5. Samsygina G.A. Koval' G.S. Problemy diagnostiki i lecheniya chasto boleyushchikh detey na sovremennom etape [Problems of diagnostics and treatment of often ill children at the present stage] Pediatriya [Pediatrics]. Moscow, 2009, № 2, P. 137-145.

6. Simbirtsev A.S. Toll-belki: spetsificheskiye retseptory nespetsificheskogo immuniteta [Toll-proteins: specific receptors of nonspecific immunity] Immunologiya [Immunology]. Moscow, 2005, №6, P. 368-377.

7. Sul'skaya YU.V. Geneticheskiy polimorfizm toll-kike retseptorov 4 tipa u bol'nykh sakharnym diabetom 2 tipa [Genetic polymorphism of toll-kike type 4 receptors in patients with type 2 diabetes mellitus] Tavricheskiy mediko-biologicheskiy vestnik [Tavrichesky medico-biological bulletin]. Simferopol', 2009, №3 (47), P.72-74.

8. Uchaykin V.F. Evolyutsiya patogeneza infektsionnykh bolezney [Evolution of the pathogenesis of infectious diseases] Detskiye infektsii [Children's infections]. Moscow, 2012, 11(4), P.4-8.

9. Yartsev M.N. Yakovleva K.P. Immunnaya nedostatochnost', chasto boleyushchiye deti i immunokorrektsiya [Immune deficiency, often ailing children and immunocorrection] Voprosy sovremennoy pediatrii [Questions of modern pediatrics]. Moscow, 2005, V.4, P.72-74.

10. Kiechl S. Toll-like receptor 4 polymorphisms and atherogenesis /E.Lorens,V.Reindl [et al.] // N. Engl. J. Med. -2002.-Vol.347. - P.185-192.

11. Lorens E. Relevance of mutations in the TLR4 receptor in patients with gram-negative septic shock /E.Lorens, J. Mira [et al.] // Arch. Intern. Med. - 2002.- Vol.162.- P.1028-1032.

12. Tantisira K. Toll-like receptor 6 gene (TLR6): single nucleotide polymorphism frequencies and preliminary association with the diagnosis of asthma / K.Tantisira, W.Klimecki, R.Lazarus //Genes Immun.-2004.-Vol.5. - P. 343-346.

Information about authors

Chita State Medical Academy, Chita, Russia:

Malezhik Lydia Pavlovna

Doctor of medical science, professor. Department of Normal Physiology of Chita State Medical Academy, Ph. 8-924-506-50-27

E-mail: lida.malezhik@mail.ru

Malezhik Margarita Sergeyevna

Candidate of Medical Sciences, assistant Department BGD and MK of Chita State Medical Academy, Ph. 8-924-271-41-45

E-mail: rita.malezhik@mail.ru

Nimayeva Dulma Tsybenovna, Candidate of Medical Sciences, assistant professor. Department of Normal Physiology of Chita State Medical Academy.

Ph. 8-924-276-89-38

E-mail: dulmanimaeva@yandex.ru

Tsentendorzhieva Valentina Batomunkuevna

Candidate of medical science, assistant professor. Department of faculty therapy of Chita State Medical Academy

G.A. Usenko, S.M. Bekmurzov, D.V. Vasendin, A.G. Usenko, E.A. Stavsky, O.M. Belkina, N.A. Shakirova

A STUDY OF THE INFLUENCE OF HELIOMETEOFACTORS ON CORTISOL AND ALDOSTERONE IN THE BLOOD OF PATIENTS WITH VARIOUS PSYCHOSOMATIC STATUSES

ABSTRACT

Arterial hypertension and ischemic heart disease continue to lead in the structure of cardiovascular diseases. In the years of high solar activity and the period of magnetic storms in the healthy and diseased organism are functional shifts, which are associated with exacerbation of cardiovascular diseases. The aim of the study was to determine the relationship between indicators of solar activity and the content of cortisol and aldosterone in the blood of able-bodied men with different temperament and high and low anxiety, hypertension. The prevailing temperament – choleric, sanguine, phlegmatic and melancholic – was identified using the psychological test John Eysenck and A. Belov, the presence and severity of depression – Je. Ahmetzhanov psychological tests. In the blood serum the content of cortisol and aldosterone radioimmunoassay method was determined. Gamma background environment was measured using the dosimeter «Master». Also took into account the morning the values of atmospheric pressure and air temperature. It is established that with increase of solar activity in the wolf numbers and radio flux at wavelength 10.7 cm is closely related to the increase in atmospheric pressure, temperature and γ-background environment (within the rules). With the increase in solar activity, atmospheric pressure, temperature and γ-background in jobs closely related to the increase in the functional activity of cells of the beam (cortisol) and decrease activity of the cells in the glomerular layer (aldosterone) adrenal sympathotonics with a predominance of choleric and sanguine temperament. In these conditions parasympathotony with the prevalence of the phlegmatic and the melancholic temperament the functional activity of cells of the beam and the glomerular layer was opposite such of choleric and sanguine. Multidirectional adaptive changes in activity of cells of the beam (cortisol) and glomerular (aldosterone) zones of the adrenal cortex in healthy choleric and sanguine and patients, in comparison with the phlegmatic and the melancholic, attests to the importance of temperament in adaptation to changes of heliogeophysical and meteorological factors.

Keywords: hypertension, solar activity, γ-background, hormones, correlation.

INTRODUCTION

Arterial hypertension (AH) and coronary heart disease (CHD) continues to lead in the structure of cardiovascular diseases (CVD) [8]. In conditions of chronic psycho-emotional stress increases the mortality rate and incidence of complications of hypertension and coronary artery disease [4]. In addition, a number of researchers find evidence that in years of high solar activity (SA) and the period of magnetic storms in the healthy and diseased organism are functional changes associated with reduction of quality of professional activity and worsening of CVD [4, 13, 15].

Objective: to establish the relationship between indicators of solar activity and the content of cortisol and aldosterone in the blood able-bodied men with different temperament and low and high anxiety suffering from hypertension.

MATERIAL AND METHODS

In the period from 1995 to 2015, the clinic surveyed 848 technical workers men aged 44-62 years (average 54±1.8 years), which in the cardiology Department established hypertension stage II (GB-II, grade 2, risk 3). Disease duration was on average 11.6±1.4 years. The presence of essential hypertension was defined according to the criteria set out in [6, 10, 11]. Controls were 422 healthy men, compatible on basic anthropo-social indicators. The prevailing temperament – choleric (Ch) sanguine (Sg), phlegmatic (Ph) and melancholic (M) was measured using a psychological test [12] by 3 times testing before treatment (0) and after 3, 6, 9 12 months of antihypertensive therapy (AHT). The amount of reactive and personal anxiety was determined according to [14]. To lowanxiety (LA) defined as those who scored 32,0±0,6 points, to highanxiety (HA) between 42.8 ±0.4 points and above. Mild depression according to the methodology [2] was only among highanxiety phlegmatic (HA/Ph) and melancholic (HA/M). At the conclusion of the psycho in the inpatient treatment they need. Highanxiety choleric (HA/Ch) and sanguine (HA/Sg) received anxiolytic that 96% Sibazon 2.5 mg in the morning and at night and HA/Ph and HA/M antidepressant that 96% Coaxil 12.5 mg morning and night (in 4% of Zoloft 25 mg./day), in addition lowanxiety (LA) individuals [13,15]. Antihypertensive therapy was carried out as an outpatient [5] and included drugs that have been approved by order No. 254 of the health Ministry of Russia dated 22.11.2004 for the treatment of hypertension: β-blockers (βAB), angiotensinase inhibitors of the enzyme, diuretics (Hydrochlorothiazide), Cardiomagnyl [9]. From βAB patients 96% received Metoprolol 200 mg/day. (4% of cases its analogues), and LA/Ch and LA/Sg for 100 mg/day.) and Hydrochlorothiazide: HA/Ch and HA/Sg at 25 mg/day, and LA 12.5 mg/day. Of aceis in patients 96% took Enalapril 20 mg/day. (4% similar) + Veroshpiron 100-200 mg/day. (75%), rarely (25%) and hydrochlorothiazide 25 mg/day, because the content of potassium in the blood have been lower than those of Ch and Sg. LA/Ph and LA/M were administered Enalapril 10 mg/day. + hydrochlorothiazide (hydrochlorothiazide) - 12.5 mg/day. All received Panangin 2 tablets./day. and Cardiomagnyl on 1 tab./day. Using the criteria [3], we have found that in healthy persons and in patients with a predominance of choleric and sanguine temperament active divisions of ANS shifted towards the sympathetic predominance, and the same persons of phlegmatic and melancholic temperament in the direction of the parasympathetic division of the ANS.

Cortisol and aldosterone in serum was conducted with radioimmunoassay method using reagents of the company «CEA-IRE-SORIN» [7]. Clinical studies were carried out from 8.00 to 10.00 in the morning on an empty stomach, before taking AHT. Data on the dynamics of SA in the wolf numbers (the WN, conv. units) and radio emission at a wavelength of 10.5 cm (RF) received from the Department of ionospheric magnetic forecasting of

the Western-Siberian administration for Hydrometeorology and environmental monitoring (Novosibirsk). Gamma (γ)-background (ur/h) environment was measured at the workplaces of respondents (dosimeter «Master») from 8.00 to 10.00 daily (20 measurements) and compared with the data of the Department of ionospheric magnetic forecasting of the Western-Siberian administration for Hydrometeorology and environmental monitoring. Variations of γ-background in the period from 1995 to 2015. do not go beyond the normal regional values (7,0-9,0 μr/h). At the same time took into account the morning the values of the atmospheric pressure (P, mm Hg) and temperature (C) air in workplaces and outside them. Data were processed by methods of variation statistics (M±m) using standard software package «Statistica 7.0» and parametric student's t–test and calculation of coefficient of correlation by Pearson (r). Were considered as statistically significant p-value<0,4. The study was performed in compliance with the Helsinki screening and treatment and approved by the ethics Committee of the Novosibirsk state medical University 20.11.2009, minutes No. 18.

THE RESULTS AND DISCUSSION

The analysis of the content of hormones for the entire study period showed a significantly higher level of cortisol and aldosterone in the blood in patients with AH compared with healthy persons of corresponding temperament, despite treatment (table. 1, 2). However, in the groups of healthy and patients with hypertension cortisol was significantly decreased, but aldosterone was increased in temperamental range from Ch to M: Ch > Sg > Ph > M (cortisol) and Ch < Sg <Ph < M (aldosterone) (table. 1, 2).

The analysis of the dynamics of Solar activity showed an increase from 1995-1996 to 2000-2002 Decline of the SA was to 2005-2006 and remained so until 2014, Again, less pronounced but significant increase in SA in 2015 noted Between the values of WN and RF is a direct, a high degree of significance correlation. The study showed a significant increase in power of γ-background in the workplaces surveyed in the same years as the increase in SA. The change in the γ-background was within the boundaries of the regional norm. The correlation analysis between WN and RF on the one hand and the power γ of the background, on the other, showed the presence of reliable, direct and high-degree of significance of the relationship. Because ionizing radiation from the Sun and space trapped by the Earth's ionosphere, the increase of γ-background in the workplaces due to the increase in the content of radioactive gas radon. It can be assumed that with increasing SA there was an increase in the allocation of radon gas from the soil. However, under these conditions showed a significant decrease of the coefficient of utilization of oxygen by tissues (CUOT) in healthy individuals and patients, increased minute volume of blood (MVB) and the proportion of persons with such complications. It can be assumed that the high level of social tension, which peaked in the years of high SA, could weaken the reserve capacity of the organism [1, 4] and contribute to the potentiation of the action of the complex of the heliogeophysical factors, including the increase of γ-background. It is possible that the decrease in CUOT in the peak years of SA – result of the exposure of any one, but rather a complex natural and social factors. The consequence of combined effects has been the development of reactions with an increase in voltage in the cardiovascular system (for MVB) and the proportion of persons with such complications.

Sympathotonics choleric and sanguine. The study showed a significant increase in cortisol and decrease aldosterone in the blood in healthy individuals and patients Ch and Sg temperament, starting with 1995-1996 (years of low SA) for 2000-2002 (high SA). In the same period significantly increased the γ-background in the workplace. In the following years there was a decrease of SA and γ-background in the workplace, which was associated with a significant reduction in cortisol and increase of aldosterone in individuals of all groups choleric and sanguine temperament. The concentration of hormones to 2005 to further reliably close or insignificantly differed from that of 1995-1996 (table. 1, 2). With the increase of SA and γ-background by 2015, we found an increase in cortisol and decrease aldosterone in the blood in healthy and patients with hypertension individuals Ch and Sg temperament (table. 1, 2). Correlation analysis between the dynamics of WN, RF and γ-background on the one hand and the content of hormones in healthy individuals and patients Ch and Sg, on the other, showed the presence of a direct and high degree of significance of the relationship with cortisol and same but opposite with the content of aldosterone. Thus, Ch and Sg sympathotonics with the increase of SA and γ-background jobs combined increase in the functional activity of cells of the beam (cortisol), and decreased activity of glomerular cells (aldosterone) zones of the adrenal cortex.

Air temperature and atmospheric pressure. The analysis performed between The air and cortisol showed a direct and weak, and Then in the workplaces surveyed average and the close degree of correlation in healthy and patients choleric, at the time, as in the group of healthy sanguine correlation was direct and secondary, and in patients With a high degree of significance. In these conditions, the correlation between The outdoor and the content of aldosterone was reversed and the close groups of patients the choleric and sanguine, and moderate in their respective groups of healthy and Ch and Sg. Between With in the workplace and the content of aldosterone in the blood in healthy and patients of Ch and Sg an inverse correlation and close relationship. These data can be interpreted as the fact that with the increase From the air combined trend of increase in cortisol, but lower aldosterone in groups sympathotonics Ch and Sg From healthy persons and patients with hypertension. However, the focus of adaptive shifts in content of hormones in response to a change in The air coincided with that of WN, RF and γ-background. It is known that in conditions of development of adaptive reactions of increased function of the cells predominantly fascicular zone of the adrenal cortex (cortisol), the activity of cells in the glomerular (aldosterone) is reduced.

The coefficients obtained between the dynamics of atmospheric pressure and the content of hormones in sympathotonics Ch and Sg, showed the presence of significant direct and close correlations with cortisol and reverse average in groups of healthy and patients, and a significant inverse close in groups of healthy and patients With temperament. On the basis of obtained data we can conclude that with increase in atmospheric pressure in the body healthy, and With and patients on the background of AHT outpatient combined increase activity of cells of the beam (cortisol) and decrease activity of the cells in the glomerular zone of the adrenal cortex.

Parasympathotony phlegmatic and melancholic. The study showed a significant decrease of cortisol and the increase of aldosteron in blood from healthy individuals and patients AH phlegmatic and melancholic temperament with 1995-1996 (low SA) for 2000-2002 (high SA) (tab. 1, 2). In subsequent years, the SA and γ-background was lower than in 2000-2002, which was associated with a decrease in the content of aldosterone and cortisol increase in these groups. The increase of SA and γ-background environment by 2015. was accompanied by a significant decrease of cortisol and

Table 1

Table 1. Dynamics of serum cortisol (nmol/l) in serum at the HA patients (P) on the empirical background of AGT and in healthy individuals (H) from 1995 to 2015.

Years		1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Just
Choleric	П. 50*	380,6 ± 2,4	380,6 ± 2,4	354,4 ± 2,2	353,2 ± 2,4	358,7 ± 2,3	568,9 ± 3,0	615,4 ± 2,8	630,5 ± 3,6	631,2 ± 2,4	665,6 ± 3,4	398,9 ± 3,7	421,1 ± 3,4	423,2 ± 3,5	425,5 ± 3,4	428,8 ± 3,4	477,8 ± 3,4	504,5 ± 3,0	589,0 ± 3,0	646,7 ± 3,4	667,8 ± 3,3	570,0 ± 3,4	500,0 ± 0,2
	Зд 50*	340,2 ± 2,4	340,2 ± 2,4	339,9 ± 2,6	337,9 ± 2,5	349,0 ± 2,5	504,4 ± 3,9	543,5 ± 3,4	446,0 ± 3,7	449,0 ± 3,2	457,0 ± 2,7	411,2 ± 2,4	419,2 ± 2,7	424,4 ± 2,3	368,9 ± 2,7	370,9 ± 2,7	387,6 ± 2,7	398,9 ± 3,3	469,9 ± 3,3	476,7 ± 2,7	630,9 ± 3,9	552,3 ± 2,7	429,4 ± 0,2
Sanguine	П. 52*	338,6 ± 2,4	338,6 ± 2,4	383,5 ± 3,3	340,9 ± 2,4	435,6 ± 2,3	506,3 ± 3,3	533,5 ± 3,5	544,5 ± 3,7	424,5 ± 3,2	435,6 ± 3,2	391,2 ± 3,3	385,3 ± 3,1	380,0 ± 3,2	373,4 ± 3,1	383,4 ± 3,1	383,3 ± 3,1	400,9 ± 3,6	436,7 ± 3,6	523,6 ± 3,1	578,9 ± 3,3	520,0 ± 3,1	430,4 ± 0,3
	Зд 50*	316,7 ± 2,4	346,7 ± 2,4	342,2 ± 2,9	345,6 ± 2,4	356,5 ± 3,3	393,3 ± 3,9	398,0 ± 3,3	398,2 ± 3,9	405,9 ± 3,3	399,5 ± 3,0	399,5 ± 3,3	390,0 ± 3,2	348,0 ± 3,4	347,0 ± 3,2	344,0 ± 3,2	311,8 ± 3,2	311,9 ± 3,6	301,9 ± 3,6	301,7 ± 3,2	400,9 ± 3,3	393,3 ± 3,2	356,8 ± 0,3
Phlegmatic	П. 54*	279,6 ± 3,9	279,6 ± 3,9	270,6 ± 3,8	264,1 ± 3,9	260,6 ± 3,8	224,9 ± 3,0	234,5 ± 3,6	245,9 ± 3,6	279,3 ± 3,3	289,3 ± 3,6	367,6 ± 3,3	370,0 ± 3,7	356,6 ± 3,3	338,4 ± 3,7	281,0 ± 3,7	291,2 ± 3,7	300,9 ± 2,6	320,0 ± 2,6	330,0 ± 3,7	250,0 ± 3,3	248,7 ± 3,7	289,7 ± 0,2
	Зд 52*	312,6 ± 4,6	312,6 ± 4,6	299,8 ± 3,3	309,6 ± 4,0	298,0 ± 3,3	250,5 ± 3,6	245,9 ± 3,3	270,9 ± 3,9	278,0 ± 3,3	288,8 ± 3,8	360,6 ± 3,3	397,6 ± 4,2	355,0 ± 3,3	379,6 ± 3,8	363,6 ± 4,2	363,6 ± 4,2	345,6 ± 3,2	343,3 ± 4,2	378,9 ± 4,0	288,9 ± 3,3	255,6 ± 3,4	319,0 ± 0,2
Melancholic	П. 50*	265,5 ± 1,5	265,5 ± 1,5	263,5 ± 3,3	266,9 ± 1,5	261,7 ± 3,3	236,3 ± 2,0	226,3 ± 3,3	230,6 ± 2,0	246,6 ± 0,06	247,0 ± 3,0	277,7 ± 3,3	271,1 ± 3,0	288,3 ± 3,3	267,4 ± 3,0	263,9 ± 3,0	269,3 ± 3,0	276,3 ± 3,6	239,4 ± 3,6	240,6 ± 3,0	235,6 ± 3,3	234,3 ± 3,0	255,9 ± 0,1
		290,4 ± 4,8	290,4 ± 4,8	284,0 ± 3,4	293,9 ± 3,8	289,1 ± 3,3	245,5 ± 3,8	246,7 ± 3,3	260,0 ± 4,1	278,8 ± 3,3	288,8 ± 4,2	358,9 ± 0,04	380,6 ± 4,2	288,4 ± 3,3	289,9 ± 4,2	298,9 ± 4,2	290,0 ± 4,2	295,5 ± 4,0	289,7 ± 4,0	270,4 ± 4,2	252,2 ± 3,3	250,5 ± 4,2	282,5 ± 0,1

Note: here and below *- the number of individuals in the group; the number of blood samplings from one specimen 4,2±0,2 30 days of 46.2 ±1.2 per 12 months.

Table 2

Table 2. Dynamics of the content of aldosterone (PG/mg) in the blood serum of the HT patients (P) on the empirical background of AGT and in healthy individuals (H) from 1995 to 2015.

Years		1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Just
Choleric	П. 50*	71,6 ± 0,3	71,6 ± 0,3	65,5 ± 0,5	58,9 ± 0,4	51,7 ± 0,4	51,7 ± 0,4	57,9 ± 0,4	58,9 ± 0,6	63,4 ± 0,3	60,6 ± 0,5	68,9 ± 0,4	69,4 ± 0,6	58,9 ± 0,3	59,8 ± 0,3	72,4 ± 0,6	72,4 ± 0,6	65,6 ± 0,3	64,4 ± 0,6	63,7 ± 0,5	54,7 ± 0,5	57,0 ± 0,5	62,8 ± 0,03
	П. 50*	60,6 ± 0,4	60,6 ± 0,4	58,5 ± 0,4	55,8 ± 1,2	47,7 ± 1,2	46,7 ± 1,1	51,5 ± 0,4	48,1 ± 1,3	50,1 ± 0,5	53,1 ± 0,9	60,8 ± 0,5	59,9 ± 1,2	61,5 ± 0,8	62,6 ± 1,1	62,6 ± 1,1	62,6 ± 0,8	60,1 ± 0,9	48,5 ± 1,3	59,6 ± 0,9	50,7 ± 0,5	50,0 ± 0,8	55,8 ± 0,03
Sanguine	П. 52*	84,5 ± 0,3	84,5 ± 0,3	74,9 ± 0,5	70,2 ± 0,5	57,8 ± 0,5	58,7 ± 0,4	57,9 ± 0,5	59,0 ± 0,4	61,4 ± 0,3	66,4 ± 0,3	76,4 ± 0,5	76,8 ± 0,5	80,9 ± 0,4	80,9 ± 0,4	83,8 ± 0,3	83,8 ± 0,3	78,6 ± 0,5	78,4 ± 0,4	78,4 ± 0,3	68,4 ± 0,4	60,0 ± 0,4	72,8 ± 0,04
	П. 50*	62,9 ± 0,6	62,9 ± 0,5	63,8 ± 0,3	58,3 ± 0,8	58,9 ± 0,4	51,7 ± 0,3	50,9 ± 0,4	48,1 ± 0,3	50,0 ± 0,4	56,9 ± 0,6	57,0 ± 0,5	58,3 ± 0,4	59,9 ± 0,5	64,6 ± 0,6	64,8 ± 0,4	64,8 ± 0,4	60,8 ± 0,4	59,7 ± 0,4	48,0 ± 0,5	52,7 ± 0,5	50,8 ± 0,5	57,5 ± 0,03
Phlegmatic	П. 54*	95,7 ± 0,4	95,7 ± 0,4	97,5 ± 0,3	99,7 ± 0,5	103,6 ± 0,4	106,3 ± 0,5	102,2 ± 0,4	103,2 ± 0,3	99,9 ± 0,4	88,1 ± 0,4	89,0 ± 0,4	90,0 ± 0,3	91,2 ± 0,5	93,2 ± 0,5	94,8 ± 0,4	94,8 ± 0,4	96,6 ± 0,3	97,0 ± 0,3	97,6 ± 0,4	97,9 ± 0,3	99,9 ± 0,5	96,9 ± 0,02
	П. 52*	86,4 ± 0,7	86,4 ± 0,7	88,8 ± 0,5	92,0 ± 0,5	96,6 ± 0,5	99,6 ± 0,5	100,9 ± 0,4	98,8 ± 0,5	98,6 ± 0,3	94,0 ± 0,4	79,6 ± 0,4	77,6 ± 0,5	78,0 ± 0,3	79,3 ± 0,4	83,6 ± 0,4	83,6 ± 0,4	92,6 ± 0,4	85,6 ± 0,4	89,0 ± 0,5	93,8 ± 0,3	94,9 ± 0,3	89,5 ± 0,03
Melancholic	П. 50*	113,6 ± 0,4	113,6 ± 0,4	114,7 ± 0,3	115,7 ± 0,4	121,2 ± 0,6	121,2 ± 0,3	129,5 ± 0,3	133,3 ± 0,6	122,2 ± 0,3	106,3 ± 0,6	98,5 ± 0,3	100,0 ± 0,3	95,7 ± 0,4	96,0 ± 0,4	113,6 ± 0,3	113,8 ± 0,6	115,8 ± 0,6	110,6 ± 0,4	115,6 ± 0,5	116,9 ± 0,6	116,6 ± 0,6	113,2 ± 0,04
		99,4 ± 0,4	99,4 ± 0,3	99,0 ± 0,4	102,0 ± 0,4	99,2 ± 0,5	103,8 ± 0,4	104,8 ± 0,5	104,8 ± 0,4	104,7 ± 0,5	101,6 ± 0,5	84,9 ± 0,4	84,6 ± 0,4	79,9 ± 0,4	88,4 ± 0,5	89,6 ± 0,3	89,6 ± 0,4	91,6 ± 0,5	94,8 ± 0,4	97,8 ± 0,4	101,9 ± 0,5	102,8 ± 0,5	96,4 ± 0,03

increase of aldosterone in the blood in healthy and patients with hypertension individuals Ph and M of temperament (table. 1, 2). The correlation analysis between WN, RF and γ-background of the shops on one side and dosage on the other, showed the presence of mainly opposite, and close correlation with the content of cortisol, and the same, but the direct extent with the content of aldosterone (table. 1, 2). On this basis we can conclude that with the increase of SA and γ-background environment combined development of adaptive reactions, which focus on functional activity of cells of the glomerular and fascicular zones of the adrenal cortex was opposite that of Ch and Sg.

Air temperature and atmospheric pressure. With the environment significantly affects the functional changes in the body, however, between The outdoor and the content of hormones in the blood, Ph and M individuals of the correlation relationship was very weak. However, between Then workplaces and cortisol there is a significant inverse medium and high degree of significance of the correlation relationship, and the contents of the aldosterone – direct and also of high to medium importance. At the same time, between the dynamics of atmospheric pressure and cortisol there is a significant inverse and close to the average (in groups Ph and M patients) and moderate significance (group of healthy Ph and M individuals) of the correlation relationship. Between the dynamics of P and the content of aldosterone statistically significant direct medium and strong degree of significance of correlation relationship. The data obtained allow to conclude that with increase in atmospheric pressure in the body of a healthy parasympathotony Ph and M individuals and patients on the background of AHT were observed adaptive changes in the functional activity of HPAS hypothalamic-pituitary-adrenal system (cortisol) and RAAS the renin-angiotensin-aldosterone system (aldosterone) opposite to those at Ch and Sg With.

Thus, overcoming the body environmental conditions (increase of SA, γ background, C and P) were combined with a reduction in CUOT. Sympathotonics healthy, and With individuals and patients (on the background of AHT) reducing CUOT was accompanied mainly by increasing the functional activity of cells of the beam (cortisol), and the corresponding groups Ph and M – increase of functional activity predominantly glomerular cells (aldosterone) zones of the adrenal cortex. In groups lowanxiety healthy individuals and patients the relationship between heliometeotropic and the content of hormones was the same orientation as the highanxiety of persons of a corresponding temperament, but the degree of correlation in 67% of cases were moderate importance.

CONCLUSION

1. With the increase in solar activity in the wolf numbers and radio flux at wavelength 10.7 cm is closely related to the increase in atmospheric pressure, temperature and γ-background environment (within the rules). 2. With increasing solar activity (h Wolff, the flux of radiation), atmospheric pressure, temperature and γ-background in the shops, is closely related to the increase in the functional activity of cells of the beam (cortisol) and decrease activity of the cells in the glomerular layer (aldosterone) from the adrenal cortex in healthy individuals and patients AH sympathotonics with a predominance of choleric and sanguine temperament. In these conditions, parasympathotony healthy individuals and patients of hypertension with the prevalence of the phlegmatic and the melancholic temperament the functional activity of cells of the beam and the glomerular layer was opposite such choleric and sanguine. 3. Multidirectional adaptive changes in activity of cells of the beam (cortisol) and glomerular (aldosterone) zones of the adrenal cortex in healthy, and With persons and in patients of hypertension, compared with Ph and M, demonstrates the importance of temperament in adapting to changing heliogeophysical (WN and RF, γ is the background environment) and meteorological (P, To C) factors.

REFERENCES

1. V.N. Krasnov [et al.]. Antidepressanty koaksil i zoloft v kompleksnom lechenii bol'nyh arterial'noj gipertenziej s rasstrojstvami affektivnogo spektra [Antidepressants coaxil and zoloft in treatment of patients with arterial hypertension with affective disorders spectrum] Rossijskij medicinskij zhurnal [Russian journal of medicine], 2004, № 1, pp. 15 - 18.

2. Ahmetzhanov Je.R. Shkala depressii. Psihologicheskie testy [Depression scale. Psychological tests]. Moscow: List Publ., 1996, 320 p.

3. Vejn A.M. Vegetativnye rasstrojstva: klinika, lechenie, diagnostika [Autonomic disorders: clinical, treatment, diagnosis]. Moscow: MIA Publ., 2000, 752 p.

4. G.A. Usenko [et al.]. Vzaimosvjaz' mezhdu soderzhaniem magnija v krovi i naprjazheniem magnitnogo polja Zemli u bol'nyh stenokardiej naprjazhenija s razlichnym temperamentom i urovnem trevozhnosti [The relationship between the content of magnesium in the blood and strain of the Earth's magnetic field in patients with angina with a different temperament and level of anxiety] Vestnik Rossijskoj voenno-medicinskoj akademii [Vestnik of Russian military medical Academy], 2015, №1 (49), pp. 29 –33.

5. Gogin E.E. Vybor taktiki lechenija bol'nyh gipertonicheskoj bolezn'ju: ego individualizacija i kriterii [The choice of tactics of treatment of patients with essential hypertension: it individualization and criteria] Terapevticheskij arhiv [Therapeutic archive], 2010, №. 12, pp. 5 – 10.

6. Diagnostika i korrekcija narushenij lipidnogo obmena s cel'ju profilaktiki i lechenija ateroskleroza. Klinicheskie rekomendacii VNOK [Diagnosis and correction of lipid metabolism disorders prevention and treatment of atherosclerosis. Clinical guidelines GFCF] Kardiovaskuljarnaja terapija i profilaktika [Cardiovascular therapy and prevention], 2009, № 6, appl. 3.

7. Kishkun A.A. Rukovodstvo po laboratornym metodam diagnostiki [Guidelines on laboratory diagnosis]. Moscow: GEOTAR Publ., 2007, 800 p.

8. Oshhepkova E.V. Smertnost' naselenija ot serdechno-sosudistyh zabolevanij v Rossijskoj Federacii v 2001 – 2006 gg. i puti po ee snizheniju [Mortality from cardiovascular diseases in the Russian Federation in 2001 – 2006 and ways to reduce it] Kardiologija [Cardiology], 2009, № 2, pp. 67 – 73.

9. Prikaz № 254 Ministerstva zdravoohranenija i social'nogo razvitija RF ot 22.11.2004 «Ob utverzhdenii standarta medicinskoj pomoshhi bol'nym arterial'noj gipertoniej» [Order № 254 of the Ministry of health and social development of the Russian Federation of 22.11.2004 «On approval of the standard of care in patients with arterial hypertension»].

10. Profilaktika, diagnostika i lechenie arterial'noj gipertenzii: Rossijskie rekomendacii (vtoroj peresmotr) [Prevention, diagnosis and treatment of arterial hypertension: the Russian advice (second revision). Moscow, 2004.

11. Profilaktika, diagnostika i lechenie arterial'noj gipertenzii: Rossijskie rekomendacii (tretij peresmotr) [Prevention, diagnosis and treatment of arterial hypertension: the Russian advice (third revision)] Kardiovaskuljarnaja terapija i profilaktika [Cardiovascular therapy and prevention], 2008, №7, appl. 2, pp. 5 – 16.

12. Stoljarenko L.D. Oprosnik Ajzenka po opredeleniju temperamenta. Osnovy psihologii [Eysenck Questionnaire by definition temperament.

Fundamentals of psychology]. Rostov-na-Donu: Fenix Publ., 1997, 736 p.

13. Usenko G.A., Vasendin D.V., Usenko A.G. Primenenie antigipertenzivnoj terapii, osnovannoj na korrekcii simpatikotonii i aktivnosti renin-angiotenzin-al'dosteronovoj sistemy u bol'nyh arterial'noj gipertenziej s razlichnymi temperamentom i trevozhnost'ju [The use of antihypertensive therapy based on the correction of sympathicotonia and activity of the renin-angiotensin-aldosterone system in hypertensive patients with different temperament and anxiety] Vestnik Rossijskoj voenno-medicinskoj akademii [Vestnik of Russian military medical Academy], 2015, №4 (52), pp. 27 –31.

14. Hanin Ju.L. Issledovanie trevogi v sporte [Study of anxiety in sport] Voprosy psihologii [Questions of psychology], 1978, № 6, pp. 94 – 106.

15. G.A. Usenko [et al.]. Jeffektivnost' antigipertenzivnoj terapii, osnovannoj na kupirovanii osobennostej psihosomaticheskogo statusa pacienta [The effectiveness of antihypertensive therapy based on the relief features of the psychosomatic status of the patient] Uchenye zapiski Sankt-Peterburgskogo gosudarstvennogo medicinskogo universiteta im. akad. I.P. Pavlova [Record of the I.P. Pavlov St. Petersburg State Medical University]. 2013, Vol. XX, №4, pp. 62 – 66.

Information about the authors:

Gennady Aleksandrovich Usenko, doctor of medical sciences, Professor of Department of hospital therapy of the medical faculty of Federal state educational institution of higher professional education «Novosibirsk state medical University» Ministry of healthcare of the Russian Federation, 630091, Novosibirsk, 91, Krasny Av., 52; +7(913)9393370 (phone); E-mail: usenko1949@mail.ru

Sergei Mukhtarovich Bekmurzov – head of Federal state institution «Military hospital №425» Ministry of defense of the Russian Federation: 630017, Novosibirsk, 17, Military street, 1. Tel/Fax: 8(383)2660811; E-mail: 425-vg@mail.ru

Dmitry Viktorovich Vasendin – (corresponding author) – candidate of medical sciences, associate Professor, associate Professor of mobilization training of health and disaster medicine of the Federal state educational institution of higher professional education «Novosibirsk state medical University» Ministry of healthcare of the Russian Federation, 630091, Novosibirsk, 91, Krasny Av., 52; +7(913)9433792 (phone); E-mail: vasendindv@gmail.com

Andrey Gennadievich Usenko – candidate of medical sciences, the doctor of functional diagnostics office, the state budget institution of health of Novosibirsk region «Novosibirsk regional hospital №2 for war veterans», 630005, Novosibirsk, Family Shamshinykh Str., 95a; Phone/Fax +7(383)2240338. E-mail: h2vv@mail.ru

Evgeny Alexandrovich Stawski – doctor of medical sciences, head of Department of mobilization training of health and disaster medicine, faculty of preventive medicine, Federal state budgetary educational institution of higher professional education «Novosibirsk state medical University» Ministry of healthcare of the Russian Federation, 630091, Novosibirsk, 91, Krasny Av., 52. Tel/Fax: 8(383)2222880; E-mail: eastavskiy@yandex.ru

Olga Mikhailovna Belkina – candidate of medical sciences, associate Professor; associate Professor of mobilization training of health and disaster medicine, faculty of preventive medicine, Federal state budgetary educational institution of higher professional education «Novosibirsk state medical University» Ministry of healthcare of the Russian Federation, 630091, Novosibirsk, 91, Krasny Av., 52. Tel/Fax: 8(383)2222880; E-mail: zyalbert@yandex.ru

Natalia Anatolievna Shakirova – head of ionospheric magnetic forecasting Federal state budgetary institution «Western-Siberian administration for Hydrometeorology and environmental monitoring»: 630099, Novosibirsk, 99, street Soviet, 30. Tel/Fax: 8(383)2225188; E-mail: rsmc@meteo-nso.ru

METHODS OF DIAGNOSIS AND TREATMENT

V. G. Ignatyev, N. V. Vinokurova, M. Yu. Vinokurov, V. P. Zorin, R. R. Gatilov, E.A. Bodunova

ROLE OF MRI «TOTAL BODY» IN EARLY DIAGNOSIS OF VARIOUS DISEASES

ABSTRACT

This article dwells on whole-body MRI «Total Body» efficacy as the choice method for whole-body screening for the purpose of early diseases diagnostics. On the basis of whole-body MRI analyses during one and a half year we've got the results allowing speaking about a new precise and reliable method for revealing pathology of minimal dimensions in any organ, including malignant tumors.

Keywords: screening, whole-body MRI, CT, diseases, radiation.

INTRODUCTION

Whole body Magnetic and Resonance Tomography (MRI) allows studying a morphological picture of all organs and tissues with the detailed image that provides diagnose the development of many malconditions at early stages.

Accumulation of the large volume of statistical data obtained as a result of magnetic and resonance tomography methods penetrated into common diagnostic practice leads to the expected number of new methodologically issued standards of protocols of program MRI researches. Some new protocols of the MRI program settings allow conducting complex «blind» trial searching of various malconditions on the background of lack of complaints and, apparently, the complete wellbeing of the patient. These complex researches are united by:

- the larger size of the explored area together with its natural and pathological tissues polymorphism – it investigates whole body or its majority with all organs and systems of organs and tissues of the explored site;
- technologies complexity – in the course of the research, according to prearranged program, MR-tomograph switches on/off various modes of scanning and processing of the received images for identification of pathological changes, different in structure;
- cross-sectional study – whole body testing of the patient or its majority

part is made in a continuous cycle, for one positioning of the patient ;

- noncontact, noninvasive – means the result of high-contrast native images of all organs and tissues.

As a result of such researches - they can be united under the name MRI «TOTAL BODY» (whole body) or in abbreviation «TB» - in a number of cases, there is an identification of the pathological changes, absolutely unexpected for the patient, which are not accompanied with any symptomatology [2]. Besides, it should be noted that validity of MRI «TOTAL BODY» is defined by absolute harmlessness and safety of this research, there is no radiation exposure and minimum contraindications. Frequency of the research and age groups are without restrictions, and recently, foreign researches proved MRI safety for pregnant women [6,10,12,15,16]. Practical accumulation of the considerable number of the performed TB, with the revealed pathological deviations, allows starting analyses of its diagnostic value and possible new, more extended possibilities.

Recently the considerable attention was concentrated on visualization screening of whole body for early disease diagnostics [14]. Screening means systematic survey of the body for detection of the unexpected, latent pathologies. The optimum candidate for the screening is the person without any symptoms of any disease. Good screening - the test has to be highly sensitive and specific to reduce number of false positive results.

Until recently the Computer tomography (CT-screening Total body) has been used, however, this method possesses a number of weak points: radiation, obligatory use of the intravenous contrast agent. Also, there is a growing concern in medical community that CT - screening of Total body leads to a large number of the doubtful conclusions demanding padding procedures, including operations, creating padding scratches and expenses for the patient [8]. In this connection interest in receiving «safe» MR-screening - the tests displaying internal structure of whole body of the patient throughout the head to toe [2], without obligatory use of the contrast agent has increased. The potent magnetic field and radio-frequency energy of MRI are safe, it cannot be the cause of cancer or anomalies of fetus, unlike the ionizing radiation (X-rays) used in CT which is the known reason of cancer and anomalies of fetus [11]. Gadolinium containing intravenous contrast agents used in MRI is also much safer, than similar agents on the basis of iodine used in CT. The smaller association with causing injury of kidneys is noted much, less allergic reactions, including heavy which can lead to death [3,5]. In general, when comparing both screening methods of visualization of whole body we have revealed that MRI screening Total body proves more diseases (malignant/benign) than CT. In this quality, MRI surpasses CT [7,9,13]. The main objective of MRT research «TOTAL BODY» - early diagnostics of neoplasms; which can considerably change treatment type, available to the patient. Other revealed problem areas which are not falling into to cancer can promote prime changes in the way of life of the person, such as eating/sports habits. Now MRI - screening of Total body is regularly used in such countries as the USA, Great Britain, Japan [1].

The aim of the research is to estimate the frequency, quantity and nature of the revealed changes among the population of various age groups during the native (noncontact) MRI testing «Total Body».

MATERIALS AND METHODS

127 trials of MRI group «TOTAL BODY» have been done (2014 - 27, 2015 - 42, during 9 months 2016 – 58 researches) on clinical base of medical institute of NEFU – in MRI centre of Victory Clinic, from March, 2014 till September, 2016. Researches were conducted on the modern digital MR-system of GE 1,5 Tesla Optima MR360 Advance. The program MRI «TOTAL BODY» used: T1, T2 STIR modes in coronary projections, T2 in sagittal, T2, T1, FLAIR, DWI in axial projections; the specialized programs allowing to unite images from different anatomic floors in a single whole. Thickness of cuts was from 1 to 8 mm. The field of the review of the patient – from the head to the top third of tibia. The research didn't test mammary glands, lungs, heart for the reasons of «method limit» and need of padding specialized opportunities of the device were not estimated.

We've carried out the retrospective analysis of the clinic researches for diagnostic of technique value for new possible indications of preventive research to early identification of pathological processes.

By sex: male – 60, female – 67;

By age:

From 16 to 45 years – 40 (31,5%)

From 45 to 60 years – 57(44,9%)

Over 60 years – 30(23,6%)

For authentic analysis patients were distributed into two groups:

1 group: patients with healthy background («for themselves» - 38 (29,9%);

2 group: patients with available symptoms and anamnesis of a disease – 89 (70,1%), among them: 2A with common complaints – 80 (63%); 2B with oncological anamnesis – 8 (6,2%); 2C with specific tubercular anamnesis – 1 (0,8%).

The received results were divided into 3 types: the 1st type – a low significance, not demanding further treatment and observation, the 2nd type – a moderate significance, demanding observations perhaps treatment and the 3rd type - an essential or potential significance, demanding treatment or immediate measures to define the nature of changes.

RESULTS

We have established that in the first group of patients as a result of the conducted «blind» MRT test «TOTAL BODY» there were 3 patients (2,3%) with no pathology; 4 cases (3,1%) with the changes requiring close attention (the 3rd type); other patients - 31 patients (24,4%) had some changes which we referred to small and average pathology (the 1st and 2nd type) with no threat for life but demanding dynamic observation and, perhaps, treatment.

Table 1 Anxiety life-threatening pathology (Type 3)

In the second group of patients (2A), with the available common complaints and the anamnesis to the postponed diseases, in 72 cases (56,6%) changes of the 1st and 2nd type, in 8 patients (6,2%) changes of the 3rd type have been revealed.

Table 2 Anxiety life-threatening pathology (Type 3)

In the second group of patients (2B) with the established oncological diagnosis, after operative therapy, without serious complaints the program MRI «TOTAL BODY» was chosen for the purpose of specification of recurrence, metastasing, assessment of surgical treatment. Among the above described group, given for the continued growth, a recurrence, metastasing, were not revealed in 5 cases (3,9%), change-types 2 were revealed. In three cases (0,2%) the mediastinum lymphadenopathy (in the anamnesis the operated malignancy of thyroid gland), abdominal cavity and pelvis (in the anamnesis the operated malignancy of uterus/ovaries) which was regarded as metastatic affection – change-types 3 was revealed. One of patients of this group has passed repeated dynamic Total Body (2014 and 2016) after the carried-out mastectomy

Table 1

Table 1 Anxiety life-threatening pathology of group 1(Type 3)

Pathology	Number of the diagnosed cases
growth in right lung	1
urinary bladder growth	1
large intracerebral meningioma	1
aneurism of intracranial vessels	1
TOTAL	4

Table 2

Table 2 Anxiety life-threatening pathology of group 2A (Тип 3)

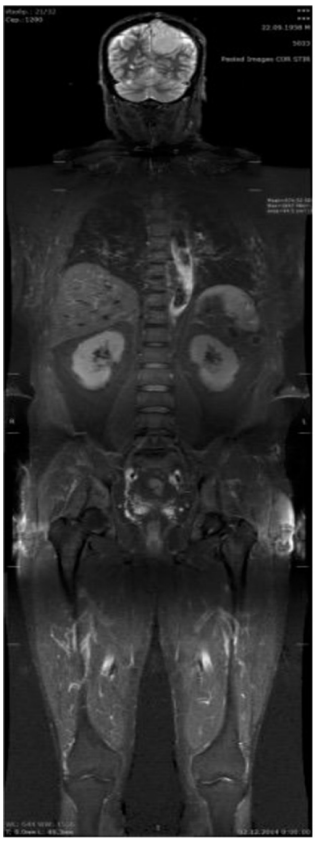
Pathology	Number of the diagnosed cases
growth in pancreas	2
chest cavity with hydrothorax growth	1
growth in kidney with metastasing in lymph nodes and perinephric fat, lymphadenopathy in portal fissures	1
aneurysm of intracranial vessels	1
liver growth, with metastasing in lymph nodes, brain	1
liver growth, rectum with metastasing in lymph nodes	1
growth in abdominal cavity, head of pancreas, moderate vascular pathology of brain, moderate degenerative changes of backbone (state after cholecystectomy)	1
TOTAL	8

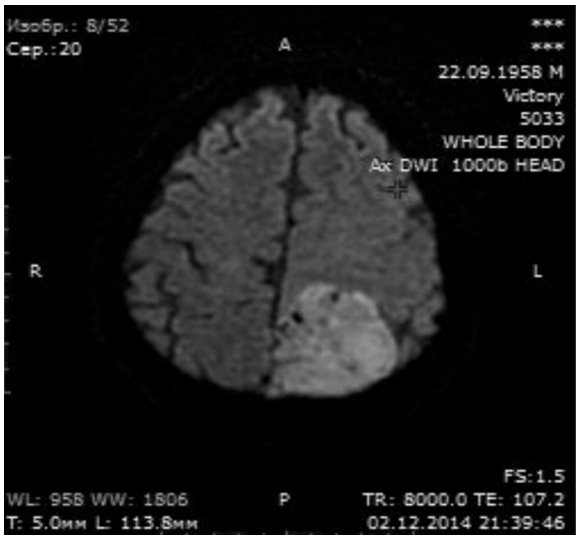
(in 2012) concerning a malignancy of mammary gland.

In the second group (2C) with the tubercular anamnesis widespread inflammatory changes of backbone, spondylitis, spondylarthritis, ankylosis of sacroiliac joints, prostatitis have been revealed (change-types 2).

Having analysed quantity of zones with the revealed changes, we came to a conclusion that in most cases the revealed changes were found in three and more zones (in calculations 119 cases from 127 were considered).

Among the found changes which we referred to the 1st and 2-groups, benign neoplasms (cysts, hemangiomas, myomas) of various localization (liver, kidneys, ovaries, uterus), degenerative changes of backbone, arthroses, arthritises of various degree of expressiveness, hernia and protrusion of disks, focal vascular changes of brain, postinfarction changes, aneurisms of vessels of brain, inflammatory and proliferative (adenoma) changes of prostate have been revealed. However, in patients of middle and senior age groups, often, the pathology revealed for the first time which had bright proliferative character met more often on the basis of neglect pathological process, poor previous medical examination.





Diagnostic cases:

Fig. 1 Patient of 58 years. Without complaints. Large asymptomatic meningioma of brain. Operative treatment. The diagnosis has been verified.

CONCLUSION

1. MRI test of whole body is safe and reliable method of early diagnostics of various pathological conditions of any age group, and also identification of complications to patients with earlier established diagnosis.

2. High quality scanning of the MRI program «TOTAL BODY» allows revealing minimum size pathology in any organs for short time.

Practical recommendations

1. The program MRI «TOTAL BODY» is recommended to be used for the purpose of monitoring of the revealed earlier pathological states, processes, and also for assessment of effectiveness of treatment.

2. For the purpose of prophylaxis of oncological and other diseases use of MRI program «TOTAL BODY» is recommended to all citizens older 40 years 1 time in three years and 50 years old patients are recommended do it annually.

3. It is expedient to include MRI program «TOTAL BODY» as the quota paid researches compulsory health insurances of high technologies.

Literature

1. Al-Shahi Salman R, Whitely WN, Warlow C. Screening using whole-body magnetic resonance imaging scanning: who wants an incidentaloma? Med Screen. 2007;14(1):2-4.

2. Baumgart D, Egelhof T. Preventive whole-body screening encompassing modern imaging using magnetic resonance tomography. Herz. 2007 Aug;32(5):387-94.

3. Berns A. Nephrotoxicity of contrast media. Kidney Int. 1989;35:730-740.

4. Berrington de Gonzalez A,

Fig. 2 Patient of 51 years old. Examination «oncology». Self-reversal. Without particular complaints. Liver growth. Growth of sigmoid department of intestine. Metastasing in regional lymph nodes of paraproctium.

Darby S. Risk of cancer from diagnostic X-rays: estimates for the UK and 14 other countries. Lancet. 2004;363:345-351.

5. Brezis M, Epsetein FH. A closer look at radiocontrast-induced nephropathy. N Engl J Med. 1989;323:179-181.

6. Choi JS, et al. A case series of 15 women inadvertently exposed to magnetic resonance imaging in the first trimester of pregnancy. J Obstet Gynaecol 2015

7. Gillman S. Imaging the brain: second of two parts. N Engl J Med. 1998;338:889-896.

8. Ko J, Casola G. Whole Body MR Screening Found Feasible. Whole Body CT Screening. Available to Members Through the RSNA Web site: http://www.rsna.org Accessed June 14, 2004.

9. Low R, Semelka R, Woranwattanakul S, Alzate G, Sigeti J. Extrahepatic abdominal imaging in patients with malignancy: comparison of MR imaging and helical CT, with subsequent surgical correlation. Radiology. 1999;210:625-632.

10. Reeves MJ, et al. Neonatal cochlear function: Measurement after exposure to acoustic noise during in utero MR imaging. Radiology 2010;257:802-809.

11. Rustam Al-Shahi Salman, William N Whiteley, Charles Warlow. J Screening using whole-body magnetic resonance imaging scanning: who wants an incidentaloma? Med Screen 2007;14:2–4

12. Santos XM, Papanna R, Johnson A, Cass DL, Olutoye OO, Moise KJ Jr, et al. The use of combined ultrasound and magnetic resonance imaging in the detection of fetal anomalies. Prenat Diagn 2010;30:402–7.

13. Semelka R, Martin D, Balci C, Lance T. Focal liver lesions: comparison of dual-phase CT and multisequence multiplanar MR imaging including dynamic gadolinium enhancement. J Magn Reson Imaging. 2001;13:397-401.

14. Sivy M. A high-tech way to know yourself. Money. August 2003:121-122. http://www.medscape.org/viewarticle/478330

15. Strizek B. Safety of MR imaging at 1.5 T in fetuses: A retrospective case-control study of birth weights and the effects of acoustic noise. Radiology 2015;275:530-7.

16. Yves Patenaude, Denise Pugash, Kenneth Lim. The Use of Magnetic Resonance Imaging in the Obstetric Patient. No. 306, April 2014

The authors:

Ignatyev Victor Georgievitch, PhD, MD, professor, head of general surgery department of Medical Institute NEFU, ignat_prof@mail.ru; Vinokurova Nadezhda Vladimirovna, radiotherapist, vinokurova.nadin@gmail.com; Vinokurov Mikhail Yuryevitch candidate of medical sciences 451307@gmail.com, Zorin Vitaliy Pavlovitch, radiotherapist, Gatilov Radislav Revoryevitch radiotherapist, Bodunova Elena Alekseevna organizer of public health 677000, Lermontov Str. 25/a, Yakutsk, Republic Sakha (Yakutia), Russia.

V.S. Danilova, N.N. Kozhevnikov

UNIVERSAL APPROACH TO STUDY THE HUMAN

ABSTRACT

The modern universal approach to the study of human problems, developing on the basis of the concept of the world coordinate system based on the limits of deterministic chaos' dynamic equilibriums. According to this concept, all natural formations tend to limit to three fundamental equilibriums: identification, communication-networking, and limiting rhythm of world harmony. This approach allows you to set the interaction between the extreme states in all spheres of the person, his fundamental structural levels and sustain the dynamic equilibrium between them.

We consider four areas of human activity, which manifest the universal approach to the description of the processes inherent in human most clearly. Among them: the interaction all rhythms of the human body; its relationship with noobiogeocenosis; influence of intellectual and spiritual catalysts on human health; relationship between secular asceticism with human well-being. All these areas are aimed at mobilizing the body's resources.

Consideration of human problems in terms of dynamic equilibriums opens up possibilities for the analysis of limiting conditions of his life and death. Man has always been building the imaginary concept of immortality; however, more descriptive view of one is associated with a cell of the noobiogeosphere connected with the world's coordinate system. Destiny – is a human life in the natural coordinate system, its states in the knots separated by intervals corresponding to the oscillation frequency of the rhythms of nature's fundamental limits (the totality set of the life's bifurcation points). A key man's threshold starts with counting his life from the date of the death, not the birth. This date no one knows, but after that threshold a person begins to evaluate the parameters of his life with accordingly the period of time that he began to feel it. The destiny which is linked with the coordinate system should be regarded as a vocation, which should obey and follow it even when the target is not feasible for the individual because of its comprehensiveness and infinity.

Keywords: dynamic equilibrium, life, death, destiny, coordinate system, rhythm, noobiogeocenosis, catalyst, asceticism, health.

INTRODUCTION

A great number faces of problems related to the human, requires a modern universal approach the basis of which in the present work is a world coordinates' system on the basis of limit dynamical equilibriums of deterministic chaos [1]. The methodology developed by us there is three basic limits: identification, communication, limit of the world harmony's rhythms and correlated them the coordinate axes [2]. This approach allows you to set the interaction between the extreme states in all spheres of human (prelife, life, death, bifurcation points), as well as its fundamental structural levels (unconscious, intellectual, spiritual) and sustain dynamic equilibrium between them.

According to the WHO charter, «health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity». In the health statistics, according to WHO, a health at the individual level refers to the absence of identified disorders and diseases, and in population - the decline in mortality, morbidity and disability. These definitions focus on the equilibrium states that are useful to consider in terms of the fundamental limits developed by our approach.

THE METHODOLOGY AND THE MAIN DIRECTIONS OF RESEARCH

According to the concept of the world coordinates' system the all natural formations seek to three limit fundamental equilibriums: identification (I - limit), communication-network (C - limit) and limiting rhythm of world harmony (K - limit), which compares the three corresponding «coordinate axis».

The natural formations are reached never of these equilibrium limits (I, C, K) as a result of environmental protection. However, each stage of the change's process of any natural formation can be associated with intermediate dynamic equilibrium F, H, T, which are connected with I, C, K by calibration ratios. Within the intermediate cell (F, H, T) equilibrium is established between an arbitrary natural formation and intermediate limits of its possible dynamic equilibriums: the phenomenon (F), the horizon (H), and the limiting rhythm of world harmony (T). «Calibration» nodes are separated by intervals corresponding to the oscillation frequency of the fundamental limits (the fundamental rhythms of the world). In the development of these «steps» and the rhythms the cell connected with the coordinate system may exist in the world millions and billions of years, such as galaxies, atmosphere and hydrosphere of the Earth. In case of deviation from these rhythms - natural objects are destroyed.

From the point of view these limit states related to the aforementioned world coordinate system as the universal possible eidetic (everlasting and indestructible) look at the man. «Eidos is living being of the object permeated with semantic energy coming out of his depth and folding into a coherent picture of the phenomenon live face essence of the subject» [3, p. 119]. As part of our approach the Eidos let us to study the natural formation in terms of the limits of the outer (intermediate) coordinate system's cell, a clear sense of the statue, a phenomenon essence of the subject, his living being. Thus, we are developing an approach aimed at cooperation in all spheres of dynamic equilibrium of the body, including his subconscious, mind, the spiritual realm, and their mutual complementarily.

Consider the four areas of human activity, which proposed a universal approach to the description of the processes inherent in human. This approach manifests it most clearly. 1) The synergy of all the rhythms of the human body; 2) its relationship with noobiogeocenosis; 3) the influence of intellectual and spiritual catalysts on human health; 4) the relationship of secular asceticism with human well-being. All these areas are aimed at mobilizing the resources of the body, focusing on it as the course of treatment.

1. According to the basic postulates of synergetic algorithms of all fundamental processes at different levels of organization of the world are the same. Through developing our approach, these algorithms are not only similar, but have the stable interactions associated with the fundamental rhythms of the universe. It should be emphasized that the stability of the human body corresponds to the calibration sites of these rhythms, i.e. its

optimal dynamic equilibriums determined by the «steps» of this calibration.

Human inherent more than 100 daily circadian rhythms and rhythms associated with circulation of the Sun around its axis (mean approximately 27 days). Human found itself the best cycles of sleep, meal, drinking and many others for themselves, writing them in their medium-run in the equilibrium cells.

2. The interaction of man with the environment must be inextricably linked with the biocenosises and biogeocoenosises, but still it is practically unable and unlikely at the present stage of technology development and behavioral strategies may fit into these cenosises. However, the man is quite capable to provide the organization of noobiogeocenosis and provide them with a stable dynamic equilibrium, associate them with their intellectual and spiritual spheres. Man is capable at the time of his life to create noobiogeosphere's cell, including its dynamic equilibrium base and thereby bind itself to the natural coordinate system. Information sphere must also be organized on the model of noobiogeocenosis, it will allow to collect unnecessary information to optimally connected blocks and mark it in a certain way.

Nature is also associated with the Earth and the solar rotation periods, but in addition there are many other cycles of solar activity, climate, Sun's rotation around the galactic center. A.L. Chizhevsky substantiated communication activity of biological and social earth processes with the solar activity.

3. Catalytic processes in the intellectual and spiritual spheres have to play the same role in ensuring the sustainability and human health, which act as a catalyst in the world of the non-living and living (enzymes) to accelerate the reaction in the hundreds of thousands times.

Catalytic processes in the intellectual sphere must be directed to special remaking information, preventing natural formations go beyond their allowable existence. To do this, you must provide a combination of internal and external views of the same concepts and phenomena. That is any element of the knowledge must be identified on the one hand, and on the other hand – must be included in the knowledge's system about the high-level structures. Another type of catalytic processes in this sphere is a conscious imitation of the features of a healthy lifestyle based on cultural memes – discrete units of culture, which accumulates and transmit the cultural information. The collection of memes including tunes, ideas, expressions, ways of cooking, leisure activities aimed to promoting a healthy lifestyle are the new replicators, forming our biological and cultural evolution at the present stage of her. Memes spread using a man as a copying machine and its ability to synthesis and simulation distribution.

Among the catalytic processes of the spiritual sphere can also identify several types. The first - it is the catalysts provide interaction of intellectual and spiritual spheres through a coordinate system based on the limit dynamic equilibriums. The second are the catalysts promoting the formation of noobiogeocenosis that are involved in the formation of planet-civilization systems of the Earth's shells.

4. The presentation of secular (cultural) asceticism apart from the concept of «the coordinate system based on the limits of dynamic equilibrium,» correlate with the concept of «emptiness», «middle way», rhythms of world harmony (Taoism, Buddhism, Zen Buddhism) well. When these concepts begin to determine the path of development of nature, society and the man, they gain the stability and optimality of existence. Secular asceticism presupposes permanent complementarily cleansing of the body, soul and mind, when the formation of «emptiness» in one of these areas helps to clean the other.

Catalytic processes of intellectual and spiritual spheres, as well as secular asceticism contribute to the formation of different types of «equlibrium-net» formed on the basis of random processes (metabolic type). In equlibrium-net, the web itself is a network of interactions is more important than their sources, so that the basic information resources of spirituality contained within the network, which allows it to maintain the dynamic equilibrium of the human as if feeding them.

Problems of death, destiny with point of view of the philosophy and the sciences interacting with it

Consideration of human problems with point of view dynamic equilibriums opens up possibilities for the analysis of limiting conditions of his life and death. This is the subject of philosophy's study, which is different from the problems that are available for scientific methodology and is aimed at the limiting foundations of science and culture.

Death is a natural completion of a human life, however, man, unlike the animals usually does not take it, performing imaginary concept of immortality, which, however, helped him to overcome the difficulties of life. From a philosophical point of views of human immortality can be considered as continuation of his life in the genes and in art creativity. However, a more clear type of immortality is associated with a cell of the noosphere connects with the world coordinate system. Such a cell can create each person, moreover it is one of the main tasks of his life. However, the few who succeed. Especially visually coordinate system associated with human destiny, fate and the key threshold of life when someone begins to count his life not from birthdate but from the date of death. This date, no one knows it is securely hidden from all living and is perfectly correct - people have naturally fear for death. But after this threshold a person begins to figure his life in line with the period that he began to feel for himself. Held a kind of «calibration» process of life - the signal sent somewhere into the unknown, the transcendental, comes back and lets you know that there is still time for such a case, specific creative frontiers, the development of something new, the rework old and so on. After that, unsparingly starts are screened all the excess associated with vanity, life line becomes clearer, the next calibration signal further clarifies it, etc.

Destiny - the concept of having a more mythological and religious than scientific interpretation. «In Greek mythology, the destiny personified ... the goddess of fate have a personal tyranny, but they do not have a distinct «personality «... With the crisis of the polis lifestyle to the forefront destiny as luck, chance ... With the triumph of the Roman Empire the fate interpreted as an all-encompassing and indisputable determination, alienated from individual being - «fate» ... Christian countered the idea of destiny, faith in meaningful action «providence» ... in Modern time, the development of natural-science outlook pushes the idea of fate in the sphere of narrow-minded ideas ... at the end of the 19th century in the philosophy of life the word «destiny» begins to communicate with the requirement of irrational activity» [4, p. 663].

A key pass for a man starts to count his life from the date of death. This date no one knows, but after that pass a person begins to evaluate the parameters of his life in line with the period that he began to feel.

On the basis of our ideas destiny is a man's life in the natural coordinate system, its status in the calibration knots separated by intervals corresponding to the oscillation frequency of the

fundamental limits of rhythms of nature (the set of bifurcation points of the life). Sufficiently to start once in sustainable interaction with the system of coordinates and it only will widens and deepens. That is expressed well, for example, in the existential prayer, where the person brings life as a sacrifice to their purpose, so that the person can be defined as «the willingness to make sacrifices». In contrast to the everyday fear (loss of life or the good things of life), the ontological fear - the fear has not found a worthy destination to sacrifice their lives, and these benefits. Destiny if it is related with the coordinate system should be regarded as a vocation, which should obey and follow it even when the target is not feasible for the individual because of its comprehensiveness, and infinity.

There are many examples from the life of famous philosophers who not only believed in his destiny and purpose, but regarded them as an extension of his life. For example, Socrates, who was sentenced to death by Areopagus, had many opportunities to avoid it, but decided that such an outcome would be beneficial to spread his philosophy. It is important that the inner voice of Socrates – "daymonion" who warned him in a life of wrong decisions in the case of his death remained silent, that is, as would have approved of his choice.

The ancient Chinese believed that the philosophical concept is only true when it is embodied in the life of its creator. This corresponds exactly to the following of a life in accordance with the rhythms of the natural coordinate system. In addition, many thinkers, prophets have emphasized that the right to the destiny given not for everyone. The central philosophical question, a thread linking the ideas of the Upanishads, Confucius, Kant, and many other great concept - it is a moral law which determines a person's life that some people hear, while others do not.

Thus in the Upanishads of ancient India this law is determined by the harmony between Brahman and Atman. Brahman - is the world around us, strung on the spiritual structure and Atman is the cell of the Brahman for a particular person. Such spiritual cell is present in every individual, but people manage it differently. One individual lovingly cultivates it, so that it becomes decisive for his «I», but at the same time correspond to universal norms. Another one purposefully destroys it, which requires a lot of effort, as the voice of conscience sound in every human. Alcohol, drugs, bad friends help many people destroy their own individual Atman or very flatten it. These philosophical ideas are very well matched dynamic equilibrium cells of the approach described above.

CONCLUSION

The coordinate system is opened and directly available to everyone. Indeed the system of interconnected dynamic equilibrium can be reached by developing of the sensory representation, using abstract and theoretical models, as well as creating a combination of different variants of these types. To interact with the coordinate system does not need a special theoretical training. The most important thing to know, to feel that there is a system of coordinates, and then it will provide individual existence «awake regime», set it to its rhythm, and will maintain a stable relationship with this man, more and more strengthening it.

The coordinate system is characterized by spatial location, time structure, but no localization or any space constraints for it does not exist. It is present in every part of nature, at all levels of its structural organization. Thus «natural coordinate system» is not identical with the concepts of «absolute», «preferred» or «truly objective» reference frame. On the one hand coordinate system is adjusted to the process, if the latter is «caught» for any type of dynamic equilibrium. On the other hand, entered into accidental contact with the process, it helps him find a stable equilibrium, that is, go to one of the fundamental (rhythmic) interactions.

Due to the coordinate system is great potential for dialogue and communication (internal and external), as the most profound form of dialogue is the dialogue: a man - «coordinate system» and «coordinate system» - another man, or other dynamic equilibrium inside of the person. Conversation with itself should also be made through it. All natural formations that have strong ties with her taking part in the formation of this coordinate system. The coordinate system interacts with open systems, which have a tendency to self-organization, self-development, developing through the bifurcation point, forming a unique set of bifurcation points - the destiny of life.

REFERENCES

1. Kozhevnikov N.N. Sistema koordinat mira na osnove predel'nyh dinamicheskih ravnovesij [The coordinate system of the world on the basis of limit dynamic equilibria]. Jakutsk: Izdatel'skij Dom SVFU Yakutsk: Publishing House of NEFU, 2014, 176 p.

2. Losev A.F. Muzyka kak predmet logiki [Music as a subject of logic]. Moscow: Izd. Losev A.F. [Losev A.F. Publishing House], 1927, 264 p.

3. Nikolay N. Kozhevnikov, Vera S. Danilova. The world coordinate system on the basis of limit dynamic equilibriums // European Journal of Philosophical Research. - 2016, Vol. 5, Is.1, pp.18-26.

Information about authors

Kozhevnikov Nikolay N., Doctor of philosophical science, Professor of Philosophy, Yakutsk, North-Eastern Federal University, Professor, Department of Philosophy, 677013, Yakutsk, Oiunsky st. 41, Apart. 37, Tel.: (4112) 32-09-59, E-mail: nnkozhev@mail.ru;

Danilova Vera S., Doctor of Philosophy (ontology and epistemology), Docent of Philosophy, Yakutsk, North-Eastern Federal University, Professor, Department of Philosophy Tel.: (4112) 32-09-59, E-mail: nnkozhev@mail.ru.

ORGANIZATION OF HEALTHCARE, MEDICAL SCIENCE AND EDUCATION

S.A. Bogachevskaya, A.N. Bogachevskiy, N. A. Kapitonenko

CARDIOVASCULAR MEDICAL CARE IN THE FAR EAST FEDERAL DISTRICT IN THE PUBLIC HEALTH OFFICIALS' OPINION

ABSTRACT

This article presents a study of the views of the health officials of the availability and quality of medical care for the circulatory system diseases in the institutions of the Far Eastern Federal District, based on the materials of sociological research from 2013 to 2015 (197 respondents). Reveled passivity of the health officials to assess the situation and making the potential administrative decisions under the circulatory system diseaseshas a negative impact on the process of provision and the development of medical care to the population of the region and indicates the presence of defects in the health care management system. Itdoes notfavor social and economic attractiveness of the Far Eastern Federal District, which according to a tenth of the respondents is one of the ways to reduce the mortality of the circulatory system diseases in the region. A comparative analysis of the views of patients, doctors and managers seems to be more informative that will allow identifying problems and suggesting solutions.

Key words: structure of cardiovascular medical care, evaluation with medical care satisfaction, the levels of care, continuing medical education standard.

INTRODUCTION

Cardiovascular diseases (CVD) are the main cause of temporary disability and death in Russia and abroad [1, 2]. Today the analysis of efficiency of functioning of medical institutions in terms of the quality of specialized medical care and achievement a positive effect through satisfaction rate gains in particular importance [5]. First, there are questions of the patients' competence in the evaluation of various aspects of institution functioning as well as practitioners' competence in the assessment of organizational issues in the medical service.

Often patients as consumers of medical service have no opportunity to compare the quality of services for key parameters. It is easier for them to appreciate the elements of the process, where they have a wide field for comparisons [4].Practitioners often have difficultiesto assess organizational issues. This requires the involvement opinion ofhealth organizersin research. It seems that the assessment of the organizational aspects of medical care servicefor CVDby health organizers will allow approaching more objective to the evaluation of medical care in general and on the key parameters.

MATERIALS AND METHODS

We used materials of a poll of health organizers (197 respondents) in the years 2013-2015 to assess the quality of care for CVD in the Far Eastern Region (FER): accessibility ofmedical care for the population, the quality of services and specialist knowledge in the diagnosis and treatment of CVD [6]. Statistical processing was realized using Microsoft Excel Statistic package of statistical programs. Statistical significance was conducted based on the results of reliability parameters using sampling error and confidence limits of the relative values of the universe. The level of statistical significance was accepted asp <0.05 (CI: 95.0%).

RESULTS

The respondents of 7 territorial subjects of the FER were involved in the study. 30.5 ± 3.3% of respondents were men and 69.5 ± 3.3% of them were women. The most numerous groups among our respondents were aged from 41 to 50 years (34.0 ± 3.3%) and from 51 to 60 years (33.5 ± 3.4%). Representatives of the regional institutions were 53.8 ± 3.6%; ones of the administrative centers of the Russian Federation subjects were 49.8 ± 3.6%, ones of the countryside were a fifth part of all respondents (20.3 ± 2.9%). Health organizers on the basic profession were 42.6 ± 3.5%, in addition 28.9 ± 3.2% of respondents had the second occupation in health organization.

More than 2/3 of the respondents (70.1 ± 3.3%) were in touch with the cardiology service. The need in cardiology and cardiovascular surgery for medical institutes of the FER was 57.9 ± 3.5% and 25.4 ± 3.1 % respectively and the need in both professionals was 18.3 ± 2.8%.

Each of the medical care levels in the FER has received more than 62% of positive opinion (3-5 points) with the largest number of them (70.6 ± 3.3%) at the level of therapeutic cardiovascular hospital and with the least amount of negative opinion (1.0 ± 0,7%) at the federal level (Tabl. 1).

Only a quarter of respondents (25.4 ± 3.1%) were satisfied with the organization of cardiovascular care in the FER.. According to respondents, the fourth level of cardiovascular care (primary medical care) in the FER was worst organized (30.5 ± 3.3% of all respondents and ¾ of the respondents dissatisfied with the situation of cardiovascular care in the region at any level). The level of specialized medical care, including high-tech medical care (HTMC) looks most advantageous: only 8.6 ± 2.0% of unsatisfied.

The presented poll included questions about the possibilities of improvement and restructuring of cardiac care. The third part (29.4 ± 3.3%) of respondents believed that the provision of a variety of medical facilities with consumables and equipment should be centralized under the compulsory medical insurance (25.9 ± 3.1%) for monitoring, planning and effective spending resources; as well as in HTMC (8.1 ± 1.9%). A fifth part of respondents (20.3 ± 2.9%) thought negatively about centralization of provision with medical equipment and consumables, they believed that a negative experience would be received. A significant number of respondents (49.7 ± 3.6%) couldn't answer this question.

82.7 ± 2.7% of respondents agreed with that improvement of physicians in cardiology would help change the situation in the field of prevention, diagnosis and treatment of CVD for the better. In addition,43.2 ± 3.2% of respondents were ready to send physicians to theme cardiology courses; 26.4 ± 3.1%of respondents had a

need, but didn't have the financial and organizational possibilities for this. 44,2 ± 3,5% of respondents doubted the attainability of the WHO goal of reducing mortality from CVD by 25% by the year 2025 for the Russian healthcare.

Discussion

The most likely portrait of the health organizer in medical institutes of the FER were women (69.5%) of 41-60 years old (67.5%) working in district(53.8%) institutes in cities (79.7%) and in 28.5% of cases didn't have a specialization for health professionals.

Taking into account the needs (57.9%) and the presence of professionals in the staffing table (58.9%), most medical institutions of the FER (98.3%) needed cardiologists on staff positions. The need for cardiovascular surgeons was 2.2 times higher than the actual number of established posts in the FER (25.4% vs. 11.7%).

Medical care satisfaction results greatly differed using various approaches, for example evaluation as whole and separate components of the process. Some contradictions between them were noted (for separate components medical services satisfaction quotients (MSSQ) were from 63.5 to 70.5% and for evaluation as whole it was just over 25%). Respondents as consumers faced often with primary medical care, which was estimated most negatively (more than 30% of respondents). Such projection the most negative assessment of the components on the overall situation (and vice versa) in the result doesn't allow using generalized questions on topics in the analysis of respondents' opinions.

The federal Centers playa special role in HTMC service: they account for more than 71% of the total amount of HTMC, and among the most complex methods they account for more than 91% [4]. Since the Federal Center of Cardiovascular surgery(FCCVS) in the FER has started to work most of respondents (51.8%) noted the cardiovascular service in the region took a turn for the better.

Delegation of public authorities most of the financial obligations for public health at the level of subjects of the federation in terms of their economic inequalities resulted previously in significant differences in the financing of necessary medical resources [3]. Of the 69.0% of the organizers, who have a need in the direction of physicians within their major field of study, 25.9% of all respondents didn't have the financial and organizational capabilities to send their practitioners to them cardiology courses. At the same time, 82.7% of respondents positively assessed this program of professional improvement.

Satisfaction with the medical care for CVD organization estimated by health officials of the FER

The level of care		Evaluation of satisfaction scores, p <0.05 (CI: 95.0%)					Difficult to answer
		1	2	3	4	5	
4	in a district clinic, %	2,5±1,1	18,3±2,8	37,1±3,4	25,4±3,1	5,1±1,6	10,2±2,2
3	in a therapeutic district hospital, %	1,5±0,9*	13,7±2,5	33,5±3,4	27,4±3,2	3,1 ±1,2	20,3±2,9
2	in a therapeutic cardiovascular hospital, %	1,0±0,7*	1,5±0,9*	19,8±2,8	38,6±3,5	12,2±2,3	26,9±3,2
1	in a cardiac surgery hospital,%	3,6±1,3	3,6±1,3	15,2±2,6	33,5±3,4	13,7±2,5	30,5±3,3
	in a Center for Cardiovascular Surgery, %	0,5±0,5*	0,5±0,5*	8,6±2,0	34,0±3,4	23,9±3,0	32,0±3,3

Note: * The level of statistical significance was accepted as p>0,05.

In spite of the positive feedback on the FCCVS functioning overall negative assessment of the Russian health care efforts prevailed. There is a lack of trust to the Ministry of Health in the region carried out the health reform.

The main proposals for improving the most problematic primary medical care were conducting competent personnel policy and the strengthening of work motivation (15.7% of all respondents); professional development in CVD as one of the most common pathologies among the population (15.2%); revision of the working time on medical examination of patients (7.1%).

The main proposals of respondents to reduce mortality from CVD were an implementation of adequate primary and secondary prevention and clinical examination (53.8%), access to free medical care for patients with CVD (13.2%), increasing social and economic attractiveness of the FER (9.7%), the availability of the examination of patients (9.1 %), increasing cardiovascular care at the prehospital level (6.6%), as well as standardization of the CVD management (5.6%). Such proposals as the growth of science and modern technologies in the CVD treatment and the development of rehabilitation services noted only 3.1% of respondents.

Proposals to improve the examination of patients and ensure them drugs were rather poorly represented in the opinion of the health organizers. Unfortunately, only 2.5% of respondents decided to pay attention to the development of science and modern technologies, as well as rehabilitation services for patients with CVD.

Thus, the opinion of the organizers and their proposals could be crucial in finding organizational solutions for developing of cardiovascular care in FER, but «difficulties» in making management decisions by respondents in this poll alert: from24 to 50% of them found it difficult to answer questions about the possibilities of improvement and restructuring of cardiovascular care.

CONCLUSION

The passivity of the organizers of the FER in assessing the situation and making the potential of administrative decisions make a negative effect on the process of cardiovascular care to the population of the region. Analysis of executive personnel and health organizers sociological survey indicates the presence of institutional flaws and shortcomings in the management of the medical care system for patients with CVD, as well as the presence of underestimated problems of rehabilitation of these patients (including rehabilitation after HTMC). Insufficient financing continues to have a negative impact on the basic processes of the organization of cardiovascular care services and the level of provision of equipment facilities and qualified personnel, the availability of HTMC for population. None of these moments contribute to the social and economic attractiveness of the FER as one of the ways to reduce the mortality of CVD in the region. A comparative analysis of the views of patients, doctors, executive personnel and health organizers seems to be more informative and could allow identifying important problems and suggest solutions better.

References

1. Belenkov Y. V., Gorokhov S.G. Organizacija kardiologicheskoj pomoshhi v Rossii [Organization of cardiac care in Russia] Kardiologija: nacional'noe rukovodstvo / pod red. Ju.N. Belenkova, R.G. Oganova [Cardiology: national

guidelines / ed. Y.N. Belenkov, S.G. Oganov]. Moscow: GEOTAR Media, 2010, P. 18-37.

2. Bokeria L.A., Gudkova R.G. Serdechno-sosudistaja hirurgija – 2009. Bolezni i vrozhdennye anomalii sistemy krovoobrashhenija. [Cardiovascular surgery. Diseases and congenital anomalies of the circulatory system]. Yearbook, 2006-2013,Moscow: Bakoulev Center for Cardiovascular Surgery, 2009, p. 3-11.

3. Kovalev S.Y., Blum I.Y., Zaitseva I.N. Reformy sistemy zdravoohranenija v Rossii: social’nye posledstvija kommercializacii [Health System Reform in Russia: the social consequences of the commercialization] Region: jekonomika i sociologija [Region: Economics and Sociology]. 2005, № 3, P. 58-67.

4. Skvorcova: federal’nye centry VMP dolzhny poluchat’ sredstva naprjamuju [Skvortsova: federal HTMC centers should receive funds directly]. 03.03.2014 // Vademec.ru - Retrieved from: http://vademec.ru/news/detail15848.html?print=Y (access date 10 Yule 2016).

5. Tokareva Y. M. Primenenie Swot – analiza dlja ocenki kachestva medicinskoj pomoshhi [Swot - analyzes application to assess quality of medical care]: Cand. Soc. Sci., Volgograd, 2010, 122 p.

6. Ob utverzhdenii Metodicheskih rekomendacij «Organizacija provedenija sociologicheskogo oprosa (anketirovanija) naselenija ob udovletvorennosti dostupnost’ju i kachestvom medicinskoj pomoshhi pri osushhestvlenii objazatel’nogo medicinskogo strahovanija»: Prikaz FFOMS ot 29.05.2009 g. № 118 (v red. ot 26.04.2012 № 86) [On approval of the Methodological Recommendations «Organization of the opinion polling (questionnaire survey) for satisfaction with the accessibility and quality of medical care in the implementation of compulsory health insurance»: the Order of CHIFF on May 29, 2009 № 118 (as amended on 26.04.2012 № 86)] Tfoms22.ru - Retrieved from: http://www.tfoms22.ru/docs/prakazi-ffoms/29052009-118/ (access date 20 Yule 2016).

The authors:

Bogachevskaia Svetlana (Academic degree: Candidate of Medical Sciences, doctoral candidate)

Place of employment: the Federal Centre for Cardiovascular Surgery, Khabarovsk

Post: a Head of the functional and ultrasound diagnostics

Contact information: 680009 Krasnodarskaya str. 2v, Khabarovsk, Russia, Тел: (4212) 78-06-31

E-mail: bogachevskayasa@gmail.com;

Co-author: Kapitonenko Nikolay Alekseevich (Academic degree: Doctor of Medical Sciences, professor)

Place of employment: the Far Eastern State Medical University, Khabarovsk

Post: a Head of the Public Health and Healthcare Department, professor

Contact information: 680000 Muraveva-Amurskogo str. 35, Khabarovsk, Russia.

Тел.: (4212) 30-54-26, E-mail: ozd_fesmu@mail.ru;

Co-author: Bogachevskiy Alexander

Place of employment: the Federal Centre for Cardiovascular Surgery, Khabarovsk, cardiac surgeon

Contact information: 680009 Krasnodarskaya str. 2v, Khabarovsk, Russia, e-mail: bogachevskiy@gmail.com.

Zakharova E.K., Poskachina T.R., Nazarov A.N.

ANALYSIS OF EYE INJURY IN THE REPUBLIC SAKHA (YAKUTIA)

SUMMARY

This article presents an analysis of injuries of the eye and orbit by type of injury, severity, treatment and outcomes among adults in the Republic Sakha (Yakutia) in the period from 2014 to 2015, which revealed the following: the prevalence of home injuries (99%) among which majority of them were injuries of mild severity 66.4% in 2014 and 64% in 2015.

In nosological structure of the eye injury the bruise of the eyeball and tissues of the orbit is in the first place (46% in 2014 and 47% in 2015), the foreign body outside of the eyes is in the second place (19.7% and 22%), in the third place – the injury of conjunctiva and corneal abrasion of 19.2% and 16% respectively.

Epidemiological data on the prevalence of eye injuries in the Republic Sakha (Yakutia), delayed hospitalization of emergency patients (from 40 till 70%) demonstrate the necessity for timely diagnosis and hospitalization eye care hospital to provide specialized and, if necessary, of high-technology care for patients with acute conditions and incidence of gas and orbit, especially in remote areas of the country. This requires the consolidation of all ophthalmic services in a single national center on the basis of The Yakut Republican Ophthalmologic clinical hospital with the introduction of medical information systems and telemedicine technologies to conduct remote medical consultations, consultations, teleconferences, introduction of new technologies of diagnostics and treatment methods.

Keywords: eye trauma - thermal burn, contusion, penetrating wound of the sclera and cornea.

Urgent help in any branch of medicine including ophthalmology requires immediate and specific diagnostic - therapeutic decision making. Eye and orbit injuries make up approximately 20% of organ pathology, estimated as the main cause of blindness and low vision of the able-bodied. Achievements of modern reconstructive microsurgery and suitable pharmacotherapy significantly improve the anatomical structure and visual organ functions after eye injury [3]. However, eye injury outcome is caused by many factors, one of which is timely medical emergency care [5].

The Republic Sakha (Yakutia) (RS (Y) as one of the subjects of Russia, due to its natural and territorial conditions is considered unique in the world. The republic is located in the north-eastern part of the Eurasian continent and it is the largest region of the Russian Federation (RF). The total area of the territory of Yakutia amounted at 3.1 million square kilometers is more than 40% of its territory within the Polar circle. Till nowadays Yakutia is one of the most remote and inaccessible regions of the world in relation to transport: 90% of the territory has no year-round transport links. Natural and climatic conditions of Yakutia in many respects are characterized as extreme and the coldest of the inhabited regions of the planet. The climate is continental with long winters and short summers. The absolute value of minimum temperature (down to minus 70 ° C) and its total duration (from 6.5 up to 9 months a year) have no parallel in the northern hemisphere. Among the properties that define Yakutia is extremely low population density in the vast territory occupied by the republic of about 0.3 people per 1 sq. km. The population within the republic is unevenly distributed. Climatic and economic factors have significant impact on the settlement pattern. The highest population density is characteristic for areas with relatively favorable conditions for agricultural production: the Southern, Central, Vilyusky regions, including the cities of Yakutsk and Neryungri, Mirniy with developed industry and transport scheme (1,2-2,8 persons per 1 sq. km). The lowest density of population in an area of the Arctic region with extreme climatic conditions, unfavorable for life and economic activity (0.01 - 0.08 persons per 1 sq. km.). The number of inhabitants in other regions of the country range from 0.1 to 0.9 people per 1 square kilometer . According to statistics, the total population of Sakha (Yakutia) in 2015 amounted to 956 896 people. The urban population - 64.1%, the rural - 35.9% [1, 2, 4].

The State autonomous establishment (SAE) of the Republic Sakha (Yakutia) the Yakutsk Republican Ophthalmologic Hospital (YROH) including the in-patient department with 107 beds is considered the leading eye care specialized establishment. On the basis of YROH there is an eye care emergency consulting room, equipped in accordance with orders of the Russian Federation Ministry of Health on November 12, 2012 N 902.

Besides the medical organization the medical emergency care is urgently provided by physicians and medical mobile emergency teams in accordance with the order of the Russian Health and Social Development Ministry of November 1, 2004 N 179 «On approval of the emergency medical care.» The out-patient emergency care is conducted in ophthalmic consulting rooms and clinics CRH Yakutsk. Patients with eye and orbit diseases of severe degree are taken by emergency teams to the YROH eye care emergency department. If necessary sanitary aviation brings patients from remote regions of the republic.

In order to increase the availability of specialized eye care SAE «YROH» branches in Neryungri, Nyurba, Lensk cities and Chulman, Suntar villages were set up.

Taking into account climatic and geographic features of the republic Sakha (Yakutia), the study of prevalence of eye injury, types and severity of eye and orbit injuries, as well as provided treatments and their outcomes is of great importance nowadays.

Aim: To analyze eye and orbit injuries in accordance with types of trauma, severity, treatments and outcomes among adults in the Republic of Sakha (Yakutia) from 2014 to 2015.

In the period 2014 – 2015 in the Republic of Sakha (Yakutia) 12758 patients with eye and orbit injuries were reported. Eye injury intensive index (II) among the adult population in the Sakha Republic (Yakutia) decreased from 940 to 880 per 100 000 adults in two years, i.e., 6.8%.

Table 1 shows there was decrease at 7% of the absolute number of patients with eye and orbit injuries, addressed for medical care in two years. By types of injuries 99% were resulted from by domestic trauma, industrial traumas had lower rate at 24.6% as compared 2014, criminal eye and orbit injuries were less than 0.5% of the total number of eye and orbit injuries.

Concerning the nosological structure of the eye injury the eyeball and orbital tissue injuries were on the first - 46% in

Table 1

The injury distribution by types of trauma in RS(Y) in the adult population at 18 years and over in the period 2014-2015

Trauma types	Total		Number of patients by types of trauma					
			Industrial		Home traumatism		Criminal	
	2014	2015	2014	2015	2014	2015	2014	2015
Conjunctival trauma and abrasion of the cornea	1268	994	10	9	1258	995	7	
Eyeball and orbital tissue injury	3031	2929	25	18	3006	2896	7	15
Lacerated eye wound with intraocular tissue prolapse or loss	2	1			2	1		
Lacerated eye wound without intraocular tissue prolapse or loss	4	3			4	3		
Penetrating wound of the orbit with or without intraocular foreign body	12	8			12	8		
Eyeball penetrating wound with intraocular foreign body	9	11			9	10		1
Eyeball penetrating wound without intraocular foreign body	25	25	2		23	21	1	4
Other eye and orbital injuries of lacrimal canal	31	18			31	18	5	
Foreign body in the eye outer part	1302	1364	16	8	1286	1356		
Thermal and chemical burns of ocular region	230	219	6	5	224	216		1
Other eye and orbit injuries	674	598	6	9	668	597		2
Total	6588	6170	65	49	6523	6121	21	23

2014, 47% in 2015, a foreign body in the eye outer part were on the third place - 19.7% and 22% respectively, on the third conjunctival injuries and abrasion of the cornea - 19.2% and 16%. Penetrating wounds of the eyeball constituted a small part of 0.6% over two years.

According to Table 2 among industrial accidents there was high prevalence of injuries of moderate severity, accounting for 49.2% in 2014 and 48.9% in 2015. Among home injuries the minor injuries were revealed at 66.4% and 64%, respectively. The ratio of severe injuries is small and was 0.9% and 0.8%.

At 99% patients with minor trauma of eyes and orbit injury and 92% patients with moderate severity the outpatient care was provided (taible 3).

100% patients with severe injury were admitted to the in-patient departments.

Emergency hospitalization for injuries of moderate severity was 47% in 2014 and 25% in 2015, with severe injuries of 40% and 70%, respectively.

Specific gravity of HTMC among hospitalized patients with injury of moderate severity was 13% in 2014 and 5% in 2015, with severe injury of 16% and 11%, respectively.

According to Table 4 there was recovery (0.3 VA) at 99% in 2014 and in 2015 as well. As a result one eye blindness is registered at 5 - 9 patients with penetrating injury of the eyeball, including 50% of a foreign body.

Thus, the analysis of eye and orbit injuries by types of injury, severity level, treatments and outcomes among adults in the Republic of Sakha (Yakutia) in the period 2014 to 2015 has found out:

1. Decrease of the absolute number of patients with eye and orbit injuries to 7% (from 6588 to 6170), intensive index (II) 6.8%.

2. The prevalence of home injuries (99%), moderate severity of injury making up the higher rate among them (66.4% and 64%). Penetrating wounds were noted in a lower rate (0.6%) for two years.

3. Among the industrial injuries there was predominance of moderate injuries (49.2% and 48.9%), severe injuries accounted for less than 1%.

4. As for the nosological structure of eye injury in the first place the eyeball and orbital tissue injury has been noted (46, 47%), followed by a foreign body of the outer ocular part (19.7 and 22%) and the third - conjunctival trauma and corneal abrasion (19 2 and 16%).

5. Out-patient medical care to the majority of patients with eye and orbit injuries of minor to moderate severity was provided (99% and 92%), with severe injury of 100% in the hospital.

Table 2

The injury distribution by severity level of the injury in the adult population at 18 years and over in the Sakha Republic (Yakutia), in the period 2014 – 2015

Types of trauma	Total		Number of patients by types of traumatism					
			Industrial		Home trauma		Criminal	
	2014	2015	2014	2015	2014	2015	2014	2015
Minor injury	4359	3940	28	22	4331	3921	12	10
Moderate severity	2166	2178	32	24	2134	2151	6	8
Severe trauma	63	52	5	3	58	49	3	5
Total	6588	6170	65	49	6523	6121	21	23

Table 3

The distribution by eye and orbit injury treatment among the adult population aged 18 and over in the Sakha Republic (Yakutia) in the period 2014 – 2015

Type of trauma	Total		Number of patients by								Bed-days in hospital	
			амбулатор-ное		стационар-ное		Urgently hospitalized					
							Total		HTMC*			
	Year	2015	2014	2015	2014	2015	2014	2015	2014	2015	2014	2015
	4359	3940	4319	3906	40	24	5	9			96	144
Minor injury	2166	2173	2034	2006	132	167	62	41	8	2	1056	1336
Moderate severity	63	52	-	-	63	52	25	36	4	4	672	485
Severe trauma	6588	6155	6353	5912	235	243	92	86	12	6	1824	1965
Total												

* HTMC - a high-tech medical care.

Table 4

Treatment outcomes by type of injury among adults aged 18 and over in the Sakha Republic (Yakutia) in 2014 and 2015

Trauma types	Total		Number of patients after visual acuity treatment							
			Recovery after treatment		Disablement					
					VA* lower than 0,3		в том числе			
							One eye blindness		Two eyes blindness	
	2014	2015	2014	2015	2014	2015	2014	2015	2014	2015
Eyeball and orbital tissue injury	3031	2914	3025	2926	6	2		1		
Lacerated eye wound with intraocular tissue prolapse or loss	2	1			1	1	1			
Lacerated eye wound without intraocular tissue prolapse or loss	4	3	3	3	1					
Penetrating wound of the orbit with or without intraocular foreign body	12	8	6	7	4	1				
Eyeball penetrating wound with intraocular foreign body	9	11	7	7	2	2	2	2		
Eyeball penetrating wound without intraocular foreign body	25	25	18	10	5	9	2	6		
Other eye and orbital injuries of lacrimal canal	1302	1364	1302	1364						
Foreign body in the eye outer part	230	219	228	216	2	3				
Thermal and chemical burns of ocular region	4615	4545	4589	4533	21	18	5	9		
Other eye and orbit injuries										
Total										

* VA - visual acuity.

6. Emergency hospitalization in traumas of moderate and severe injury is provided at 40 - 70% of the whole number of injuries admitted to the in-patient department . Of them, the specific gravity of HTMC ranged from 11 to 16%.

7. Recovery as the treatment outcome of patients with eye and orbit injuries was noted at 99%, blindness in one eye is fixed at 0.2%.

Epidemiological data of the prevalence of ocular injuries in the Sakha Republic (Yakutia), delayed admission of emergency patients (40 to 70%) testify to the need for timely diagnosis and hospitalization in ophthalmic hospital to handle up-to-date specialized and high-tech care for patients with eye and orbit diseases of severe degree, especially from remote areas of the country. This requires the consolidation of the entire ophthalmic services in the single republican center based in YROH with the implementation of health information systems and telemedicine technology for remote medical consultations, consuls for physicians, teleconferencing, inculcation of new technologies and methods of diagnosis and treatment.

REFERENCES:

1. Gogolev A.I. Jakyti. Problemi etnogenesa i formirovania kylturi [Yakuts. Problems of ethnogenesis and formation of culture] Izdatelstvo JGY [YSU Publishing House], Yakutsk, 1993, p.200.

2. Gogolev A.I. Istoria Jakyti (obzor istorisheskih sobitii do nashala XX veka [History of Yakutia (review of historical events before the beginning of the XX century)] Izdatelstvo Jkutskogo Universiteta [Publishing House of the Yakutsk University], Yakutsk, 2000, p.201.

3. Kochergin S.A. Sergeev N.D. Issledovanie statisticheski znachimih otlichii pokazatelei kachestva gizni patientov posle mechaniheskoi travmi glasa i prakticheski zdorovih lydei [The study of statistically significant differences of patients' quality of life indicators after mechanical eye injury, and healthy people] Practicheskaj Medicina. Ophthalmologia [Practical Medicine. Ophthalmology]. Moscow, 2012, V. 2, p. 199 - 203.

4. Prokhorov B.B. Ecologia cheloveka. Ponjtiino-terminologicheskii slovar [Human Ecology. Conceptual and terminological dictionary]. Rostov-on-Don, 2005.

5. Stepanov A.V. [et al.] Sochetannaj travma glas v usloviah ekstremalnih sityacii [Combined eye injury in extreme situations] Medicina Katastrov [Disaster Medicine]. Moscow, 2011, № 1. (73), p. 25-27.

Authors:

1. Zaharova Ekaterina Kimovna, the head of in-patient department, the main non-staff ophthalmologist of MH RS (Y), State Budget Establishment RS(Y) «YROC», 677005 Yakutsk, 15, Sverdlova Str., ph. 89142757704, e-mail: Katya1961@mail.ru <mailto:Katya1961@mail.ru>

2. Poskachina Tamara Romanovna, the kand. of medical sciences, the senior lecturer, the head of ophthalmologic department Medikal Institute NEFU, 677000 Yakutsk, 5/1 Ordzhonikidze Square 28 ph. 89248766662 e-mail: doka14@list.ru <mailto:doka14@list.ru>

3. Nazarov Anatoly Nikolaevich, the Head Physician, SBE RS (Y) «YROC», 677005, Yakutsk 15, Sverdlov Str., ph. 89142757704, e-mail: nazarov_anatoly@mail.ru mailto:nazarov_anatoly@mail.ru

ARCTIC MEDICINE

O. N. Ivanova, M. A. Togullaeva, A. S. Golderova

FEATURES OF CLINICAL AND IMMUNOLOGICAL COURSE OF ACUTE PNEUMONIA IN CHILDREN

ABSTRACT

The article dwells on the study of the etiological factors of acute pneumonia in children, as well as changes in the immune status. It was revealed that the most frequent causative agent of pneumonia is Streptococci pneumonia, the second most frequent is Klebciella pneumonia, followed by a combination of C. pneumonia, Pseudomonas aureginosa, Chlamidia pneumonia. At analyzing the changes in the immune status in children with acute pneumonia, in comparison with the group of healthy children, the greatest decrease in T-cell (CD3 +, CD4 +, CD16 +), complement components C3 and C4, B-cell link of CD22 + was found.

Keywords: pneumonia, streptococcus, microbiological examination, Klebciella.

Lung inflammatory diseases dominate in the pathology of children's age forming persistent deviations in the health status of children; have a significant impact on child mortality. One of the factors of the climate of Yakutia, affecting directly or indirectly on the human body, is cold (-40, -50 C). Although, in a period of great and prolonged cold weather, our children most of their time spend in artificially heated rooms, due to large temperature difference inside and outside the building they are exposed to sudden temperature changes [1, 2, 3, 4].

Objective: to study the features of immunological system at children of early age with acute pneumonia.

Materials and methods. We analyzed 320 case histories of children from 6 months up to 8 years at the Children's infectious hospital of Yakutsk. Among the patients were 126 girls and 194 boys. All patients underwent clinical, laboratory and radiological examinations. The results of microbiological studies of sputum in 64 children with acute pneumonia, hospitalized at Children's city clinical hospital №2, Yakutsk in the period from January 2012 to March 2013 were analyzed. The analysis was carried out using computer program software WHONET version 5.6. The isolation and identification of pathogens were carried out by conventional microbiological methods.

Determination of subpopulations of T - and B - lymphocytes was performed by ELISA using monoclonal antibodies.

Determination of antibodies was carried out turbodimetrically by means of the intention of the speed of light in the formation of immune complexes in the kinetic measurement at multiscan.

The level of IL-1, IL-13, FNO, IFN in serum was determined using ELISA method according to instructions attached to sets of antibodies.

Material processing included calculation of arithmetic units (M), error medium (m), the frequency of occurrence of abnormal variant, expressed in percent, assessment of reliability of Student ($p<0.05$)

Results and discussion. Initially, we thought it appropriate to describe the group of examined children according to clinical variants of acute pneumatic self-harmony.

As it can be seen from Table1, the highest percentage of morbidity in children of early age falls on the focal and interstitial bronchopneumonia.

64 examined children older than 6 years are taken sputum flora. Patients rinse the mouth with a weak antiseptic solution (furacillin), and then with boiled with water.

A positive result is obtained in 30 cases, the overall structure was dominated by gram-positive bacteria -41,4%. 41 conditionally pathogenic microorganisms were allocated.

As it can be seen from table 2, the most frequent causative agent of pneumonia – pneumonia Streptococci, the second place on frequency is Klebciella pneumonia, then a combination of Klebciella pneumonia,Ps.aureginosa, Chlamidia pneumonia.

In the analysis of changes of immune status in children with acute pneumonia in comparison with healthy children we revealed the largest decline in T-cell levels (CD3+, CD4+, CD16+), components of complement C3 and C4, the decline In-cell link CD22+ (Table 3). These changes indicate antigenic stimulation and decrease immune resistance in children with acute pneumonia. The number of investigators indicated the decrease in the content of b-lymphocytes in acute pneumonia [1], which coincides with the results of this study.

CONCLUSIONS:

1. Focal bronchopneumonia predominates of clinical variants of acute pneumonia in all age groups.

2. At the analysis of sputum cultures in children with acute pneumonia, it was found that the most frequent causative agent of pneumonia is pneumonia of streptococcus, second place in frequency is occupied by Klebsiella pneumonia, then a combination of Klebsiella pneumonia, Ps. aureginosa, Chlamydia pneumonia.

3. At analyzing the changes in the immune status in children with acute pneumonia, in comparison with the group of healthy children, the greatest decrease in the T-cell level (CD3 +, CD4 +, CD16 +), complement components C3 and C4,

Table 1

Clinical variants of acute pneumonia

Clinical variants	Focal	Focal confluent	Segmental	Interstice
The frequency of occurrence	270(75%)	8(2,5%)	8(2,5%)	46(20%)

Table 2

Etiological factors of acute pneumonia in children

Pathogen	Absolute number	Relative number
Streptococc pneumonia	60	70 %
Klebciella pneumonia	15	20%
Klebciella pneumonia, Ps.aureginosa, Chlamidia pneumonia.	7	5 %

Table 3

Indicators of immune status in children of Sakha (Yakutia) with acute pneumonia

Indicators	Standards indicators for children(n = 100), M ± m	Children with acute pneumonia((n = 106), M ± m
CD3+	52,6 ± 1,7	20,1 ± 1,02*
CD4+	26,3 ± 0,7	11,2 ± 0,7*
CD8+	22,5 ± 0,23	16,2 ± 1,0
CD16+	23,2 ± 0,54	4,6 ± 1,1*
ИРИ	1,18 ± 0,64	0,7 ± 0,02
IgA	2,34 ± 0,69	1,3 ± 0,3*
IgG	13,3 ± 0,16	9,2 ± 0,7
IgM	1,6 ± 0,03	0,9 ± 0,09
CD22+	19,8 ± 0,16	9,9 ± 1,9
C3	0,67 ± 0,12	0,20 ± 0,02*
C4	0,34 ± 0,05	0,11 ± 0,02*
ЦИК	96,8 ± 0,132	194,2 ± 1,5*

*p < 0,05 между нормативами и полученными показателями в каждой группе.

and decrease in the B-cell link of CD22 + was revealed.

REFERENCES:

1. Bolezni organov dykhaniya u detej [Diseases of the respiratory system in children]/ Pod red. Rachinskogo S.V., Tatochenko V.K. Moscow: Meditsina, 2007, 496 p.

2. Vel'tishhev Yu.E. Immunodefitsitnye sostoyaniya [Immunodeficiency]. Prikladnaya immunologiya //Pod red.A.A.Sokhina. Kiev: Zdorov'e, 2014, P. 76-105.

3. Vel'tishhev Yu.E. Ostrye pnevmonii u detej [Acute pneumonia in children.]. Moscow: Meditsina, 2015.

4. Gavalov S.M. Ostrye pnevmonii u detej [Acute pneumonia in children.]. Novosibirsk: Izdatel'stvo Novosibirskogo universiteta, 2014.

Information about authors:

Ivanova Olga Nikolaevna, MD, professor of the Department of Pediatrics and Pediatric Surgery of the MI NEFU named after M.K. Ammosov, Yakutsk, Republic Sakha (Yakutia), Russia olgadoctor@list.ru;

Togrullaeva Matryona Afanasyevna, deputy head physician of the Children's city clinical hospital №2, Yakutsk, Republic Sakha (Yakutia), Russia;

Golderova Aitalina Semenovna, MD, chief research officer of the YSC CMP, Yakutsk, Republic Sakha (Yakutia), Russia, hoto68@mail.ru.

E.F.Argunova, S.N.Alexeeva, A.L. Sukhomyasova, F.F. Vasilyev, M.E.Nikiforova, G.I.Danilova, A.F. Zhelobtsova, Sh. B. Pirnazarova

ANALYSIS OF THE RESULTS OF NEONATAL SCREENING FOR CONGENITAL HYPOTHYROIDISM IN THE REPUBLIC SAKHA (YAKUTIA)

ABSTRACT

Congenital hypothyroidism (CH) is a disease characterized by insufficiency of thyroid hormones produced by the thyroid gland. CH leads to delay of development of all organs and systems, primarily from a lack of thyroid hormones Central nervous system suffers. Neonatal screening for congenital hypothyroidism is an effective method of early diagnosis and treatment of disease to prevent the development of disabling complications. With timely treatment of CH rate of physical and mental development of the child conforms to the norm. Currently, the optimal age of initiation of therapy drugs levothyroxineis considered the first 2 weeks of life.

The article analyzes the data of neonatal screening for congenital hypothyroidism in the Republic Sakha (Yakutia) from 1996 to 2016. The study revealed that prevalence of congenital hypothyroidism in the Republic Sakha (Yakutia) for reported twenty years was lower than in other regions of the Russian Federation. Congenital hypothyroidism is three times more prevalent in girls, than in boys and is more often observed in children from countryside. Organization of neonatal screening for congenital hypothyroidism in the Republic Sakha (Yakutia) allowed achieving a high percentage of newborn screening, reducing observation time and early initiation of replacement therapy and prevention of disability of patients.

In the period before the implementation of the PNP, there were revealed two children with mental retardation, after the introduction - one. According to the data of neonatal screening peak enhancement detection of CH as in 2006, out of 6954 newborn past research on CH, the diagnosis was confirmed in 4 of the studied (1:1739). In 2010-2011, the detection rate was lowest and amounted to 1 person per year with a frequency of 1:15877. Organization of neonatal screening on congenital hypothyroidism in the Republic of Sakha (Yakutia) allowed achieving a high percentage of newborn screening, reducing time of inspection and early replacement therapy, prevention of disability of patients.

Keywords: children, congenital hypothyroidism, neonatal screening.

INTRODUCTION

Congenital hypothyroidism (CH) is a disease characterized by insufficiency of thyroid hormones produced by the thyroid gland. CH leads to delay of development of all organs and systems, primarily from a lack of thyroid hormones suffering Central nervous system [2]. Congenital hypothyroidism occurs with a frequency of 1 in 4000-5000 newborns. In girls, the disease is detected in 2-2,5 times more often than in boys [3]. Prior to the introduction into practice of health care programmes neonatal screening of CH was one of the most frequent causes of early mental retardation. Neonatal screening for congenital hypothyroidism is an effective method for early diagnosis and timely treatment of the disease to prevent the development of disabling complications. In Russia, neonatal screening for CH is from 1993 in the Republic of Sakha (Yakutia) – till 1996; in the early years in neonatal screening

in the RS (Y) were involved only 15 out of the 36 districts (Uluses). Currently are involved all the municipalities of the Republic. Within this time, the coverage rate of neonatal screening increased from 42% to 99.6% [4]. The main purpose of screening for CH – early identification of all babies with elevated thyroid stimulating hormone (TSH) in the blood. All newborns with abnormally high TSH levels require urgent in-depth examination for final diagnosis and immediate commencement of substitution therapy [4].

In the previous investigations there was a direct relationship between the age at which treatment was started, and the index of intellectual development of the child in the future. In case of timely treatment CH rate of physical and mental development of the child conform to the norm. Currently, the optimal age of initiation of therapy by preparations levotiroksineis considered the first 2 weeks of life [3]. The main clinical symptoms are non treated CH are delayed growth and mental development leads to mental retardation. In most cases (85-90%) prevails primary congenital hypothyroidism. Among the cases of primary congenital hypothyroidism about 85% are sporadic, 15% are hereditary [2].

MATERIALS AND METHODS

In the framework of the priority national project (PNP) «Health» by the Ministry of health and social development of the Russian Federation was issued a decree No. 185 of 22 March 2006 «On mass newborn screening for hereditary diseases».To organize screening, introduction of new methods, organization of diagnostic and medical care published the following normative documents: the order of the Ministry of Health of RS (I) from March 20, 2006 01-8/4-134a «On the implementation section of the national project «Health» for examination of newborn babies for hereditary diseases»; The order of the state Autonomous institution of Sakha (Yakutia) «Republican hospital №1-national center of medicine» («RHN№1-NCM») of 31 August 2006 №01-0108/91 «About rendering of medical aid to children with cystic fibrosis, adrenogenital syndrome, galactosemia, phenylketonuria and congenital hypothyroidism identified by neonatal screening» [4]. Screening for CH is based on the determination of TSH levels in whole capillary blood spot on filter paper by the method of immunofluorescence. As the upper allowable limit for infants 3-4 days of lifetaken TSH level of 20 Miu/L. In the level of TSH more than 20 Miu/l is retestedfrom the same spot of capillary blood. In case of positive result, the child is sent to an endocrinologist. At very high TSH result is reported to the pediatrician at the place of residence of the child and immediately is assigned to the substitution therapy with levothyroxine.

The data on neonatal screening for the period 1996-2016.is provided by the laboratory Medical genetic center (MHC) Perinatal center «of RBN№1-NCM». Information on patients with CH were obtained from specialists endocrinology Department of the Pediatric center, «RBN№1-NCM». A retrospective study was carried out on stationary cards of children diagnosed with congenital hypothyroidism. Information on patients is taken from the register of patients of endocrinology Department (form 001).

THE RESULTS AND DISCUSSION

In RS (Y) within 1996-2016 on screening were examined 259587 newborns on CH, 53 children were identified with CH, the coverage was 88.6%. The frequency of CH was 1:4898. Newborn screening for mass screening in the RS (YA) on CH can be divided into two periods: from 1996 to 2005 and 2006 to 2016, i.e. the periods before and after the implementation of the PNP «Health». In the period from 1996-2005 were examined 101530 newborns, among which were identified 24 children with CH, coverage of screening amounted to 73.7%. The frequency of CH during this period was 1:4230. From 2006-2016 158057 newborns were examined, among them there were identified 29 children with CH, the coverage amounted to 99%. The frequency of CH was 1:5450 (table. 1). Thus, the prevalence of CH in the Republic of Sakha (Yakutia) is lower than in the Russian Federation – 1 in 3950 and its regions: Urals FD 1:2600, Central, northwestern, Volga, southern and Siberian Federal district varies from 1:4000 up to 1:4800 [1].

According to the data of neonatal screening peak enhance of the detection of CHwas in 2006 and 2016. In 2006 6954 newborn past research on CH, the diagnosis was confirmed in 4 amounting 1:1739. In 2016, the frequency of CH was 1:3846. In 2010-2011, the detection rate was the lowest and amounted to 1 person per year with a frequency of 1:15877.

Over 20 years of neonatal screening in the Republic of Sakha (Yakutia) were identified 53 children with CH. Among children with CH: 11 boys (20,7%), 42 girls (79.3 per cent), the ratio of semi – 1:3,8, ie predominantly affected girls, which corresponds to literature data. Place of residence: urban – 24 (45,2%) rural 29 (54,8%) children. Nationality: 31 (58.4 per cent) the child of the Yakut nationality, 15 (28,3%) of Russian nationality, 7 (13,2%) children with other nationalities.

According to the ultrasound in almost all patients with CHwas revealed hypoplasia of the thyroid gland with diffuse changes. The level of TSH on neonatal screening in average amounted184,45±17,2 mkme/ml (limits of oscillation from 88.79 per to 369,16),is retest 300,5±33,2 mkme/ml (limits of oscillation from 113,94 to 654,9). TSH levels at initial hospitalization – 194,2 ± 94,2 mkme/ml (limits varying from 14.1 to 1034 mkme/ml).

All patients with CH received replacement therapy with levothyroxine since set diagnosis in the individual dosage depending on the age (from 15 up to 150 mg per day). Delayed psychomotor development was observed in 9 (16,9%) patients, in 5 of them (9,4 %) was revaled delayed psycho-speech development. Mental retardation (mental retardation) diagnosed in two children (3.7 percent). Both were baby girls, 1992 and 1998 Children with mental retardation, children who were not included in the program of mass screening, and their treatment started after 1 year. Patients with a diagnosis of CH had the following concomitant diagnoses: residual encephalopathy (DRE) – 18 (33,9%), iron deficiency anemia – 2 (4,5%), small anomalies of the heart (patent foramen ovale) – 3 (5,6%), CHD (ASD) – 1 (1,8%), CHD (VSD) – 1 (1,8%), obese – 1 (1,8%), umbilical hernia – 1 (1,8%), hemangioma – 1 (1,8%), nevus – 1 (1,8%).

CONCLUSIONS

Organization of neonatal screening for congenital hypothyroidism in the Republic

Screening of newborns for mass screening in the RS (Y) for 1996 – 2016

Years	The number of people born in the RS (Y)	Surveyed: VG	Coverage	Revealed
1996-2005	137684	101530	73,7	24
2006	13623	6954	51	4
2007	15152	14931	98,5	3
2008	15254	11054	72,5	2
2009	15783	11196	71	3
2010	15877	15662	99	1
2011	16173	16092	99,5	1
2012	16922	16832	99,5	3
2013	16611	16546	99,6	3
2014	16964	16946	99,8	3
2015	16469	16459	99,9	2

of Sakha (Yakutia) allowed achieving a high percentage of newborn screening, reducing time of inspection and early replacement therapy, prevention of disability of patients. At the beginning of screening for CH in the Republic of Sakha (Yakutia) attended only 15 of all districts, at this time, involved all the municipalities of the Republic. Coverage of neonatal screening from 42% in the first years of its introduction has increased up to 99.6%. In the period from 1996 to 2016, the frequency of CH was 1:4898, which is comparable to the literature data.

REFERENCES:

1. Vadina T.A. Vrozhdennyj gipotireoz: jepidemilogija, struktura i social'naja adaptacija: avtoref. dis. kand. med. nauk [Congenital hypothyroidism: epidemilogy, structure and social adaptation: author. diss. kand. med. sciences]. Moscow, 2011, 20 p.
2. Peterkova V.A. Vrozhdennyj gipotireoz u detej: neonatal'nyj skrining, diagnostika i lechenie [Congenital hypothyroidism in children: neonatal screening, diagnosis and treatment]. Moscow, 2006, 28 p.
3. Peterkova V. A. Vrozhdennyj gipotireoz [Congenital hypothyroidism] Lechashhij vrach [Attending physician]. Moscow, 2004, № 6, P. 5-7.
4. Suhomjasova A. L. Realizacija prioritetnogo nacional'nogo proekta «Zdorov'e»: massovoe obsledovanie novorozhdennyh na nasledstvennye bolezni obmena v Respublike Saha (Jakutija) [the Implementation of priority national project «Health»: mass newborn screening for hereditary metabolic diseases in the Republic of Sakha (Yakutia)] Jakutskij medicinskij zhurnal [Yakut medical journal]. Yakutsk, 2009, № 2, P. 69-72.

Information about authors:

1. Elena Filippovna Argunova, Associate Professor of the Department of Pediatrics and Pediatric Surgery MINEFU, eargunova@mail.ru, Yakutsk, Republic Sakha (Yakutia), Russia
2. Sargylana Nikolaevna Alekseeva, Associate Professor of the Department of Pediatrics and Pediatric Surgery MI NEFU, sargylanao@mail.ru, Yakutsk, Republic Sakha (Yakutia), Russia
3. Aitalina Lukichna Sukhomyasova, Head of the Educational and Scientific Laboratory «Genomic Medicine» NEFU, Head of the Medical Genetic Center SAI RS(Y) «RH №1-National center of medicine», AitalinaS@yandex.ru, Yakutsk, Republic Sakha (Yakutia), Russia
4. Philip Filippovich Vasilyev, Scientific employee of the educational-scientific laboratory «Genomic medicine», NEFU, vasilyevmd@gmail.com, Yakutsk, Republic Sakha (Yakutia), Russia
5. Margarita Egorovna Nikiforova, Head of the Endocrinology Department of the Pediatric Center SAI RS (Y) «RH №1- National center of medicine», N_kynnei@mail.ru, Yakutsk, Republic Sakha (Yakutia), Russia
6. Danilova Galina Ivanovna, Candidate of Medical Sciences, Chief non-staff pediatric endocrinologist Mof HR S (Y), Child endocrinologist of the highest qualification category, dan_galina@mail.ru, Yakutsk, Republic Sakha (Yakutia), Russia
7. Zhelobtsova Ayana Fedotovna, A pediatric endocrinologist of the first qualification category, aynazhe@gmail.ru, Yakutsk, Republic Sakha (Yakutia), Russia
8. Pirnazarova Shahzoda Bahtijorovna, Student medical school M.K. Ammosov NEFU, vshahv2112@yandex.ru, Yakutsk, Republic Sakha (Yakutia), Russia.

ACTUAL TOPIC

Ivanova O. N., Golderova A. S.

POLLINOSIS IN CHILDREN OF THE SAKHA REPUBLIC (YAKUTIA)

ABSTRACT

The article is devoted to an actual problem of modern pediatrics - the incidence of pollinosis in children living in the Far North. The aim of the study was to investigate the etiological factors of hay fever in the child population of the Sakha Republic (Yakutia) according to allergen testing of school children suffering from hay fever - 100 people at the National center of Medicine, Yakutsk. Considering the obtained data on the importance of sensitization among children and adolescents of Sakha (Yakutia) Republic it is necessary to introduce the calendar dusting of plants in the work of allergists and pediatricians.

Keywords: incidence, allergen testing, allergy, immunoglobulins, immunity, sensitization, prevention.

Hay fever – a reaction of an inflammatory character from the mucous membranes or skin as a result of increased sensitivity of the child's body to the pollen. The disease has a pronounced seasonality from April to September.

Difficulties in determining the accurate number of creating geographical differences in the pollen composition, a wrong interpretation of symptoms by patients or doctor error in diagnosis [1,2,7].Hay fever is a common Allergy in children. Malta pollinosis identified U14,7% of children aged 5 to 8 years [2]. In Europe and the USA by hay fever suffers 20% of adolescents. From 1991 to 2000, the incidence of hay fever has increased more than 2 times [3]. In the Republic of Belarus, according to official statistics, allergic diseases affect 10 to 15% of the population. Annually increase the incidence of allergic rhinitis: in 2002 of 102.3 cases per 100 thousand population; in 2003 112, 1 [3, 4, 5, 6]. However, health statistics, based on the appealability to curative preventive institutions do not correspond to true values of the incidence and prevalence of pollinosis among the population.

In the Republic Sakha (Yakutia) a study of etiological factors of pollinosis among the pediatric population has not been conducted, so this study is of scientific interest [1, 2, 3, 8, 9].

The purpose of the study: to study the etiological factors of hay fever (AR) in children population of the Republic of Sakha (Yakutia).

MATERIALS AND METHODS

The authors present the analysis of allergen testing of schoolchildren, patients with pollinosis living in the North of the Republic and 100 people at the National center of medicine of Yakutsk in the age from 4 years to 18 years. Of the 100 surveyed children 50% were girls and 50% boys. 32% of the surveyed children showed atopic dermatitis. We conducted allergen testing to value all children of the studied group. Allergic examination was conducted by prick test method to

standard pollen allergens (early-flowering - birch, alder, hazel, late-flowering-poplar, weed grasses - timofeevka, meadow grass, fire, sagebrush, reygrass, dandelion, wheat grass) cereals (rye, oat, fescue). Severity of skin reactions was assessed (+_ ,++, --).

Statistical calculations are performed on the basis of applied programs «SAS» and «SPSS». Comparison of mean values was assessed by univariate dispersion analysis using T-student criterion to assess the equality of average F-Fisher criterion to assess the equality of variance. The relationship between parameters was assessed using the coefficients of the linear and rank correlation.

RESULTS OF THE STUDY:

Pupils showed a high sensitization to the pollen of plants, of which mugwort, birch and Prairie grass.

In children with pollinosis highest percentage of sensitization was observed on birch pollen (40%), then wormwood (32,1%) . Prevention of exacerbations of hay fever needed a hypoallergenic diet given cross-sensitization in patients with pollinosis. Below is a calendar dusting of plants of the Republic of Sakha (Yakutia), developed by the Ivanova O. N., Kardashevskiya V. E. in 2006 (Table 2).

Thus, in the period of dusting birch (May, June) the patient with a reaction to birch should not eat any stone fruit, honey, carrots. Patients with sensitization to Prairie grasses (fescue) should not be included in the diet of cereals in the period dusting of grass (July). Students with sensitization to weeds do not use seeds, vegetable oil, honey and halva in the period dustings of quinoa and sage (July, August). In the Republic of Sakha (Yakutia) range pollonaruwa plants and less time dusting in short, because of climate and geographical features of the far North.

Given the regional peculiarities of the Republic of Sakha (Yakutia) features of the spectrum pollonaruwa herbs necessary to implement regional programs taking into account the calendar dusting of plants of RS (I) for a dispensary observation of patients with pollinosis.

CONCLUSIONS:

1. According to the analysis of allergies there of the students are above sensitization to the pollen of plants, of which mugwort (32,1%), birch (49.8%) and meadow grass (20,5%).

Table 1

The frequency of sensitization to pollen allergens from children and adolescents with pollen allergy (according to skin tests)

Plant	% positive reactions
Alder	10,2
Ambrosia	21,1
Quinoa	13,8
Poplar	10,9
Wormwood	32,1
Birch	49,8
Fescue	20,5
Ryegrass	16,9
Dandelion	25,1
Wheatgrass	28,1
Timothy	10,1
Bluegrass	10,6
Oats	8,2
Rye	7,9

Table 2

The calendar dusting of plants of the Republic of Sakha (Yakutia)

Plants	Flowering time	
	the beginning	the end
Trees *Birch* *Alder* *Iva* *Pine* *Poplar (only in the South-Western districts)*	20–25 may 1–2 June 20–25 may 20–25 June 10–15 June	5–10 May 10–20 June 2–9 June 10 July 20-30 June
Grass *Timothy* *Foxtail* *Bluegrass* *Fescue* *Wheatgrass* *Dandelion*	10-15 July C 15 July July July Beginning of July 20 мая	10-15 August To late 15 August August August the end of July 1–25 June
Weeds *Wormwood* *Quinoa*	July July	August August

Medicinskaya kniga [Medical book], 2004, p. 158.

2. Korotkov N.V. Rykova N.E. Etiologiya pollinozov u detej Central'noj Sibiri [The etiology of hay fever in children of Central Siberia] Aktual'nye problem allergii v pediatrii. Ch. 1. [Problems of allergy in pediatrics. Part 1]. Kobuleti, 1987, 50 p.

3. Koryukina I.P. Kliniko-patogeneticheskie osobennosti ostryhstenozov verhnih dyhatel'nyh putej u detej (klinika, diagnostika, lechenie): Avtoref. dis. dokt. med. nauk [Clinical and pathogenetic features of acute stenosis of the upper respiratory tract in children (clinical picture, diagnosis, treatment): author. dis. doctor. med. sciences]. Moscow, 1992, 35 p.

4. Ksenzova L.D. Balabolkin I.I., Belyaeva E.V. Primenenie parenteral'noji sublingval'noj allergen specificheskoj immunoterapii u detej i podrostkov, bol'nyh pollinozom [The use of parenteral and sublingual allergen specific immunotherapy in children and adolescents with pollinosis] Voprosy sovremennoj pediatrii [Issues of modern pediatrics]. Moscow, 2003, V. 2, App. 2, p.55.

5. Kuvshinova E.D. Ksenzova L.D. Ryleeva I.V. Effektivnost' sublingval'noj allergenspecificheskoj immunoterapii detej, stradayushchih pollinozami [The efficacy of sublingual allergen-specific immunotherapy in children with pollinosis] Allergol. iimmunol. [Allergol. and immunol.]. Moscow, 2001, V. 2, p. 171–175.

6. Lysikova I.V. Rasprostranyonnost' allergicheskih zabolevanij u detej po rezul'tatam mul'ticentrovyh issledovanij v ramkah mezhdunarodnoj programmy ISAAC: Avtoref. dis. kand. med. nauk [The prevalence of allergic diseases in children according to the results of multicentre studies in the framework of the international program ISAAC: author. dis. kand. med. sciences]. Moscow, 1999, 20 p.

7. Molokova T.M. Kliniko-immunologicheskie osobennosti pollinoza u detej: Avtoref. dis. kand. med. nauk [Clinical and immunological features of pollinosis in children: author. dis. kand. med. sciences]. Tomsk, 1997, 18 p.

8. Ryzhova E.G. Prisyazhnaya M.M. Kliniko-immunologicheskie osobennosti pollinozov u detej v Primorskom krae [Clinical and immunological features of pollinosis in children in Primorsky region] Pul'monologicheskaya pomoshch' detyam: Sb. nauch. tr. [Medical assistance for children: Collectoin of scientific papers]. Vladivostok: Izdatel'stvo Dal'nevostochnogo un-ta [Publishing house of Far Eastern University], 1990, p. 27–31.

9. Sadovnichaya L.T. Ambrozij nyj pollinoz u detej: Avtoref.dis. dokt. med. nauk [Ambrosial hay fever in children: author.dis. doctor. med. sciences]. Moscow, 2002, 48 p.

Information about the authors:

Ivanova Olga Nikolaevna - doctor of medical sciences, Professor, Department of Pediatrics and pediatric surgery of the Medical Institute NEFU. Tel 89142906125 olgadoctor@list.ru;

Golderova Ajjtalina Semenovna - doctor of medical sciences, chief researcher of the YSC of complex medical problems.

HEALTHY LIFESTYLE. DISEASE PREVENTION

Rad Y.G., Douglas N.I., Garmaeva D.K., Pavlova T.Y.

PROPHYLAXIS OF CERVICAL CANCER IN SAKHA (YAKUTIA) REPUBLIC ON THE BASIS OF A SURVEY OF WOMEN IN THE "WHITE ROSE-SAKHA" MEDICAL DIAGNOSTIC CENTER

ABSTRACT

Currently cervical cancer holds one of the leading positions in reproductive organs oncology. Unfortunately, increasing number of women of young and very young age is developing the disease. Screening diagnostics is now being introduced for the purpose of early diagnosis of this pathology. It involves examining the cervix on the mirrors with advanced colposcopy, examining the cervical smears and the cervical canal for oncocytology and HPV (human papillomavirus) infection. Together, this makes it possible to diagnose and timely treat a disease as serious as cervical cancer at an early stage.

Keywords: cervical cancer, HPV, oncocytology, screening, diagnosis.

INTRODUCTION

Cervical cancer (CC) has the second highest prevalence of cancer of the female reproductive system in the world and the leading cause of female cancer mortality in developing countries.

According to WHO (World Health Organization), around 500,000 cases of cervical cancer are recorded each year, every second of which ends in the patient's death within the first year after diagnosis. The number of deaths from cervical cancer in 2015 increased to 320 thousand, and in 2030 it is expected to increase to 435 thousand [1]. In economically developed countries, the average patient is growing younger – the incidence in women of reproductive age has doubled in the last 10-15 years. In the Russian Federation, the incidence of cervical cancer in recent years is 10.8 per 100 000 women, and the mortality rate is 5 per every 100 000. Early diagnosis of precancer provides the possibility of primary and secondary prevention. Primary prevention is a system of measures to identify risk factors for cervical cancer and their elimination. This is primarily the promotion of healthy lifestyles, increasing education for the population, combating smoking, using barrier methods of contraception, preventing and identifying the risk factors for the spread of papillomavirus infection (PID) and other sexually transmitted infections (STIs), developing and implementing preventive vaccines. Secondary prevention is cervical screening, i.e. A survey of all women to identify and timely treatment of precancerous changes in cervical cancer. The screening program for cervical cancer detection must meet two basic requirements: to be effective and inexpensive in cost. The screening test should be simple, non-invasive, sensitive and specific, safe, inexpensive and affordable.

In recent years, it has been established that an important role in the development of precancerous conditions belongs to infectious agents, among which HPV takes the first place. The International Agency for Research on Cancer (IARS) officially declared HPV 16 and 18 types of carcinogenic factors [1].

In the diagnosis of precancerous diseases and cervical cancer, various methods are used, but the clinico-visual method, the use of colposcopy, molecular biological methods (polymerase chain reaction-PCR or DIGENE test), and one of the morphological methods: cytological examination of smears and histological Investigations of the sight taken biopsy of the cervix [2].

Modern management of patients with cervical pathology for one category of patients requires adequate monitoring, for another category of patients - a targeted biopsy under the control of colposcopy, ablation (destruction) of the epithelium, or (which should often be used in precancerous processes) cervical excision. The decision should be made by an experienced physician who is able to assess the benefit and risk in accordance with the clinical situation [2].

Objective: To analyze the uptake of cervical screening as a method of early diagnosis of precancerous lesions and early forms of cervical cancer.

MATERIALS AND METHODS

Cards of outpatients with the results of screening diagnostics of patients who were examined at the "White Rose-Sakha" MDC for 2016-2017, in the amount of 5733.

RESULTS OF THE STUDY

The "White Rose-Sakha" Medical Diagnostic Center started its work in September 2016 and conducts all the main methods of screening for cervical diseases, namely: advanced colposcopy, examination of cervical smears and cervical canal for oncocytology, examination for HPV types 16-18, which are assuredly effective, affordable, and non-invasive diagnostic methods, together providing a high chance of timely early diagnosis of cervical cancer.

In 6 months, during the period from November to April 2017, 5733 women aged 18 to 85 were examined at the "White Rose-Sakha" MDC.

All women in 99.9% of cases (except Virgo) underwent an oncocylotogy examination with a pap test. Diagnosis was carried out by staining the glasses with Pappanikolaou (PAP) and the interpretation was completed using the same method, PAP1-PAP5.

To date, the cytological exams using pap smears is not entirely informative, the efficacy of the cytological smear ranges from 46-98% [1]. Today only liquid oncocytology is a highly informative method for diagnosing cervical pathology, the accuracy of which is 98% [1], but unfortunately in our Republic this method of research is still not available.

The diagnosis of cervical dysplasia of various severity is delivered to 115 patients and is 2% of the total number of women examined. 106 patients had dysplasia of 1-2 degrees, which is 1.9%. 9 women had grade 3 dysplasia, which is considered a severe cervical dysplasia and is 0.15% of the total number of women surveyed and 7.8% of all cervical dysplasias in the study group; 3 women had PAP4 oncocytology, regarded as carcinoma in situ.

Cervical cancer clinically diagnosed and cytologically confirmed was detected in 3 cases and amounted to 0.05% and 2.6% of the total number of subjects and the number of dysplasias, respectively.

In the conditions of screening diagnostics at the "White Rose-Sakha" we also take material from the cervix for HPV types 16-18. These oncomarkers are the most oncogenic, but other strains of the HPV virus can cause malignant

changes in the cervix, especially in conjunction with STDs. Therefore, women with suspected cervical dysplasia are recommended to undergo an HPV test, where the study of HPV strains is significantly expanded, which is important for more accurate prognosis.

Taking into account the fact that at the MDC we can study only HPV types 16 and 18, it is impossible to give an unambiguous answer about the relationship between dysplasia and the carrier state of the virus according to our results. But, all women with PAP4 and PAP5 have HPV types 16 and 18. That stand to confirm the viral etiology of this disease.

Clinical case: Patient I., 49 years old, was examined at the MDC, where a complete screening examination of the cervix was carried out. Colposcopic picture: Adequate colposcopic picture. Atypical zone of transformation due to acetobelic epithelium with different caliber mosaic. The site of atypia is located in the epithelium interface at 9 o'clock in the first zone, 0.7 cm in size. HPV 16 (+), HPV 18 (-). PAP3 oncocytology dysplasia of the 2nd degree. Preliminary diagnosis: 2nd stage cervical dysplasia. Carrier of HPV type 16. Given the age of the patient is 49, 2nd stage HPV16 (+) dysplasia, and atypical colposcopic picture, to clarify the diagnosis and treatment of the cervix the patient was sent to undergo a diathermic excision after previously conducted remediation. Result of histological examination: dermoid cancer. The depth of infestation is 3 mm.

On the basis of which the final diagnosis is: 1st stage dermoid cancer of the cervix. 1 clinical group. The patient was transferred to YROC (Yakutsk Republican Oncology Center) for specialized treatment.

In our clinical example, there was no correlation between cytological and histological diagnoses. But thanks to the well-timed management of the patient, she was promptly diagnosed and treated accordingly.

CONCLUSION

The wide introduction of screening programs should significantly reduce the incidence and mortality from cervical cancer thanks to early diagnosis and timely treatment of the precancerous conditions of the cervix. In detection and treatment of inflammatory and precancerous cervical conditions such as dysplasia are one of the main cervical cancer prevention methods.

But we must not forget that oncocytology is a screening method. Therefore, all women who are diagnosed with cervical dysplasia with the presence of an abnormal colposcopic pattern and the presence of an HPV infection, should be on strict medical check-up at a gynecologist, which implies mandatory dynamic observation, as well as: control of oncology of the cervix and cervical canal once every 3-6-9 months. The use of cervical biopsy / diathermoxcis with cervical canal scrapings should necessarily accompany a cytologic examination in the case of PAP3, especially in women over 30 years of age, and be a method of not only detailing the diagnosis but also cervical treatment. All 3rd stage dysplasia must be treated by a gynecologist oncologist.

Timely screening diagnosis and treatment of cervical disease opens up prospects for women globally.

REFERENCES

1. Rogovskaya I.S., Liovaya E.V. Shejka matki, vlagalishhe, vul'va. Fiziologija, patologija, kol'poskopija, jesteticheskaja korrekcija [Cervix uteri, vagina, vulva. Physiology, pathology, colposcopy, aesthetic correction]. Status Praesens [Publisher: Status Praesens], 2014, p. 831

2. Rogovskaya I.S. Papillomavirusnaja infekcija u zhenshhin i patologija shejki matki 2-e izdanie ispravlennoe i dopolnennoe. V pomoshh' praktikujushhemu vrachu [Papillomavirus infection in women and pathology of the cervix uteri", 2nd edition, corrected and supplemented. Practicing doctor guidance note]. Moscow, Izdatel'stvo [Publisher: GEOTAR-Media], 2014, p. 192.

The authors:

Yakutsk, Republic Sakha (Yakutia), Russia:

Radj Yana Gennadievna – Candidate of Medical Sciences, Associate Professor of the Department of Obstetrics, Gynecology, Faculty of Postgraduate Training of Doctors, Medical Institute, M.K. Ammosov North-Eastern Federal University, iana.rad@yandex.ru, tel. +79248735555

Douglas Natalia Ivanovna – Head of the Department of Obstetrics and Gynecology, Faculty of Postgraduate Training of Doctors, Medical Institute, M.K. Ammosov North-Eastern Federal University, nduglas@yandex.ru , tel. +79246626722

Garmaeva Darima Kyshchetovna – Professor of the Department of Normal and Pathological Anatomy, Operative Surgery with Topographic Anatomy and Forensic Medicine of the Medical Institute, M.K. Ammosov North-Eastern Federal University, dari66@ mail.ru, tel. +79142349680

Pavlova Tatyana Yurievna – Candidate of Medical Sciences, Associate Professor of the Department of Obstetrics and Gynecology, Faculty of Postgraduate Training of Doctors, Medical Institute, M.K. Ammosov North-Eastern Federal University, tatyanaupavl@mail.ru, tel. +79248727164

SCIENTIFIC REVIEWS AND LECTURES

S.S. SEPTSOVA, A.E. EFIMOV, H.A. KURTANOV

ROLE OF POLYMORPHISM OF I148M GENE PNPLA3 IN THE PROGRESSION OF LIVER DISEASES IN PATIENTS WITH CHRONIC VIRAL HEPATITIS B, C

Abstract

The article presents an overview of the relationship between I148M, PNPLA3, and fibrosis, liver cancer in patients with chronic hepatitis B and C.

Key words: I148M, PNPLA3, adiponutrin, chronic viral hepatitis B, chronic viral hepatitis C, steatosis, fibrosis, HCC, CHC, CHB, CHD

Introduction

Currently, more than 350 million people are chronically infected with the hepatitis B virus and about 1 million people die each year from the effects of hepatitis B and approximately 130-170 million worldwide are infected with the hepatitis C virus [4].

In the Russian Federation, viral hepatitis B and C are widespread, the total number of patients with chronic viral hepatitis B (HBV) and HBsAg carriers is about 5 million, the number of patients with chronic hepatitis C (HCV) and carriers of hepatitis C virus is at least 2 million people [4].

The Republic of Sakha (Yakutia) is considered hyperendemic region of the Russian Federation for the prevalence of viral hepatitis B, C and D [4]. The level of registration of chronic viral hepatitis does not tend to decrease, the incidence rate in 2011 was 1502.5 per 100 thousand population and is, according to the Reference Center for the Supervision of Viral Hepatitis, the highest in the Russian Federation. According to the register «Chronic viral hepatitis in the Republic of Sakha (Yakutia)» for 2016, 14 391 people are registered, (excluding carriers of hepatitis B virus - 570 people), of them with chronic hepatitis B - 6404, C - 6224, D - 889, mixed - 821, unspecified etiology – 57, liver cirrhosis - 544 patients, 59 patients with primary liver cancer.

The first genetic studies in the pathology of liver disease

It is believed that the additional factors of liver damage in CHB and CHC are pathological conditions such as abdominal obesity, hypertriglyceridemia, insulin resistance, metabolic syndrome leading to steatosis of the liver and its progression to steatohepatitis followed by the development of fibrosis and then cirrhosis.

It is established that the fat content in the liver is determined not only by the way of life and the presence of risk factors, but also associated with genetic factors.

The first studies of genetic polymorphisms in the progression of liver diseases were carried out in 2008 by Romeo S. et al. [15] who found that polymorphism I148M PNPLA3 gene associated with steatosis in patients with non-alcoholic fatty liver disease (NAFLD). After that, a large number of studies have been conducted on the relationship between I148M polymorphism and liver disease [10].

PNPLA3 gene function

It is believed that the PNPLA3 gene located on the long arm of chromosome 22q13.31 is expressed in the membranes of hepatocytes and is responsible for intrahepatic lipid metabolism by coding the synthesis of adiponutrin, a protein regulating the activity of triacylglycerol lipase in adipocytes [24].

I148M polymorphism consists in replacing the sequence from cytosine to guanine, which in turn leads to the replacement of the amino acid isoleucine by methionine in residue 148, which leads to disruption of the mechanism of lipid metabolism in the liver.

The hypotheses of the I148M polymorphism impact:

1. Mutant adiponutrin reduces the activity of triacylglycerol hydrolases, thereby reducing the hydrolysis of triglycerides and increasing their concentration in liver cells [21];

2. Accumulation of free fatty acids in hepatocytes occurs, which leads to the development of oxidative stress, and as a result, a direct cytopathic effect on liver cells takes place [16];

3. An alternative hypothesis is that the substitution of amino acids entails an increase in the activity of the acyltransferase, leading to an increase in the synthesis of triglycerides [5];

4. Adiponutrin affects the differentiation of adipocytes (fat cells) through activation of the PPAR-γ receptor [16].

Influence of I148M polymorphism on the progression of CHC

Since the I148M polymorphism was recognized as a genetic determinant of the development of hepatic steatosis in patients with NAFLD and alcoholic liver disease, it was suggested that this polymorphism is also associated with steatosis and progression of fibrosis in patients with CHC [14].

The prevalence of liver steatosis in CHC patients ranges from 35 to 81% and is associated with progression of liver fibrosis, inefficiency of antiviral therapy, and the development of HCC [10, 1]. Possible risk factors for the development of steatosis in CHC patients include obesity, hyperlipidemia and insulin resistance, as well as direct virus cytopathic effect [29]. In sum, these risk factors, combined with predisposing factors of the body itself, lead to the emergence of steatosis in CHC patients. Also, the degree of development of steatosis depends on the genotype of the virus, in case of chronic HCV infection caused by virus genotype 3a, steatosis of the liver occurs significantly more often than with the 1b genotype of HCV (almost 2-fold). [2]

In 2011, Valenti et al. first reported a possible association between I148M polymorphism and CHC. In the study of two independent groups of patients with CHC, it was found that I148M is associated with the development of not only steatohepatitis, but also liver fibrosis in these patients [19].

Influence of polymorphism I148M on the progression of CHB

The prevalence of liver steatosis in CHB is (according to the data of different authors) from 27 to 51% [11], and its role in the progression of fibrosis and cirrhosis in these patients has not been fully determined [9]. Yet some authors argue that the steatosis of the liver affects the development of fibrosis and the progression of CHB [17].

But whether genetic factors contribute to the development of steatosis and fibrosis in CHB patients is not yet known, although there are reports that I148M polymorphism is an independent predictor of severe steatosis in patients with CHB [20]. Other authors have not reported this genetic association between I148M polymorphism and steatosis in patients with CHB [12]. Data on the effect of I148M polymorphism on the course and progression of CHD are not available at this time. Probable route of influence of polymorphism I148M on the progression of CHC and CHB in combination with various risk factors is presented in Figure 1.

Polymorphism I148M and allele G

It was found that I148M recessive G allele is associated with the highest risk of development of steatosis and severe liver fibrosis and in patients with NAFLD, including patients with CHC and CHB [24, 26, 18].

The effect of I148M polymorphism on a sustained virological response (SVR)

In an early study, Valenti et al. reported that patients with CHC combined with fibrosis (virus genotype 1 and 4) carrying I148M polymorphism less often achieved SVR [19], while others did not observe an association between I148M polymorphism and SVR level [6]. It is possible that the cause of low SVR in antiviral therapy is steatosis, mediated by metabolic rather than genetic factors [6]. However, the effect of I148M polymorphism on the SVR level is still controversial and should be studied in future researches.

The influence of polymorphism I148M on the development and progression of hepatocellular carcinoma (HCC)

In his first study, Valenti et al. demonstrated the relationship of polymorphism I148M to the development of liver cancer [19], which was confirmed later [25], also confirmed by other authors [28, 8]. These reports indicate the important role of I148M polymorphism in the development and progression of HCC in various liver diseases, including patients with CHB and HCV.

Thus, the carriers of polymorphism I148M have a predisposition to HCC, moreover HCC does not depend on the stage of steatosis and cirrhosis, developing in the early stages of liver disease, including CHC, and the polymorphism I148M affects the rapid progression of cancer and low survival of patients with HCC [25].

Effect of I148M polymorphism on liver transplantation efficiency

CHC is the most common cause of liver transplantation in Western countries [7].

A number of studies have demonstrated that the presence of I148M polymorphism in donors and recipients affects the results of liver transplantation in patients with CHC, in particular the frequent development of post-transplant metabolic disorders, diabetes mellitus, steatosis and liver fibrosis, liver transplantation, high incidence of lethal cases [13, 22].

I148M polymorphism and ethnic predisposition

The frequency of the allele G of polymorphism I148M varies depending on ethnicity, with the highest prevalence in early studies among Hispanics (49%), and the approximate frequency of homozygotes is 25%. It is reported that the frequency of homozygotes 148M among the population of Italy is approximately 10% (8-14%). In contrast, the frequency of homozygotes in Germany is lower (5.5%) [27]. Among the Asian population, the frequency of polymorphism 148M, due to the lack of qualitative research at the moment, is not known [26].

I148M polymorphism and other risk factors

It is believed that the presence of I148M polymorphism in combination with risk factors, such as abdominal obesity, insulin resistance, hypertriglyceridemia, impaired carbohydrate metabolism, alcohol consumption leads to faster progression of steatosis, fibrosis and cirrhosis [23].

Mackawy, A. M., et al. [18] showed that I148M polymorphism is not associated with the presence of risk factors such as age, gender, BMI, total cholesterol and triglyceride levels, but found significant association with alanine aminotransferase (ALT), aspartate aminotransferase (AST), gamma-glutamyl transferase (GGT) level and viral load in patients with CHC.

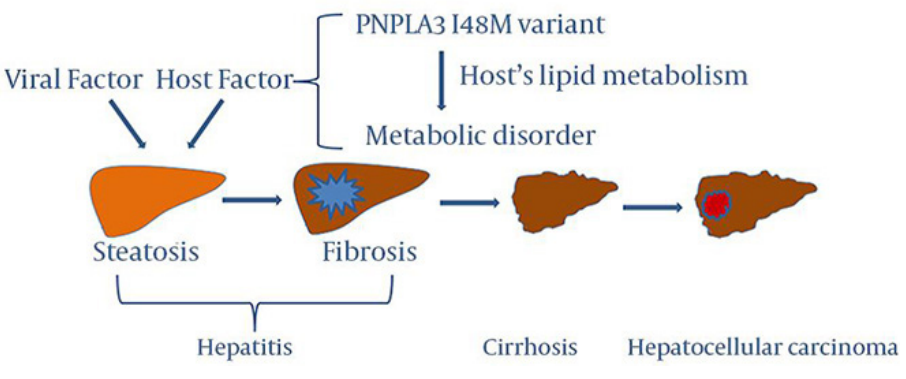


Fig. 1. Probable route of influence of polymorphism I148M on the progression of CHC and CHB in combination with various risk factors.

Conclusion

In conclusion, the results of the studies indicate a significant association of I148M polymorphism with the severity and progression of steatosis, fibrosis and HCC in patients with CHB and CHC, the outcome of liver transplantation depends on the presence of I148M polymorphism in both donors and recipients. It was found that the frequency of polymorphism I148M varies depending on ethnicity. Also, I148M polymorphism was associated with ALT, AST, GGT level in peripheral blood, however, association I148M polymorphism with age, sex, BMI, total cholesterol and triglyceride levels were not observed.

REFERENCES:

1. Abdurachmanov D.T. Steatoz pecheni pri khronicheskom gepatite C: mekhanizmy razvitiya i rol' v progressirovanii porazheniy pecheni [Hepatic steatosis and chronic hepatitis C-infection: route of development and role in the progressive of liver disease]. Klinicheskaya gepatologiya [Clinical Hepatology], 2005, no. 1, pp. 25-28.

2. Tselicovsky A.V. Vliyanie steatoza pecheni na effektivnost' kombinirovannoi protivovirusnoi terapii khronicheskogo gepatita C [Elektronnyi resurs] [Impact of liver steatosis on the effectiveness of combined antiviral therapy of chronic hepatitis C]. Sovremennyye problemy nauki i obrazovaniya [Modern problems of science and education], 2012, no. 6, URL: http://science-education.ru/ru/article/view?id=7387 (Date of extraction: 19.04.2017)

3. Zhdanov K.V. Lobzin Y.V. Virusnye gepatity [Viral hepatitis]. St. Petersburg, Folio, 2011, 304 p.

4. Sleptsova S.S. . Rakhmanova A.G. Rol' virusnykh gepatitov v razvitii pervichnogo raka pecheni v Yakutii [The role of viral hepatitis in the development of primary liver cancer in Yakutia].

Infektsionnye bolezni [Infectious diseases], 2015, no. 3, pp. 76-82.

5. Adiponutrin functions as a nutritionally regulated lysophosphatidic acid acyltransferase / M. Kumari [et al.] // Cell Metab. – 2012. - Vol. 12. - № 5. – P. 691–702.

6. Aghemo A. Understanding the role of PNPLA3 genetic vari¬ants in patients with chronic hepatitis C infection // Dig Dis Sci. – 2012. – Vol. 57. – № 8. - P. 1977–1979.

7. Akamatsu N. Liver transplantation and hepatitis C [Electronic resource] / N. Akamatsu, Y. Sugawara // Int J Hepatol. - 2012. – Vol. 2012. - URL: http://dx.doi.org/10.1155/2012/686135 (Date of extraction: 24.04.2017).

8. Association between PNPLA3 rs738409 polymorphism and hepatocellular carcinoma risk: an updated meta-analysis / L. Zhang [et al.] // Genes & Genomics. - 2016. - Vol. 38. - № 9. - P. 831–839.

9. Association of nonalcoholic fatty liver disease with insulin resistance / G. Marchesini [et al.] // Am. J. Med. - 1999. - Vol. 107. - P. 450–455.

10. Association of PNPLA3 I148M Variant With Chronic Viral Hepatitis, Autoimmune Liver Diseases and Outcomes of Liver Transplantation [Electronic resource] / N. Geng [et al.] // Hepatitis Monthly. – 2015. - Vol. 15. - № 4. - URL: http://hepatmon.com/?page=article&article_id=26459 (Date of extraction: 21.01.2017).

11. Brunt E.M. Nonalcoholic steatohepatitis: definition and pathology // Semin. Liver Dis. - 2001. - Vol. 21. - P. 3–16.

12. Correlation between patatin-like phospholipase domain-containing protein 3 gene polymorphisms and liver cirrhosis in a chinese han population with chronic hepatitis B [Electronic resource] / J. Tong [et al.] // Hepat Mon. – 2014. - Vol. 14. - № 8. - URL: http://hepatmon.com/?page=article&article_id=18943 (Date of extraction: 08.04.2017).

13. Donor PNPLA3 rs738409 genotype affects fibrosis progression in liver transplantation for hepatitis C / W. Dunn [et al.] // Hepatology. - 2014. - Vol. 59. - № 2. - P. 453-460.

14. Genetic polymorphisms of IL28B and PNPLA3 are predictive for HCV related rapid fibrosis progression and identify patients who require urgent antiviral treatment with new regimens / N. Tamaki [et al.] // PLoS ONE. - 2015. - Vol. 10. - № 9. - P. 1–12.

15. Genetic variation in PNPLA3 confers susceptibility to nonalcoholic fatty liver disease / S. Romeo [et al.] // Nat. Genet. - 2008. - Vol. 40. - P. 1461–1465.

16. Genetic variants regulating insulin receptor signalling are associated with the severity of liver damage in patients with non-alcoholic fatty liver disease / P. Dongiovanni, [et al.] // Gut. – 2010. – № 59. – P. 267–73.

17. Hepatic steatosis and insulin resistance are associated with severe fibrosis in patients with chronic hepatitis caused by HBV or HCV infection / S. Petta [et al.] // Liver Int. - 2011. - Vol. 31. - № 4. - P. 507-515.

18. Mackawy A. M. H. Patatin-like phospholipase domain containing-3 gene (PNPLA3) I148M polymorphism and liver damage in chronic hepatitis C Egyptian patients / A. M. H. Mackawy, M. E. H. Badawi, O. Megahed // Egyptian Journal of Medical Human Genetics. - 2015. - Vol. 16. - № 4. – P. 333-441.

19. Patatin-like phospholipase domain-containing 3 I148M polymorphism, steatosis, and liver damage in chronic hepatitis C / L. Valenti [et al.] // Hepatology. - 2011. - Vol. 53. - № 3. - P. 791–799.

20. Patatin-Like Phospholipase Domain-Containing 3 I148M Variant Is Associated with Liver Steatosis and Fat Distribution in Chronic Hepatitis B / R. Zampino [et al.] // Digestive Diseases and Sciences. - 2015. - Vol. 60. - № 10. - P. 3005–3010.

21. Patatin-like phospholipase domain-containing 3 (PNPLA3) I148M (rs738409) affects hepatic VLDL secretion in humans and in vitro / C. Pirazzi [et al.] // J. Hepatol. - 2012. - Vol. 57. - № 6. - P. 1276-1282.

22. Patatin-like phospholipase domain-containing protein 3 rs738409-G in recipients of liver transplants is a risk factor for graft steatosis / A. Finkenstedt [et al.] // Clin Gastroenterol Hepatol. – 2013. - Vol. 11. - № 12. – P. 1667–1672.

23. PNPLA 3 I148M genetic variant associates with insulin resistance and baseline viral load in HCV genotype 2 but not in genotype 3 infection / K. Rembeck [et al.] // BMC Med Genet. - 2012. - Vol. 13. - № 1. - P. 1.

24. PNPLA3 I148M polymorphism and progressive liver disease / P. Dongiovanni [et al.] // World Journal of Gastroenterology. – 2013. – Vol. 19. - № 41. - P. 6969-6978.

25. PNPLA3 I148M Polymorphism, Clinical Presentation, and Survival in Patients with Hepatocellular Carcinoma [Electronic resource] / L. Valenti [et al.] // PLoS ONE. - 2013. - Vol. 8. - № 10. - URL: http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0075982 (Date of extraction: 22.01.2017).

26. PNPLA3 rs738409 Polymorphism Associated with Hepatic Steatosis and Advanced Fibrosis in Patients with Chronic Hepatitis C Virus: A Meta-Analysis. / J.-H Fan [et al.] // Gut and Liver. – 2016. - Vol. 10. - № 3. – P. 456–63.

27. Rembeck K. Impact of IL28B, ITPA and PNPLA3 genetic variants on therapeutic outcome and progression of hepatitis C virus infection / K. Rembeck, M. Lagging // Pharmacogenomics. - 2015. - Vol. 16. - № 10. - P. 1179-1188.

28. Significant Association Between Adiponutrin and Hepatocellular Carcinoma Risk [Electronic resource] / H.-G. Li [et al.] // Medicine. – 2015. - Vol. 94. - № 45. - URL: http://journals.lww.com/md-journal/page/results.aspx?txtkeywords=e2019 (Date of extraction: 08.04.2017).

29. Yoon E.J. Hepatitis C virus (HCV) infection and hepatic steatosis / E.J. Yoon, Hu. Ke-Qin // Int. J. Med. Sci. - 2006. - Vol. 3. - № 3. - P. 53–56.

Information about authors:

Sleptsova Snezhana Spiridonovna - MD, associate professor, head of «Department of Infectious Diseases, Phthisiology and Dermatovenereology» of the Medical Institute of the «M.K. Ammosov North-Eastern Federal University», Yakutsk, Russia, e-mail: sssleptsova@yandex.ru;

Efimov Alexander Egorovich - post-graduate student of medical institute, Yakutsk, Russia;

Kurtanov Khariton Alekseevich - PhD, head of the Department of Molecular Genetics, FSBSI «Yakutsk Science Center of Complex Medical Problems», Yakutsk, Russia, e-mail: hariton_kurtanov@mail.ru.

Davyodova L.E., Gubanova M.N., Ayupova R.F., Zarubin M.V., Gaponova T.V., Paramonov I.V., Khalzov K.V., Moor Y.V., Zhiburt E.B., Ermolaev A.R.

DONORS PLATELET TRANSFUSIONTOB

ABSTRACT

The article summarizes recent data on the safety and efficacy of preparation and transfusion of donor platelets. There are discussed the features of a) the recruitment and selection of donors; b) the advantages and disadvantages of different methods of platelet concentrates production; c) platelet concentrates inventory management; d) immunological and infectious safety of platelet concentrates; e) deal with undesired constituents remaining in platelet concentrates. There are made the practical recommendations for better choice of platelet concentrate for patient safety. In conclusion, it is noted that in Russia should be normalized timing for: buffy-coat isolation and pooling, platelet concentrate leukodepletion, as well as a gradual transition to 100% transfusion of pathogen-reduced platelet concentrates.

Keywords: blood, donor, platelets, apheresis, pooling, transfusion, pathogen inactivation, immunization, safety

INTRODUCTION

In recent years a successful improvement in infectious and immune safety of allogeneic blood components has been observed. The implementation of quality systems in blood transfusion organisations, technical support and government regulations provided a comprehensive level of safety and efficacy in blood components [1-6]. Along with this, as a result of globalisation and evolution of microorganisms, new threats of infections arise [7-13]. Also, the blood component recipient spectre is changing as well: more patients with oncohematology are required to have frequent blood transfusions for a longer period of time. This increases the compound risk of allogeneic impact [14-20].

Whilst executing platelet transfusion certain safety procedures should be followed::

- sufficient amount of platelet concentrate (PC/CP) must be stored;
- timely delivery of appropriate PC must be in place for the patients;
- blood transfusion infections screening;
- decrease of immunological risks;
- blood transfusion goal achievement;
- unnecessary transfusion rejections;
- monitoring and testing of side effects [21-36].

There two principal methods of donor platelet production:

1) apheresis from another donor
2) extraction from the whole donor blood

The latter can be of two types:

1) platelet enriched plasma
2) extract of the platelet concentrate from the pool of leuko platelet layers (LPL) [37-40].

In theory, it is fair to assume the patients who receive the pool of platelet from 4-6 donations face lower risk of infection and allogeneic impact than the recipients of platelet concentrate apheresis of a single donor. However, the 15-year experience of European Hematological Control does not support but even proves the contrary of results [41].

Hence there is an interest to generalise recent data about the safety and efficacy of platelet production and transfusion.

Engagement and selection of blood donors

Ther requirements for donors of whole blood and apheresis are relatively similar. The latter requires certain concentration of platelets and a solid vein access.

When separating the whole blood from erythrocytes and plasma the platelets are:

- a side product;
- imply zero costs;
- being LPL discard.

Therefore, the cost to produce Platelet Concentrate from the whole blood is lower than deriving it from machine apheresis [42-43].

Though it is another topic of discussion to assess the risk of contamination when conducting the pooling of LPL. Theoretically the risk can be higher on one hand. On the other hand it might be lower due to the neutralisation of bacteria with phagocytes and plasma opsonins (antibodies, complement). According to many national norms and standards the minimum time required for conducting leukodepletion is 2 hours and maximum is 24. Further to this, the amount of bacteria in contamination of apheresis can be higher due to a large volume of collected transfusion environment. This also demands thorough disinfection of a donor's skin [44-46].

Apheresis:

- prolonged;
- is usually conducted in a small group of carefully selected donors;
- can not be performed in transporting conditions;
- carries the risk of citrate intoxication and demineralisation of bones [47].

Production of platelet concentrates: advantages and disadvantages

The quality and safety of platelet concentrates, regardless of their initial source - whole blood or apheresis, might depend on various factors such as the types of containers (configuration and plastic, separator type, method of blood extraction) types of leukofilters, types and usage of scaling (additional) solute, technology and usage of pathogens inactivity, usage of X-Ray or Gamma-Ray, and finally, expiration dates). The combination of these factors are summarised in the table below.

Whilst comparing these products it is crucial to not only compare the "pooled" against "apheresis" platelets concentrates, but also take into account all the factors. In addition, it is also important to consider the before and after

The process of platelet concentrate production from whole blood and apheresis method

Donation

Whole blood	**Apheresis**
LPL	Apheresis Platelet Concentrate
Preparation	
Container	Container
Scale-stirring	Machine
Temperature (before transportation)	Filter
Transportation (time, temperature)	
Recycle	
Store before initiation	
Leukodepleation	
Centrifuge	
Extraction	
Pooling (manual, machine)	
Scaling Solute	
Pathogens Inactivation	
X-Ray	
Store/Stirring	
Delivery	
More than 5 million variations	More than 10 thousand variations

Figure 1. LPL pooling: wash of primary containers with scaled solutions

side effects experienced by donors.

A revolutionary progress in quality of platelet concentrate from the pool of LPL was made after the machine implementation of automatic separation of blood from components and hemacontainers “up-down” (pic. 1, 2). The advantages of such systems are:

- fast and precise production of any necessary blood components;
- no manual work (with the Macropress Smart REVO system cannula breaking in tubes of hemacontainers is automatic without human involvement) (pic. 2-5);
- the maximum amount of platelets produced (in Irkutsk, approximately 1×1011 of cells from a single donor);
- minimum loss of hemoglobin and plasma [48, 49].

Management of platelet concentrate stock

Managing the stock of platelet concentrate is a challenge due to the fact that the maximum period of storage is 5 days as per the regulations in Russia. The delivery of platelet concentrates is highly affected by the long weekend days as well as by inappropriate epidemiological conditions which result in delays of patient’s treatment. Further to this the Chikungunya and Dengue fever waves are also well known for influencing the delivery time. In Russia, the period of delivery time may increase due to the unique 18-hour delay of of the blood diagnostics initiation [50].

On the other side, exceeding amount of platelet preparation may lead to its obsolete and significant cost.

Both situations lead to serious ethical problems. The depreciation of platelets is hardly acceptable for volunteering. The obsolete platelet concentrates may be used for preparation of Lysate, the universal growth factor for cultural laboratories. Nevertheless, only a few clinics have opportunities to utilise depreciated platelet concentrates [51].

The platelet stock management has to consider the biological specificities of each product such as phenotypes ABO and Rh, HLA and/or HPA, as well as cytomegalovirus-negative status (although the characteristics of the latter is non-crucial after the leukodepletion and pathogen inactivation) Creoconcentration and long storage of platelets is complicated and leads to a large loss of cells. The alternative methods of long storage such as lyophilisation - changing the pressure and atmosphere are yet to be developed.

Safety of platelet concentrate: main goals

There are two main goals of concentrate platelet safety:

1) to minimise the risk of blood transfusion infection;

2) to minimise the risk of alloimmune impact;

Leukodepletion or in other words leukoreduction is an important process

Figure2. Centrifugeof LPL pool

Figure 3. Machine separation on Platelet Concentrates from the LPL pool: canule breakage

that links the two problems stated above.

Leukodepletion (leukoreduction)

Leukodepletion is a decrease or reduction of leukocytes by 3 log10 and in Russia the platelet concentrate dose contains no more than 1 × 106 of cells (1 million leukocytes).

There are built-in filters in the modern machine apheresis systems that eliminate leukocytes. The Platelet Concentrate produced from the LPL pool is filtered at the early stages, 18-24 hours after the blood collection. The implementation of universal (from 100% doses) leukodelpletion led to a rapid decrease in transferring innercell viruses such as cytomegalovirus, T-lymphotropic human virus and the Epstein–Barr virus. For the recipients of numerous transfusions Platelet Concentrate leukodepletion is a key element of HLA-alloimmunisation prevention [52].

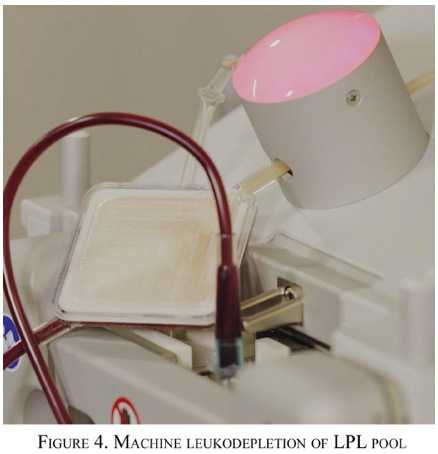
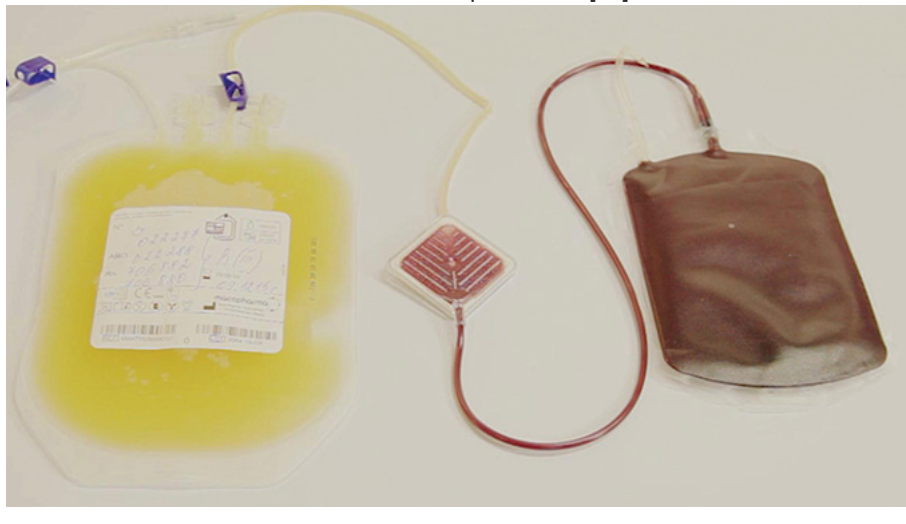


Figure 4. Machine leukodepletion of LPL pool



Immunomodulation and immunomodulation danger

The majority of immunomodulating effects of transfusion are related to the leukocytes content in the blood components. Therefore the leukodepletion reduces the transfusion-related immunomodulation (TRIM) the effects of which are mostly harmful.

Leukodepleted concentrated platelets are effective to prevent Non-Hemolytic Reactions (NHR) and alloimmunisation. It is universally acknowledged that leukodepletion decreases the proinflammatory effects of donated leukocytes - the excesses of inducible synthase of oxide nitrogen, cytokines, chemokines, which are the main indicators of high fever and ague (typical for NHR).

The anti-inflammatory effects of early leukodepletion are more advanced as opposed to bedside leukodepletion effects, as leukocytes begin to disintegrate and released proinflammatory factors of Platelet Concentrate within 24 hours after blood preparation. For that reason, the early leukodepletion also decreases alloimmunisation as it prevents the transfusion of dissoluble antigens of donated leukocytes.

In half of the registered NHR cases Platelet Concentrates is the source of it even though it is only 10% of transfused blood components [53]. It also considered that platelets are the source of majority of inflammatory mediators. However, the proinflammatory factors, released by leukocytes, and activating the proinflammatory factors of platelets, should not be excluded either.

The mechanisms of transfused alloimmunisation are not fully investigated, and perhaps there many more factors to discover. Nevertheless, some progress in the field of Platelet Concentrates transfusion was achieved. It is proved that excessive B-lymphocytes play key role in anti-presenting cells [54].

Infections safety of Platelet Concentrate

The general safety regulation of blood components are applicable to platelet concentrates respectively.

The donor selection is one the crucial safety stages in blood transfusion. Recently, there are more reasons and criteria appearing against donation. Even though such reasons and criteria are implemented for safety purposes, it is not sufficiently enough to prove their justification [55-60].

Bacterial contamination: detection

The risk of bacterial contamination of Platelet Concentrate is high due the fact that the storage temperature of 22 ± 2 °C facilitates the growth of almost all types of bacteria. In Russia such casess were not registered, whilst in France in 2013, the clinical hemotransmitted bacterial infection was developed amongst 3,4 and 0,87 of recipients per 1000 apheresis and pooled transfusions of Platelet Concentrates. Despite the efforts to eliminate infections, their frequency remains stable, approximately 2,3 per 1000 transfusions in 2012 and 2013. In the last five years the apheresis of platelet transfusion leads to five times more bacterial infections than the transfusion of pooled platelets [61].

In Russia it is not obliged to test platelets for bacteria even though some oragnisations practice various globally acknowledged methods such as BactAlert (Biomerieux, France) and BACTEC (Becton-Dickinson, USA).

The search for bacteria might be compulsory in case of production release or quality control. There are certain problems of cultural bacteria detection systems such as the delay of delivery by 24 or 48 hours and the significant amount of false positive and false negative results [62]. In Europe the platelets expiration date can be extended to 5-7 days if the bacteria detection and pathogens inactivation process implemented.

The tests to detect bacteria in Platelet Concentreates with the use of varios types of ligands just before delivery and transfusion do exist and are also developing. These are BacTx ™ (Immunetics, USA) and amongst polyclonal antibodies PGD-Test (Verax, USA). The effects of these test are yet to be proved.

From the practical point of patient's safety another alternative to bacteria detection is pathogens inactivation.

Viruses in blood transfusion

As opposed to plasma, the quarantine of Platelet Concentrates is almost impossible. In comparison to erythrocytes, Platelet Concentrates apheresis is prepared from regular donors who practice frequent donations within 2-week interval. With this kind of donation the risk of "period window" - inception of virus infection non-detectable by laboratory diagnostics, increases. The increase of interval between donations (no less than 2 months for whole blood) reduces the risk of donation during "period window" of virus infection.

Following this, the virus safety of Platelet Concentrates engages:

- pooling of LPL produced from whole blood;
- plasma in Platelet Concentrates is replaced by scaled solution;
- pathogens inactivation.

Pathogens inactivation in Platelet Concentrates

There are two methods to process Platelet Concentrates to achieve pathogens inactivation:

- amotosal-HCl and UVA-A – Intercept (Cerus, USA),
- riboflavin and UVA-B - Mirasol (Terumo BCT, USA).

There is one more method that is under development and considers only UVA-C and stirring without chemical additives. - Teraflex (Macopharma, France). In Russia the Intercept method is implemented since 2003.

There are three significant advantages of pathogens inactivation.

First of all, these methods eliminate the growth of bacteria which makes them competitive enough with bacteria screening. Quite often screening provides false negative results when the bacteria amount is low which is typical for non-symptom donors with the low level of bacteria. There is no single case of bacterial infections registered by hemocontrol in France and Switzerland, as well as in the series of Intercept-processed Platelet Concentrate studies [63].

Secondly, in spite of existing pathogen inactivation methods that do not inactivate spores, they are relevant to vermins and fungus such as malaria, toxoplasma, leishmania and etc.

Finally, the pathogens inactivation reduces the level of hemotransmissive virus infections. If the high concentration of bacteria is in the blood infected by sepsis then viremia might be high in the blood non-symptom donors. The Intercept method helped to provide the clinics with safe platelets during the virus epidemy in Reunion in 2006 (Chikungunya virus) and in French Caribbean in 2006 (Dengue virus). Further to this, the Intercept method is used to process the plasma of Ebola convalescents which is later used to cure the patients. There is no risk of other virus infections such as HIV (typical for Africa) and the antibodies against Ebola are remaining [64].

It is also interesting to observe the experiment of pooling of 2 LPL, pathogens inactivation with Intercept and separation of 2 curing doses of Platelet Concentrates [65].

Non-desirable components remained in Platelet Concentrates: the strategy of preventions, culture and elimination

The transfusion of Platelet Concentrates may lead to:

- NHR (more often that other blood components);
- acute lung damage related to

transfusion (TRALI);
- allergic reactions;
- bacterial infections.

These side effects can be completely or at least prevented with special precaution methods.

Non-desirable components remained in Platelet Concentrates can be divided into two categories:
- antibodies, mainly anti-HLA, as a result of donor alloimmunisation;
- biological substances with anti-inflammatory effect.

The anti-HLA antibodies in plasma may be a consequence of previous blood transfusion and more often pregnancies.

There are three suggested strategies for prevention:
- anti-HLA antibodies screening,
- restriction of female donation,
- use of additive solutions.

The additive solutions reduce the amount of plasma in 65-80% of Platelet Concentrates. The content of various additional solutions differs and evolves. This explains its differences in platelet activation and clinical effectiveness. The morphology assessment, life duration, functional activity, metabolism and aggregated capability of platelets demonstrated that extended storage of platelets in additive solution SSP+ mainly allows to sustain its metabolic in vitro cells characteristics rather than storing it in autologous plasma [66-69].

The expiration date of Platelet Concentrates and its clinical effectiveness as well as the growth of proinflammatory effect is actively discussed in the field. The excessive of proinflammatory cytokines and other biological substances increases after 3 days of storage [70].

Each action toward Platelet Concentrates may theoretically lead to activation or apoptosis of cells. The impact of plastics, centrifuge, filters, gas, solutions and temperature changes may create stress that further leads to damages. Perhaps different platelets react to differently to other various signals. It also possible the production of biological substances determined by the donor specificities, and the reaction to biological substance injection determined by recipient's specificities.

The individual reaction of platelets is the advantage of pooled Platelet Concentrates. The adverse reaction and a breakdown of donor's stored platelets will lead to a functional deficiency of 100% of apheresis Platelet Concentrate cells, but 15-25% of pooled Platelet Concentrates.

Prevention of posttransfusion "transplant against master" disease

Some patients are needed to be irradiated with Platelet Concentartes to prevent the posttransfusion disease called "transplant against master" (PT-DTAM). The main method of inactivation of the remaining lymphocytes against the disease is either X-Ray or gamma-irradiation.

This practice is insufficient to inactivate the infectious pathogens, and it is enough to slightly damage membranes of platelets and increase its activation and apoptosis.

The damaging effect might be prevented if the prevention methods of disease are fully assessed:
- new methods of leukodepletion that are capable to reduce the amount of leukocytes in a dose to less than 105;
- pathogens inactivation methods aimed at damaging of nucleic acids but not damaging platelets. It is observed that the effectiveness of Intercept against the disease (PT-DTAM) is higher than the X-Ray irradiation. And it is confirmed not only by the certifications, but also by implementing the appropriate regulations in the norms of blood transfusion organisation of various countries (Kuwait, Saudi Arabia). On the 14th of January 2016 the American Association of Blood Banks recommended to replace the gamma-irradiation of Platelet Concentrates procedure by its Intercept method [71].

Prevention of alloimmunisation

Numerous platelet transfusions may lead to a development of alloimmunisation and a decrease in future effectiveness of transfusions. The match sampling of Platelet Concentrates with the recipient's serum is not regulated by the Russian norms. The selection of HPA antigens is also not available. The leukoreduction significantly lowers the foundation of anti-HLA antibodies among patients who receive myeloablative chemotherapy. In addition, there is no data about the effectiveness of leukoreduction for the purpose of alloimmunisation prevention among immune competitive patients. Ultraviolet which is included in all methods of pathogens inactivation of Platelet Concentrates lowers the speed of development and the rate of alloimmunisation, and also the duration of anti-HLA of antibodies [72]. The mechanisms of this effect is yet to be studied. If such pathogens inactivation behaviour confirms, then it will become more valuable.

The best choice of Platelet Concentrates for patients' safety

At first sight it is always possible to check whether there any erythrocyte adulterants in the Platelet Concentrates as it should not be red. It is also easy to determine the absence of aggregates - when pressure is applied to the lowest level of Platelet Concentrate the cell spine must be even (the effect of "snowstorm").

Unlike erythrocytes the Platelet Concentrates transfusion is not limited by the absolute immunological barriers and usually does not require a cross sampling (except the well-known alloimmunisation). The release of Platelet Concentrates is conducted on first-in/first-out basis. In different countries there are various practices of ABO-matching of Platelet Concentrates

Typical methods of safety increase and Platelet Concentrates effectiveness:
- ABO-identity;
- Transportation terms control;
- objective assessment (container solidity, cell spine);
- HLA or HPA match in the event of refractoriness and neonatal alloimmune thrombocytopenia;
- the effect of aligned platelet growth monitoring (EGP).

Practical recommendations

The pooled Platelet Concentrates from LPL must be prioritised when possible. The appropriately selected apheresis of Platelet Concentrates should be transfused to alloimmune patients. The use of additive solutions should be in place.

The HLA antibodies injection prevention policy must also be facilitated (male plasma, donor screening). The pathogen inactivated Platelet Concentrates must be used for transfusion purposes.

ABO-identity should be accomplished. The donors with low titre of anti-A, B must be selected in the events of platelet transfusion of O type to other blood type recipients with a compulsory replacement of plasma by the additive solution.

Bear in mind that the effectiveness of Platelet Concentrate diminished after 3 and more days of storage.

CONCLUSION

The methods of Platelet Concentrate safety and transfusion effectiveness are rapidly evolving. Nevertheless, the effective systems of hemacontrol contains 25-30% of transfusion reactions related to Platelet Concentrates transfusion. This means that further advancement is this field is required.

In Russia the dates should be regulated: the release of LPL, pooling of LPL, leukodepletion of Platelet Concentrates as well as moderate shift to a 100% of pathogens inactive Platelet Concentrate transfusion.

The intense search of the best platelet production and implication protocols is conducted globally. Even the quantity of dose differs throughout the world: 2×1011

of cells in Europe, 3×1011 of cells in the USA. Hence the results of the research are not always the same. It is also important to take into account the growing difference between the established practice and new developing methods of Platelet Concentrates preparation, processing, storage and implication.

By no doubt the key goal is the curing effectiveness of transfusions and patient safety. On the other hand, the economical aspects as well as the efficient allocation of donor resources and ethical issues in donor-related work are also quite crucial.

Re-evalution of prevention activities and implication of platelets for curing purposes as well as the parameters which should be selected for the effectiveness and transfusion quality, lead to some new perspectives.

REFERENCES

1. Gubanova M.N. Kopchenko T.G. Zhiburt E.B. Selection of the platelet concentrates production from whole blood. Vestnik of blood service Russia, 9, 2009. - pp. 20-22.
2. Gubanova M.N. Madazaev. S.R. Zhiburt, E.B. Infections distribution and frequency amongst donors in Russia. Questions of virology, 60(6), 2015. - pp. 29-31.
3. Zhiburt E.B. Prevention of post-transfusion hepatitis. Saint Petersburg: Terra Medica, 1998. – P.52.
4. Zhiburt E.B. Golubeva A.V. The TT Virus. The Journal of Microbiology, Epidemiology and Immunobilogy, 3, 2001. – pp. 117-220.
5. Zhiburt E.B. Transfusiology. Saint Petersburg: Piter, 2002.
6. Zhiburt E.B. Gubanova M.N. Shestakov Y.A. Maksimov V.A. New hemotransmissed infections and their prevention. Transfusiology, 7(4), 2006. - pp. 56-67.
7. Zhiburt E.B. Fedorov N.A. Reizman P.V. NAT screening of virus infections amongst donors increasing blood safety. Clinical diagnostics, 12, 2006. - pp. 22-23.
8. Zhiburt E.B. Gubanova M.N. Distant and proximate. Tropical infections in the blood services in Russia. Transfusiology, 9(1), 2008. - pp. 20-24.
9. Zhiburt E.B. Gubanova M.N. Maksimov V.A. Hemastransmissed virus of Eastern Nile. Epidemiology and Infectious diseases, 3, 2007. - pp. 28-32.
10. Zhiburt E.B. Transfusion dictionary. M., RAEN, 2012.
11. Zhiburt E.B. GMP of blood service organization. M: ID KDU, University Book, 2016.
12. Zhiburt E.B. Benchmark of blood preparation and transfusion. RAEN, M., 2009.
13. Zhiburt E.B. Madzayev S.R. Preparation and transfusion of platelets. RAEN, M., 2013.
14. Zhiburt E.B. Vergopulo A.A. Gubanova N.A. Kopchenko T.G. Blood and platelet donor effectiveness in Russian Federation subjects. Glav.Vrach, 2, 2009. - pp. 23-29.
15. Zhiburt E.B. Karavaev A.V. Vaisman D.A. Madzaev S.R. Special features of national risk assessment of infectious blood transfusion. Vestnik Roszdravnadzor, 1, 2013. - pp. 75-77.
16. Zhiburt E.B. Madzaev S.R. Mazgumova R.Z. Methodical questions in infections screening among donors. Vestnik of blood service Russia, 1, 2013. - pp. 30-32.
17. Zarubin M.V. Zaznobov M.E. Kurnosov N.B. [et al.], Platelet storage managing in regional blood service. Kazan Medical Journal, 96(3), 2015. - pp. 407-413.
18. Zarubin M.V. Kupcevich P.S. Smirnova, O.Y. [et al.]. Centralization of blood service in Irkutsk region. Siberian Medical Journal, 7, 2014. - pp. 97-101.
19. Kodenev A.T. Vashchenko G.A. Kapustov V.I. Zhiburt Y.B. Mastering of concentrate platelet production. Vestnik of blood service Russia, 2, 2010. - pp. 22-25.
20. Lyauzheva F.M. Tlenkopachev R.S. Zhiburt Y.B. Donor culling with infections markers in Kabardino-Balakar Republic. Transfusiology, 15(4), 2014. - pp. 40-46.
21. Protopopova E.B. Filina N.G. Kuzmin, N.S., [et al.]. The quality of regular platelet donations. Vestnik of blood service Russia, 2, 2015. - pp. 35-38.
22. Protopopova E.B. Mochkin N.E. Madzaev S.R. [et al.]. Platelets transfusion in transplantation of autologous stem cells. Vestnik of National Medical Surgery Center of Pirogova N.I, 10(2), 2015. - pp. 84-85.
23. Protopopova E.B. Mochkin N.E. Sultanbaev U.S., [et al.]. Thrombocytopenia after transplantation of autologous stem cells. Kazan Medical Journal, 96(3), 2015. - pp. 428-431.
24. Skorikova S.V. Buritkabaev Z.K. Savchuk T.N. Zhiburt E.B. Distribution of HIV, Heptitis C virus, Hepatitis B infections of donors in Astana. Questions of virology, 60(1), 2015. - pp. 34-36.
25. Tankayeva H.S. Makhachev B.M. Zhiburt E.B. The Evolutions of blood service in child clinics. Vestnik of blood service, 2, 2015. - pp. 43-46.
26. Fedorov N.A. Eylov A.A. Suhanov Y.S. Zhiburt E.B. NAT blood and other material testing for pathogens and mutation. Moscow: Poligraphservice. -2003.
27. Filina N.G. About the quality of platelet concentrates. Transfusiology, 12(4), 2011. -pp. 32-37
28. Filina N.G. Kolotvina T.B. Titova S.A. Zhiburt E.B. Provisional screening of donors with alanine transaminase activity has lost the economic effectiveness. Transfusiology, 12(3), 2011. - pp. 61-64.
29. Shevchenko Y.L. Zhiburt E.B. Secure blood transfusion. - Saint Petersburg: Piter, 2000.
30. AABB authorizes use of the INTERCEPT blood system for platelets to reduce the risk of transfusion-associated graft versus host disease [Online]. Available from: http://www.businesswire.com/news/home/20160114005342/en/ [Accessed 30/01/2016].
31. Cerelli E., Nocera M., Di Bartolomeo E. et al. Effect of adhesive properties of buffy coat on the quality of blood components produced with Top & Top and Top & Bottom bags. Blood Transfus. 2015; 13(2):265-73.
32. Garraud O., Cognasse F., Tissot J.D. et al. Improving platelet transfusion safety: biomedical and technical considerations. Blood Transfus. 2015; 16:1-14.
33. Jackman R.P., Deng X., Bolgiano D. et al. Leukoreduction and ultraviolet treatment reduce both the magnitude and the duration of the HLA antibody response. Transfusion. 2014; 54(3):672-80.
34. Lafeuillade B., Eb F., Ounnoughene N. et al. Residual risk and retrospective analysis of transfusion-transmitted bacterial infection reported by the French National Hemovigilance Network from 2000 to 2008. Transfusion 2015; 55(3): 636-46.
35. Petrik J., Lozano M., Seed C. R. et al. Hepatitis E, Vox Sang, 110(1), 2016. pp. 93-103.
36. Pietersz R.N., Reesink H.W., Panzer S. et al. Prophylactic platelet transfusions. Vox Sang, 103(2), 2012. - pp. 159-176.
37. Roth W.K., Busch M.P., Schuller A. International survey on NAT testing of blood donations: expanding implementation and yield from 1999 to 2009. Vox Sang, 102(1), 2012. - pp. 82-90.
38. Sandgren P., Diedrich B. Pathogen inactivation of double-dose buffy-coat platelet concentrates photochemically treated with amotosalen and UVA light: preservation of in vitro function. Vox Sang. 2015; 108(4):340-9.
39. Seghatchian J. Multilayer-strategy to enhance optimal safety of the blood supply: The role of pathogen inactivation

for optimizing recipient safety and helping health care cost containment: Moderator views. Transfus Apher Sci. 2015; 52(2):233-6.

40. van Griensven J., Edwards T., de Lamballerie X. et al. Evaluation of Convalescent Plasma for Ebola Virus Disease in Guinea. N Engl J Med. 2016 7; 374(1):33-42.

The authors:

Davydova Lyubov Yegorovna - Candidate of Medical Science, Ch. Transfusiologist of the Republic Sakha, davlyibov@mail.ru, Yakutsk, Russia;

Gubanova Marina Nikolaevna - Candidate of Medical Science, Ch. Doctor of the Stavropol Territory Blood Transfusion Station, ezhiburt@yandex.ru, Stavropol, Russia;

Ayupova Raila Fayazovna - Deputy Chief Doctor of Blood Transfusion Station of the Republic of Bashkortostan, Ufa;

Zarubin Maxim Vladimirovich - Candidate of Medical Science, Ch. Doctor of Irkutsk regional station, Irkutsk, Russia;

Gaponova Tatyana Vladimirovna, Candidate of Medical Science, Deputy Director of the Hematology Research Center, Moscow;

Paramonov Igor Vladimirovich - Candidate of Medical Sciences, Director of the Kirov Institute of Hematology and Blood Transfusion, Kirov, Russia;

Khalzov Konstantin Vasilievich - Ch. Doctor of Novosibirsk region station of blood transfusion, Novosibirsk, Russia;

Moore Yulia Vladimirovna - Deputy Chief Doctor of Novosibirsk region station of blood transfusion, Novosibirsk, Russia;

Zhiburt Evgeniy Borisovich - MD, prof., Head of Department of Transfusiology of the National Medical and Surgical Center, Moscow.

L.G. Marinova, N.V. Savvina

OBESITY AS A METABOLIC FACTOR OF THE RISK OF CARDIOVASCULAR DISEASES

ABSTRACT

Obesity is currently one of the serious problems of modern society and medicine. The article gives an overview of obesity as one of the main metabolic risk factors for cardiovascular diseases. The reasons of the development of obesity and pathogenetic mechanisms of complications development from the side of the cardiovascular system are considered against its background, as well as the risk to human health in the presence of visceral obesity. We present data on child obesity as a metabolic base of cardiovascular diseases at which a prolonged accumulation of adipose tissue leads to the most serious disorders of human organs and systems, primarily cardiovascular one.

Keywords: obesity, overweight, cardiovascular diseases, epicardial fat.

According to the WHO, overweight and obesity are determined as «abnormal or excessive fat accumulation that presents a risk to health'' [5]. Obesity plays a role in the development of a number of cardiovascular risk factors (FR). The researchers defined pathogenetic basis of the negative effect of obesity on the structural and functional activity of heart and blood vessels. An obese person has a greater risk of developing cardiovascular disease (CVD), which in turn can lead to severe heart diseases [24].

Many factors can cause obesity, including genetic (more than 50 candidate genes). But most people do not have monogenic inheritance of obesity. There are many studies being held to find candidate genes that can affect obesity and overweight. Currently, the role of mutations in the PPAR genes (peroxisome proliferator-activated receptors), fatty acid-binding protein 2, (FABP2), ADRB2 and ADRB3 (G-protein adrenergic receptors) is under study. The latter are considered as an interesting finding in nutrigenetics, confirming the hypothesis of «economical genotype». In people with a body overweight and with a mutation of the ADRB3 gene, daily energy consumption, altered lipolysis and increased abdominal obesity decrease are noted [6]. Despite the revealed interrelationships of gene mutations with overweight, the question of direct role of genetic factors in the development of obesity remains controversial. One cannot ignore environmental factors, such as lifestyle, diet, physical activity, stressful situations and bad habits. To date, according to the WHO, the main reasons of obesity are an excessive supply of nutrients with food and a low level of physical activity, which does not allow consuming the amount of energy coming from food [5, 8, 9].

Clinically obesity can be an independent disease (exogenous-constitutional obesity) or a syndrome that develops at various diseases, such as hypothyroidism, hypercorticism, polycystic ovary syndrome, Cushing's syndrome, etc. (in the latter case, excess weight can be eliminated after curing or compensation of the main disease). In this case, it must be remembered that obesity itself leads to disruption of the sexual glands, the hypothalamo-pituitary system and the adrenal glands. For example, the establishment of a diagnosis of neuroendocrine form of the hypothalamic syndrome is inappropriate, since the formation of hypothalamic stigmas such as cyanotic striae, pigmentation in places of friction, the formation of acanthosis of obese, unclean skin and functional disorders of the hypothalamic-pituitary system is not the cause, but the result and manifestation of obesity, and the degree of their severity correlates with the duration and severity of obesity [20].

Excess body weight contributes to increased levels of total cholesterol and low-density lipoprotein (LDL) and very low density (VLDL) in plasma. It has been established that the production of cholesterol (Ch) in people with obesity increases by an average of 20 mg per

each excess kilogram of fat. For every 4.5 kg of body weight, systolic blood pressure (SBP) is increased by 4.5 mm Hg [4, 19, 20].

Obesity occurs when the number or size of fat cells in the body increases. Normally, a person has 30 to 35 billion fat cells. When a person gets fat, these fat cells first increase in size, and then their number grows. When a person grows thin, the size of the cells decreases, and no matter how thin a person is, the number of fat cells remains the same. Namely for this reason, after gaining of fat mass it is very difficult to lose weight.

Dangerous to human health is visceral obesity (abdominal type of obesity), at which the adipose tissue (AT), has an uneven distribution with excess deposition in the region of the upper body and abdomen (intraabdominal visceral fat - in the omentum, mesentery, retroperitoneal area), as well as in internal organs, including the heart, kidneys and liver (extra-abdominal deposits of visceral fat). Just deposits of adipose tissue in vital organs lead to complications and high mortality. It all starts with a violation of the functional activity of AT, which is not only a depot of fat, but an active endocrine and paracrine organ. Visceral fat, being hormonally active, performs a complex role in the body: secretes estrogens (adipocytes aromatase promotes the synthesis of estrogens from adrenal androgens), angiotensinogen, prostaglandins, tumor necrosis factor α, interleukin-6, leptin, resistin, adiponectin, insulin-like growth factor 1, tissue activator of plasminogen I inhibitor, fibrinogen [4, 28].

At visceral obesity, the main target organs are heart and blood vessels. In heart fat is deposited both inside the cardiomyocytes, leading to fatty myocardial dystrophy, and externally, increasing the thickness of the epicardial fat (EF). Epicardial fat itself develops from brown adipose tissue during embryogenesis and is metabolically more active than subcutaneous adipose tissue. Normally, the EF protects the myocardium and coronary arteries from fatty acids [3]. Since epicardial AT plays an active role in the metabolism of the myocardium, an increase in its volume and activity leads to disruption of the mitochondria. Mitochondrial dysfunction and metabolic disturbance of cardiomyocytes promote systolic cardiac dysfunction in obese patients. At epicardial obesity of heart fibrosis of the myocardium can quickly develop, which accelerates apoptosis of cardiomyocytes. The excess amount of angiotensin II, secreted by the EF, increases the synthesis of fibrosis, which subsequently gives rise to the development of atrial fibrosis and the diastolic function of heart due to the LV myocardial hypertrophy. J. Shirani et al. revealed that excessive fat deposition in the atrial septum increases the prevalence of atrial fibrillation [4, 25-27]. As a result of a pathological increase in the volume of the EF around heart and inside the myocardium, conditions are created for significantly loading the course of IHD, characterized by a more severe lesion of the coronary arteries, more pronounced metabolic disorders, hypercoagulable activity, and shifts in the system of lipid transport of atherogenic orientation [3,4,22].

Currently, epicardial fat is considered as a marker of cardiovascular diseases. A statistically significant relationship with the waist circumference was revealed, with a level of low density lipoproteins. The thicker the epicardial fat, the more pronounced arterial hypertension in patients is and a higher level of insulin. According to a Park study conducted in 2008, for 30 days, in patients with acute coronary syndrome often developed fatal and nonfatal infarcts, cerebral stroke, if the thickness of their epicardial fat was 7.5 mm (against the control group of 5 Mm). According to some data, at the thickness of epicardial fat in 7 mm signs of subclinical atherosclerosis are revealed. According to other data, at epicardial fat in 9 mm with a high probability insulin resistance is diagnosed. In patients with metabolic syndrome, the epicardial fat layer is larger (6 mm) than in patients without metabolic syndrome (4.9 mm). At the moment no clear quantitative value of the layer of epicardial fat has been found [4, 7].

The most significant factors initiating the atherosclerotic process at obesity include: excess of visceral and epicardial fat, resistance index, low level of adiponectin, increased expression of proinflammatory adipokines and cytokines, hypercoagulation, hypertension, hyperglycemia, atrial septal defect [4,7,15- 17].

In the Russian Federation, the prevalence of cardiovascular disease is very high. Ischemic heart disease and cerebrovascular diseases are the main causes of death. In Yakutia over the past 15 years, mortality among the working-age population from diseases of the circulatory system has increased in 2.2 times (in the Russian Federation - 1.7 times).

In order to identify the causes of the development of cardiovascular diseases in Yakutia, a number of studies have been carried out. Medico-social studies have shown that the most significant socio-hygienic factors affecting the formation of circulatory diseases in people of working age are: employment of the population, material wellness, living conditions, the presence of bad habits and the quality of nutrition [10]. Recent populational studies have shown that among men of indigenous nationalities, coronary artery atherosclerosis is less pronounced than in non-indigenous population, with a high prevalence of hypertension (74.7% of cases) and associated hypertrophy of the left departments of heart. There are suggestions that in the development of this phenomenon in the native inhabitants of Yakutia, the presence of insulin resistance, as an independent factor of cardiovascular diseases, probably played a role [13]. Epidemiological studies of the prevalence of the metabolic syndrome and its clinical variants among the indigenous population were also conducted. The most frequent variant of the metabolic syndrome was a combination of abdominal obesity, high blood pressure and lipid metabolism disorders. This combination was more common in young people aged 20-39 years and mainly in women. After 40 years, disorders of carbohydrate metabolism were detected in 52% of the indigenous population [14]. Violations of lipid metabolism are an important issue for residents of Yakutia. In the North, lipids supply the body with the energy that means the transition of the basic metabolism from carbohydrate to fat. In indigenous people, the protein-lipid type of metabolism is genetically determined and is formed in the process of ontogenesis under the influence of external factors. According to the research, in the indigenous and non-indigenous population of Yakutia, an increase in the prevalence of dyslipidemia and differences in the lipid spectrum were detected. As a result of the violation of the ratios of atherogenic and antiatherogenic fractions of lipids, the coefficient of atherogenicity exceeded the permissible norm and was higher for the Yakuts (in the Yakuts in 2.16, for the Russians - 1.9 times) [21].

Cardiovascular diseases are largely a pediatric problem. Considering that overweight in childhood and adolescence is often transformed into obesity in adults, this phenomenon can be considered the metabolic foundation of cardiovascular disease [5, 12, 15-16].

In recent years, convincing evidence has been obtained that the atherosclerotic process leading to CVD

begins in childhood and adolescence and develops over the course of life under the influence of genetic and modifiable risk factors. According to the data of large-scale prospective epidemiological studies, the concept of risk factors, which is the basis for the prevention of CVD, has developed [5, 17, 18, 23]. Later, the concept of risk factors was extrapolated to the child population. As a result of the study, risk factors that retained stability during life were identified. Stable risk factors are hypertension, overweight, hypercholesterolemia, carbohydrate metabolism disorder, low physical activity and smoking among the child population [5, 16]. Despite a variety of risk factors, obesity is the most common risk factor for CVD in children. Critical periods for the debut of obesity are the first year of life, the age of 5-6 years and the period of puberty [8, 9]. The prevalence of excess BM and obesity among boys begins to increase rapidly at the end of puberty (after 15 years). The greater the BMI value in adolescence, the higher it's resistance in subsequent life periods and the higher the risk of excess BM and obesity in young adulthood [8, 9, 15, 16]. The development of metabolic syndrome against obesity in children increases the risk of type 2 diabetes and cardiovascular diseases in young adults. The most frequent complications of obesity (type 2 diabetes, non-alcoholic fatty liver disease, arterial hypertension) can be diagnosed already at the younger school age. Today, the prevalence of childhood obesity has increased significantly in countries with both high and low and middle income countries, and currently solving the problem of childhood obesity is an urgent public health challenge [1, 2, 5].

According to 2010 data, the prevalence of obesity in the Republic Sakha (Yakutia) as a whole was 9.4 among children 0-14 years old, among adolescents - 14.3 per 1000 children of the corresponding age. The statistically significant differences in the average incidence rates for the analyzed period in 3 groups of districts ($p < 0.001$) were revealed. The highest incidence of obesity among children aged 0-14 years was observed in the Arctic group of regions (13.3 per 1000 children), the lowest in the agricultural group (5 per 1000 children). Adolescents had high rates of obesity in the industrial group of districts (17.2 per 1,000 adolescents), the lowest in the agricultural group (11.3 per 1000 adolescents). For 2000-2010 in both age groups, a statistically significant increase in the incidence of obesity was observed in all groups of districts ($p < 0.001$). For example, among children aged 0-14 years, the incidence of obesity in the Arctic group of regions increased three-fold (from 4.6 to 13.3 per 1000), in industrial and agricultural two-fold: from 2.6 to 5 and from 5, 9 to 11.2 per 1.000 children, respectively. Among adolescents, there is also an increase in the incidence of obesity in the dynamics: in the industrial group from 5.9 to 17.2, in the Arctic group - from 4.6 to 14.6 (3 times), in the agricultural group of districts - from 2.6 to 11.3 per 1.000 teenagers (4 times). In the dynamics for 2000-2010 among the children of the Republic Sakha (Yakutia), there is a statistically significant increase in the incidence of obesity. The prevalence of obesity in agricultural areas was statistically significantly lower than in the arctic and industrial groups of areas. These differences may be due to the ethnic composition of the population, the nature of nutrition and the level of motor activity of children in different groups of areas [11].

CONCLUSION

Thus, at obesity a violation of the functional activity of adipose tissue due to excessive accumulation in vital organs leads to their functional and organic lesions, presenting a health risk. It is especially important to note the transformation of childhood obesity into adulthood and the increase in the prevalence of obesity among children. Long-term accumulation of adipose tissue leads to the most persistent damage to human organs and systems, primarily cardiovascular. An important factor is the living conditions. As the researches show, in the residents of the indigenous population of Yakutia specific clinical manifestations of metabolic risk factors for the development of cardiovascular diseases were identified, which may be the reason for its steady growth among the residents of Yakutia.

REFERENCES

1. Averyanov A.P. Bolotova I.V. Zotova S.A. Ozhirenie v detskom vozraste [Obesity in childhood] Lechashhij vrach [Therapist]. Moscow, 2010, №2, P.13-15.

2. Nasibulina E.S. Shagimaradnova R.R. Borisova A.V. Akhmetov I.I. Associacija polimorfizma gena FTO s izbytochnoj massoj tela v rossijskoj populjacii [Association of polymorphism of the FTO gene with overweight in the Russian population] Kazanskij medicinskij zhurnal [Kazan Medical Journal]. Kazan, 2012, V.93, №5, P. 823-826.

3. Bondarenko I.Z. Shpagina O.V. Patogeneticheskie osnovy razvitija serdechno-sosudistyh zabolevanij pri ozhirenii. Trudnosti diagnostiki i lechenija [Pathogenetic bases of development of cardiovascular diseases at obesity. Difficulties in diagnosis and treatment]. Ozhirenie i metabolizm [Obesity and Metabolism]. Moscow, 2015, №12 (4), P. 47-51.

4. Bubnova M.G. Rol' ozhirenija i visceral'nogo zhira serdca v zapuske serdechno-sosudistogo kontinuuma. Klinicheskie jeffekty orlistata [The role of obesity and visceral fat of heart in the launch of the cardiovascular continuum. Clinical effects of orlistat] Rossijskij medicinskij zhurnal [Russian Medical Journal]. Moscow, 2014, №2, P. 116.

5. VOZ. Global'naja strategija po pitaniju, fizicheskoj aktivnosti i zdorov'ju. Izbytochnyj ves i ozhirenie sredi detej [WHO. Global strategy on diet, physical activity and health. Overweight and obesity among children/] Mir mediciny [The world of medicine]. Minsk, 2001, №3-4, P. 28.

6. Borodina S.V. Gapparova K.M. Zainudinov Z.M. [et al.] Geneticheskie prediktory razvitija ozhirenija [Genetic predictors of obesity development]. Ozhirenie i metabolizm [Obesity and Metabolism]. Moscow, 2016. - №13 (2). - P. 7-13.

7. Gilyarevsky S.R. Korneeva O.N. Jepikardial'nyj zhir i serdechno-sosudistyj risk. Est' li svjaz' [Epicardial fat and cardiovascular risk. Is there a connection] http://internist.ru/publications/detail/6359/

8. Dedov I.I. Melnichenko G.A. Ozhirenie [Obesity]. Moscow, 2004, P. 312-328.

9. Dedov I.I. Melnichenko G.A. Romantsova T.I. Patogeneticheskie aspekty ozhirenija [Pathogenetic aspects of obesity]. Ozhirenie i metabolizm [Obesity and Metabolism]. Moscow, 2004, №1, P. 3-9.

10. Egorova A.G. Romanova A.N. Gorborukova T.V. Ocenka vlijanija social'no-gigienicheskih faktorov na formirovanie boleznej sistemy krovoobrashhenija u lic trudosposobnogo vozrasta Respubliki Saha (Jakutija) [Evaluation of the influence of socio-hygienic factors on the formation of diseases of the circulatory system in persons of working age of the Republic Sakha (Yakutia)]. Zdorov'e. Medicinskaja jekologija. Nauka [Health. Medical ecology. The science]. Moscow, 2009, №4-5 (39-40), P. 48-52.

11. Marinova L.G. Savvina N.V. Klimova T.M. Dinamika zabolevaemosti ozhireniem detej i podrostkov RS(Ja) za 2001-2010 gg. [The dynamics of the incidence of children and adolescents

of the RS (Y) for 2001-2010]. Voprosy pitanija [Issues of Nutrition]. Moscow, 2015, Vol.84, № S3, P. 134.

12. Marinova L.G. Savvina N.V. Savvina I.L. Ozhirenie u detej Jakutii: social'no-gigienicheskie aspekty i klinicheskaja harakteristika [Obesity in children of Yakutia: socio-hygienic aspects and clinical characteristics]. Jakutskij medicinskij zhurnal [Yakut medical journal]. Yakutsk, 2015, №3 (51), P. 51-53.

13. Maharova N.V. Voevoda M.I. Lyutova F.F. Vysokaja chastota arterial'noj gipertenzii i porazhenie organov mishenej u korennyh zhitelej Jakutii s verificirovannym aterosklerozom koronarnyh arterij – vozmozhnaja svjaz' s insulinorezistentnost'ju [High frequency of arterial hypertension and defeat of target organs in Yakutia natives with verified atherosclerosis of coronary arteries - possible association with insulin resistance]. Jakutskij medicinskij zhurnal [Yakut medical journal]. Yakutsk, 2011, № 1, P. 104-107.

14. Osakovsky V.L. Goldfarb L.G. Klimova T.M. [et al.] Metabolicheskij sindrom u aborigennogo naselenija Jakutii [Metabolic syndrome in the aboriginal population of Yakutia] Jakutskij medicinskij zhurnal [Yakut medical journal]. Yakutsk, 2010, №2, P. 98-102.

15. Pervichnaja profilaktika serdechno-sosudistyh zabolevanij (klinicheskie rekomendacii): materialy IV Kongressa vrachej pervichnogo zvena zdravoohranenija Juga Rossii, IX Konferencii vrachej obshhej praktiki (semejnyh vrachej) Juga Rossii, Moskva – Sankt-Peterburg – Rostov-na-Donu [Primary prevention of cardiovascular diseases (clinical recommendations): materials of the IV Congress of Primary Health Care Professionals of the South of Russia, IX Conference of General Practitioners (Family Doctors) of the South of Russia, Moscow - St. Petersburg - Rostov-on-Don], 2014, 22 p.

16. Profilaktika serdechno-sosudistyh zabolevanij v detskom i podrostkovom vozraste: rossijskie rekomendacii [Prevention of cardiovascular diseases in childhood and adolescence: Russian recommendations] Rossijskij kardiologicheskij zhurnal [Russian Cardiology Journal]. № 6 (98), Moscow, 2012. Annex 1.

17. Aleksandrov A.A. [et al.] Profilaktika serdechno-sosudistyh zabolevanij v detskom i podrostkovom vozraste: rossijskie rekomendacii [Prevention of cardiovascular diseases in childhood and adolescence: Russian recommendations] Rossijskij kardiologicheskij zhurnal [Russian Cardiology Journal]. Moscow, 2012, №4 (96), pp. 1-40.

18. Profilaktika hronicheskih neinfekcionnyh zabolevanij: rekomendacii [Prophylaxis of chronic non-infectious diseases: recommendations]. Moscow, 2013, 128 pp.

19. Rozanov V.B. Prognosticheskoe znachenie faktorov riska serdechno-sosudistyh zabolevanij, svjazannyh s aterosklerozom, u detej i podrostkov i otdalennye rezul'taty profilakticheskogo vmeshatel'stva: dis…dokt. medic. nauk: Rozanov V. B. [Prognostic value of risk factors for cardiovascular diseases associated with atherosclerosis, in children and adolescents and the long-term results of preventive interventions: dis ... doc. med. sciences: V. B. Rozanov]. Moscow, 2007, 257 p.

20. Samorodskaya I.V. Indeks massy tela i paradoks ozhirenija [Body mass index and the paradox of obesity] Rossijskij medicinskij zhurnal [Russian Medical Journal]. Moscow, 2014, №2, P. 170.

21. Khamnuyeva L.Yu. Andreeva L.S. Koshikova I.N. Ozhirenie. Klassifikacija, jetiologija, patogenez, klinika, diagnostika, lechenie [Obesity. Classification, etiology, pathogenesis, clinical picture, diagnosis, treatment]. Irkutsk, 2007, 33 p.

22. Krivoshapkina Z.N. Mironova G.E. Olesova L.D. [et al.]. Chastota dislipidemij sredi naselenija Jakutii [The frequency of dyslipidemia among the population of Yakutia] Jakutskij medicinskij zhurnal [Yakut medical journal]. Yakutsk, 2007. - №3. - P. 24-26.

23. Chumakova G.A. Veselovskaya N.G. Gritsenko O.V. [et al.] Jepikardial'noe ozhirenie kak vozmozhnyj marker metabolicheskogo sindroma [Epicardial obesity as a possible marker of metabolic syndrome] Kardiosomatika [Cardiosomatics].Moscow, 2012, № 4, P. 38-42.

24. Yartsev S.E. Faktory riska hronicheskih neinfekcionnyh zabolevanij v neorganizovannoj populjacii muzhchin trudosposobnogo vozrasta: annot. dis… kand. medic, nauk [Risk factors of chronic non-infectious diseases in the unorganized population of men of working age: annot. dis ... cand. med, sciences]. Tyumen: TGMA, 2014, 118 p.

25. Branka F. The problem of obesity in the WHO European Region and its solutions strategy / F. Branca, N. Nikogosian, T. Lobstein - WHO. - 2009. - 408 p.

26. Jacobellis G. Different «weight» of cardiac and general obesity in predicting left ventricular morphology / G. Jacobellis, C.M. Pond, A.M. Sharma // Obesity (Silver Spring). - 2006. - Vol. 14. - P. 1679-1684.

27. Relationship between epicardial adipose tissue and left ventricular mass / G. Iacobellis, M.C. Ribaudo, A. Zappaterreno [et al.] // Am J Cardiol. - 2004. - Vol. 94. – P. 1084 -1087.

28. Shirani J. Clinical, electrocardiographic and morphologic features of massive fatty deposits ("lipomatous hypertrophy") in the atrial septum / J. Shirani, W.C. Roberts // J AmCollCardiol. – 1993. - Vol. 22. – P. 226-238.

29. The adipocyte: a model for integration of endocrine and metabolic signaling in energy metabolism regulation / G. Fruhbeck, J. Gomez-Ambrosi, F. Muruzabal, M. Burrell // Am. J. Physiol. Endocrinol. Metab. 2001. Vol. 280. – P.827-847.

Information about authors:

1. Marinova Lyudmila Germanovna, assistant of the Department of Propaedeutics of Children's Diseases, MI NEFU named after M.K. Ammosov, Yakutsk, Russia.

Contact information: 677000, Yakutsk, ul. Oyunsky, 27, cab. 215; E-mail: marinovalg@mail.ru;

2. Savvina Nadezhda Valeryevna – MD, professor, head of the Department of Public Health and Healthcare, General Hygiene and Bioethics, MI NEFU named after M.K. Ammosov, Yakutsk, Russia.

Contact information: 677000, Yakutsk, ul. Oyunsky, 27, cab. 510; E-mail: nadvsavvina@mail.ru.

Ozhegov P.S., Nikolaeva T.Ya.

EPIDEMIOLOGY AND RISK FACTORS OF INITIATION HYPOXIC-ISCHEMIC ENCEPHALOPATHY

ABSTRACT

A literature review of foreign and domestic studies on hypoxic-ischemic encephalopathy in recent years has been conducted to assess the epidemiological situation in various countries of the world and in Russia, as well as to consider the risk factors for this pathology. Despite some differences in the approaches to the diagnosis of hypoxic-ischemic encephalopathy, data on the prevalence of this disease in newborns are fairly homogeneous and depend little on geographical and medico-social factors. However, in connection with the unresolved issue of distinguishing hypoxic-ischemic encephalopathy and neonatal encephalopathy, diagnostic criteria in different neonatal and neurological schools differ, which also has an impact on the results of epidemiological studies. At present, discussions continue on pathogenesis, risk factors, prevalence of perinatal encephalopathy, as well as approaches to diagnosis, treatment and rehabilitation of children.

Keywords: hypoxic-ischemic encephalopathy, perinatal lesions of the central nervous system, epidemiology, prevalence, risk factors.

INTRODUCTION

A significant increase in the incidence of the child population is an urgent problem of modern health care. A special place in this case is occupied by perinatal lesions of the nervous system, which are currently diagnosed in 85% of full-term and almost 100% of premature infants [1, 3, 5]. Perinatal hypoxic lesions of the central nervous system cause a high percentage of neurological disorders: from mild functional disorders to severe, disabling conditions (cerebral palsy, epilepsy, oligophrenia, etc.) [2, 11].

Hypoxic-ischemic encephalopathy (HIE) is an acquired syndrome characterized by clinical and laboratory signs of acute brain damage after perinatal hypoxia and asphyxia in labor and manifested by breathing disorders, suppression of physiological reflexes, reduction of muscle tone, impaired consciousness with frequent occurrence of seizures [14]. Representations about the clinical manifestations of HIE, despite the obviousness of their main manifestations, are quite contradictory. At present, there is no unity in the notions of the duration of the current and the periods of GIE. At the present time, two basic principles have been formed in the approach to the diagnosis of hypoxic brain lesions: staged (phase) and syndromological. The first of these approaches prevails abroad, the second - in Russia. In connection with the foregoing, it seems relevant to study the prevalence and risk factors for hypoxic-ischemic brain.

Objective: to evaluate the epidemiological indicators of hypoxic-ischemic encephalopathy in various countries of the world and in Russia, and to consider the risk factors for the occurrence of this pathology.

METHODS OF RESEARCH

We conducted a strategic search for the MEDLINE database using such keywords as «hypoxic-ischemicencephalopathy», «epidemiology» and «prevalence» in various combinations. To search for domestic research, a search was used based on the RINC database (elibrary.ru) using the key words «hypoxic-ischemic encephalopathy», «perinatal lesions of the central nervous system», «epidemiology», «prevalence».

RESULTS AND DISCUSSION

According to WHO, 10% of children have neurological disorders of varying severity, caused by hypoxic-ischemic damage to the brain of the fetus and the newborn [15]. In the United States, hypoxic-ischemic encephalopathy is noted in 1-8 cases per 1000 births. In Western Australia, HIE and neonatal encephalopathy occur at a frequency of 1.9-3.8: 1000, with HIE due to only hypoxia in childbirth recorded in 1.6: 10,000 births [4]. The incidence of neonatal encephalopathy is 3.0: 1000 full-term live births with fluctuations from 2.7 to 3.3: 1000, and GIE - 1.5 (1.3-1.7): 1000 [6, 11]. Retrospective study of 1864 766 newborns ≥ 36 weeks. Gestation in the state of California indicates that the incidence of neonatal encephalopathy is 1.1: 1000 births [12, 18].

Study of the incidence of HIE in the first decade of the XXI century. In Spain showed that it is 1.088: 1000 full-term newborns, and medium-heavy and severe HIE - 0.49: 1000, with a linear tendency to reduce the incidence [7, 17]. However, epidemiological studies conducted in Nepal showed that the clinic for neonatal encephalopathy occurs at a frequency of 28.1: 1000 births, with 2% of cases showing congenital anomalies, 25% having an infection, and 28% having intranatal causes. The incidence of neonatal encephalopathy due to intranatal causes is 13.0: 1000 births [9, 12]. Along with this, there are data on the epidemiology of hypoxic brain lesions in preterm infants. So, among preterm infants who died at the 1st week of life, the detection of pereventricular leukomalacia (PVL) is 7%; In children who died after 7 days of life, PVL is detected on autopsy in 75% of cases [12, 13]. In children who required a hardware breathing, the frequency of development of PVL can reach 60%, in contrast to 6% of cases of PVL in unventilated children. Prognostically the most unfavorable is the cystic form of PVL [8].

The occurrence of peri- and intraventricular hemorrhages (PIVK) largely depends on the survival of premature infants. In Canada and the United States, the proportion of live births of prematurity with a weight of less than 1500 g in the structure of all genera increased from the 1970s to the 1990s from 1.0-1.17 to 1.2-1.45%. Currently, about 85% of children born with a mass of 500-1500 g survive in developed countries [14].

In the Russian Federation, the frequency of GIE reaches 712: 1,000 children under 1 year [1].

Despite the fact that pregnancy and childbirth are natural and physiological events in human life, these underlying processes are extremely vulnerable and subject to numerous endo- and exogenous effects. The causes that adversely affect the course of pregnancy and childbirth are so diverse that it is difficult to find a factor that could not contribute to the disturbance of their harmonious course.

The most significant factors for the formation of HIE are the following:

1. Socio-demographic and prenatal factors: working mother or unemployed during pregnancy; Absence of private

(voluntary) health insurance; Epilepsy and / or neurologic diseases in a family history; Infertility treatment; Thyroid disease, preeclampsia, severe or moderate haemorrhage, viral infection during pregnancy; Gestational age less than 37 and more than 42 weeks; Birth weight less than 3 centiles; Pathology of the placenta; Late prenatal care or lack of it [12].

2. Intratinal factors: posterior view of the occipital presentation; Mother fever in childbirth; impetuous labor; Instrumental vaginal delivery or emergency cesarean section; The need for general anesthesia of the mother. Among the factors that impede the development of HIE, the authors indicate only two: delivery in time and elective cesarean section (according to indications) [2, 17]. At 70% of hypoxia-borne newborns, antenatal risk factors for HIE were detected, in 24% - a combination of antenatal and intranatal factors, and only 5% postnatal causes led to HIE [11]. Childbirth at night (from 19 to 7 hours) is associated with an increase in the development of neonatal encephalopathy, as well as asphyxia and seizures of newborns. Night delivery is an independent risk factor for the development of neonatal encephalopathy, along with a severe delay in prenatal development, the lack of prenatal care, the age of the mother, the male sex, the pervious mother [13]. The protracted second stage of labor in pregnancy serves as a predictor of a decrease in Apgar scores at 5 min below 7 points and, together with it, increases the risk of developing a syndrome of respiratory distress, the need for ventilation and the development of HIE [3].

CONCLUSION

Data on the prevalence of hypoxic-ischemic encephalopathy are fairly homogeneous and depend little on geographical and medico-social factors in those cases when the criteria for diagnosing this condition are unified. However, in connection with the unresolved issue of discrimination between HIE and neonatal encephalopathy, diagnostic criteria in different neonatal and neurological schools differ, which also has an impact on the results of epidemiological studies. Discussions are ongoing on pathogenesis, risk factors, prevalence of perinatal encephalopathy, as well as approaches to the diagnosis, treatment and rehabilitation of children [1, 18]. In addition, the relevance of the problem in question is also due to significant differences in the views of this pathology among Russian and foreign researchers.

Thus, the problem of perinatal hypoxic-ischemic injury of the central nervous system remains a serious scientific, medical and social significance.

REFERENCES:

1. Badalyan L.O. Detskaya nevrologiya [Pediatric Neurology]. Moscow: MEDpress-inform, 2001, 607 p
2. Barashnev YU.I. Perinatal'naya nevrologiya [Perinatal encephalopathy]. Moscow: Triada –KH, 200, 640 p.
3. Lavrik S.YU. Posledstviya perinatal'nykh gipoksicheskikh porazheniy tsentral'noy nervnoy sistemy u detey doshkol'nogo i rannego shkol'nogo vozrasta [Consequences of perinatal hypoxic lesions of the central nervous system in preschool and early school age children]: Avtoreferat diss. dokt. med. [abstract of the thesis of the doctor of medical sciences]. Irkutsk, 2015, 30 p.
4. Pal'chik A.B., Shabalov N.P. Gipoksicheski-ishemicheskaya entsefalopatiya novorozhdennykh [Hypoxic-ischemic encephalopathy of newborns]. St. Petersburg: Piter. 2000, 224 p.
5. Pal'chik A.B. Shabalov N.P. Shumilina A. P. Sovremennyye predstavleniya o perinatal'noy entsefalopatii [Modern concepts of perinatal encephalopathy]. Ros. pediatr. zhurn., 2001, № 1, p. 31-34.
6. Sokolova O.G. Perinatal'nyye gipoksicheskiye porazheniya nervnoy sistemy u detey pervogo goda zhizni: kliniko-diagnosticheskiye aspekty avtoref. dis.kand. med. nauk [Perinatal hypoxic lesions of the nervous system in children of the first year of life: clinical and diagnostic aspects: abstract of the thesis of the candidate of medical sciences]. Nizhniy Novgorod, 2006, 25p.
7. Stepanov A.A. Tserebral'naya ishemiya u detey pervykh mesyatsev zhizni: sovremennyye kriterii diagnostiki i printsipy lecheniya: avtoref. dis. d-ra med. nauk [Cerebral ischemia in children of the first months of life: modern diagnostic criteria and treatment principles: abstract of the thesis of the doctor of medical sciences]. Moscow, 2007, 28 p.
8. Fenichel D.M. Pediatricheskaya nevrologiya: Osnovy klinicheskoy diagnostiki: per. s angl. [Pediatric Neurology: The Basics of Clinical Diagnosis: Translation from English]. Moscow: Meditsina, 2004, 640 p.
9. Abbot N.J. Astrocyte-endothelial interactions at the blood-brain barrier / N.J. Abbot, L. Ronnback, E. Hansson // Nature Rev. Neurosci. 2006. - Vol.7- P. 41-53.
10. Factors associated with epilepsy in children with periventricular leukomalacia / P. Humphreys, N. Barrowman, M. Matzinger // J. Child Neurol. -2007. Vol. 22, № 5. - P. 598-605.
11. Jense F.E. Role of glutamate receptors in periventricular leukomalacia / F.E. Jense // J. Child Neurol. 2005. - Vol. 20, № 12. - P. 950-959.
12. Leven M, J. (ed) Neurology and Neurosugery of the Fetus and the Newborn 3-rd ed. London: Churchill Livingston, 2001.
13. McKinney A. M. Diffusion-weighted imaging in the setting of diffuse cortical laminar necrosis and hypoxic-ischemic encephalopathy / A. M. McKinney, M. Teksam, R. Felice // Am. J. Neuroradiol. 2004. - Vol. 25, № 11. - P. 1659 -1665.
14. PerlmanJ. M. Summary proceedings from the neurology group on hypoxic-ischemic encephalopathy / J. M. Perlman // Pediatrics. 2006. -Vol. 117, № 3.-P. 28-33.
15. Volpe J.J. Neonatal encephalopathy: an inadequate term for hypoxic-ischemic encephalopathy / J.J. Volpe // Ann neurol. 2012. - Vol. 72, № 2. - P. 156-166.
16. Volpe J.J. Encephalopathy of prematurity includes neuronal abnormalities / J.J. Volpe // Pediatrics. 2005. - Vol. 116, № 1. - P. 221-225.

Information about authors:

Ozhegov Pavel Sergeevich - Post-graduate student of the Department of Neurology and Psychiatry of the North-Eastern Federal University, MD, neurologist.

Contact phone: 89991739686 E-mail: ozhegov_ps@mail.ru

Address: 677000, Russia, Republic of Sakha (Yakutia), 677000, Yakutsk, Oyunsky Str. 27

Nikolaeva Tatyana Yakovlevna - professor, PhD, Head of Department of Neurology and Psychiatry of the North-Eastern Federal University E-mail: tyanic@mail.ru

Address: 677000, Russia, Republic of Sakha (Yakutia), 677000, Yakutsk, Oyunsky Str. 27.

POINT OF VIEW

M.P. Dutkin

SUICIDE AND SOCIAL MEDIA

ABSTRACT

The article provides a viewpoint, linking the decline in the suicide rate the last two decades throughout the world, according to the WHO data, with the development of information and communication technologies. Communication in social networks leads to a reduction of emotional alienation in people, contributes to the disappearance of feeling of loneliness. The feeling of community, involvement in various groups of people, joint activities lead to the realization of oneself as a full-fledged person, not prone to suicide.

In the last two decades there has been worldwide a clear trend of reduce the number of suicides and crime. The average global suicide rate from 2000 to 2012, decreased by 26%. Marked reduction in suicidal index and aggression on a global scale in recent decades cannot be explained in «sociological» hypothesis for the origin of suicide. The decrease of suicide and crime can explain the massive use of messengers. Instant messaging applications allow communication and to communicate easily, quickly. Social networking leads to a decrease in the level of «alienation» among people and contributes to the disappearance of loneliness. Alienation is a psychological cause of suicide. Communicate through instant messengers leads to a sense of community, involvement in various groups of people, sharing activities that leads to the realization of themselves as a person. Humanization of communication leads to a decrease in the level of alienation among people, leads to the disappearance of feelings of loneliness and existential «abandonment» in the world. The globalization of social, cultural, economic and political processes led to positive phenomena - reduced the number of indicators of aggressive behavior of personality. Aggressive behavior of personality is manifested in acts of self-aggression and external aggression. Suicide is now considered an extreme form of self-injurious behavior. The rate of external aggression of the individual – level violence and crime reduced. Crime in the United States during 1996-2005 has declined by 30%. During 2001-2010, the rate of violent crime in this country decreased by 20%. The introduction of information technology strongly affects the socio-historical development of human society. Humanization of communication leads to a decrease in the level of alienation among people, leads to the disappearance of feelings of loneliness and existential «abandonment» in the world. Humanization of interpersonal relations in modern society is the cause of the decrease of aggressive behavior around the world.

Keywords: suicide, suicidal index, messengers, crime, humanization, aggressive behavior, autoaggression, existential «abandonment» into the world, cybersocialization, interpersonal relations, «sociological» theory of suicidal behavior.

The problem of suicide agitated the minds of human society since ancient times. According to the eminent philosopher of the twentieth century by A. Camus believed that there is only one serious philosophical problem – a suicide problem. In the book “The Myth of Sisyphus”, he writes on the first page: “To judge that whether there is a life to be lived or it’s not worth it – so to answer the fundamental question of philosophy” [3].

The World Health Organization in 2014 published its first report on suicides in the world “Preventing suicide: a global imperative” in order improve the understanding of the public health value of suicide and to make suicide prevention one of the priority issues in the global agenda for public health [7]. According to the report in the world every year due to suicide kills more than 800 thousand people – around one person every 40 seconds.

The beginning of the XXI century differs from the past the XX century a marked decline in the number of suicides. According to the WHO, average global suicide rate from 2000 to 2012, decreased by 26% and amounted to 11,4 per 100 thousand population [7].

The rate of suicide in all parts of Europe decreased by 24-40%, following an increase observed in the mid 1990 [8].

The leading countries in the number of suicides per 100 thousand population: Guyana, Belarus, Hungary, Kazakhstan, Lithuania, Latvia, Russia, Estonia, Sweden and Finland – demonstrate a sharp decline of suicides during this period. In Belarus in 2012 the suicide rate was 18.3 per 100 thousand (in 2000 – 35,5), in Hungary in 2012 to 19.1 (in 2000 – 25,7), in Kazakhstan, respectively – 23,8 (37,6), in Lithuania – 28,2 (44,9), in Latvia 16,2 (29,0), in Estonia – 13,6 (25,0), Japan is 18.5 (18.8 in) in Finland was 14.8 (20.8 per).In Guyana, where the highest rate of suicide in the world also recorded a decrease in the number of suicides - 44.2 (48,4). Of those affected by suicide countries, only in Finland in 1986 was developed in a successful national project for the prevention of suicide aimed at improving the diagnosis and treatment of depression, improving the availability of mobile mental health teams [4].

In the UK in 2012, the suicide rate was 6.2 per 100 thousand (in 2000: 7,8) in Germany – 9,2 (11,2), in France, and 12.3 (14,9), India - 21,1 (23,3), in China and 7.8 (19,4).

In the Russian Federation is the peak of suicides occurred in 1995, 41.1 cases per 100 thousand population and in 2001 to 40 cases per 100 thousand population [1]. In the country since 2002, he planned a steady trend towards reduction of suicide, despite the economic crisis in 2008 and 2013, According to the WHO, in 2013-2014 in Russia per 100 thousand inhabitants accounted for 19.5 suicides. Therefore, the suicide index in the Russian Federation for 13 years has decreased by 50%.

Most researchers of suicide see the main cause of suicide in the socio-economic crisis, causing massive unemployment and declining living standards («sociological» hypothesis of suicidal behavior). The founder of «sociological» theory of the origin of suicide by E. Durkheim considered suicide as the result of a rupture of interpersonal relations of the individual, his alienation from the social group to which he belonged for a long time: «the Rate of suicide depends on sociological reasons, and the contingent of voluntary deaths is determined by the moral organization of society» [2].

Reduction of suicidal index on a global scale over the last decades was not due to «sociological» theory of the origin of suicide put forward by E. Durkheim. He linked the surge in suicides with the economic and social crises.

Over the last 20 years the world experienced two big economic crisis – the Asian financial crisis in 1998 (at that crisis were involved Russian Federation) and the global financial crisis of 2008. These crises have not led to a surge in suicide index.

The globalization of social, cultural,

economic and political processes led to positive phenomena - reduced the number of indicators of aggressive behavior of personality. Aggressive behavior of personality is manifested in acts of self-aggression and external aggression. Suicide is now considered an extreme form of self-injurious behavior.

The rate of external aggression of the individual – level violence and crime reduced.

Doctor of legal sciences V. E. Kvashis in the scientific article «Crime in the United States: trends and countermeasures» writes that the crime in this country over the 1996-2005 decreased by 30% [9]. Within this General trend, particularly noticeable is the annual decline in violent crime. Its level decreased by 33.4%, including murders – on 36,7%, robberies by 40%. During 2001-2010, the rate of violent crime has decreased 20%, including homicide by 14%, robbery by 20%.

The decrease of suicide and crime is due to the universalization and globalization of interpersonal relationships in modern society. Communication between people today has reached the highest level of adaptability. Progress in the development of personal computers in the 90s of the XX century (for example, «chat» communication) and mobile phones has made possible the exchange of messages within seconds (or instantly). It allows people to communicate in real time, while being even tens of thousands of kilometers from each other.

Since the production of the first cell phone by Motorola in 1983 the massive use of mobile cellular communication began in 1995 With the help of instant messaging, you can exchange not only text messages but also images, audio signals and videos.

What is an instant messenger (SMS, Whatsapp, Instagram, Skype, etc.), knows almost everyone. It is an indispensable attribute of modern society, allowing to build communication and to communicate easily, quickly and often for free. Social networking leads to a decrease in emotional alienation from people contributing to the disappearance of a sense of loneliness and existential «casual abandonment in the world.»Alienation is a psychological cause of suicide. Communicate through instant messengers leads to a sense of community, involvement in various groups of people, sharing activities that leads to the realization of themselves as a person.

The introduction of information technology strongly affects the socio-historical development of mankind, the fate of the individual, his place and role in this global historical process. In this regard, the candidate of pedagogical Sciences V. A. Pleshakov allocates one-fifth of the information technology revolution associated with the development of digital, mobile and Internet technologies [5]. In his opinion, if the evolution of humanity viewed from the point of view of evolution of information technology (cyberevolution), we can say that at the turn of XX-XXI centuries in human society has entered a new stage of development – the era of cybersocialization of the person – the life of the individual in cyberspace. Changing even the mind of modern man: «Cybersocialization – socialization of the individual in cyberspace is a process of qualitative changes in the structure of self-consciousness and the requirement of motivational sphere of the individual, occurring under the influence and as a result of human use of modern information and communication technologies...» [6].

Extensive development of communication technologies, humanity unites in a single socio-cultural integrity. Gradually formed a new humanistic culture in which a person will be treated as an end in itself of social development. A person in such a society is less likely to be exposed to forms of aggressive behavior. As a result of the universalization and globalization of interpersonal relationships has decreased the number of homicides and suicides in the modern world.

References:

1. Dutkin M. P. Flyuktuaciya suicidal'nogo povedeniya naseleniya Severa Rossijskoj Federacii [Fluctuation of suicidal behavior of the population of the Russian North]. Yakutsk: Jakutskij medisinskij zhurnal, 2013, № 1(41), PP. 94-98.

2. Durkheim E. Samoubiystvo. Sotsiologicheskiy etyud [Suicide. A study in sociology]. St. Petersburg: Soiuz, 1998, P. 363.

3. Camus A. Mif o Sizife. Esse ob absurde [the Myth of Sisyphus. Essay on the absurd].Moscow: Politizdat, 1989, P. 24.

4. Korkejla Y. Preduprezhdenie samoubijstv v Finlyandii [Suicide Prevention in Finland]. Moscow: 2013, №1 (23), PP. 46-47.

5. Pleshakov V. A. Kiberontologicheskaya koncepciya razvitiya lichnosti i zhiznedeyatel'nosti cheloveka XXI veka i problemy obrazovaniya [Cyberintelligence the concept of personality development and human life of the XXI century and the problems of education]. Vestnik Pravoslavnogo Svyato-Tihonovskogo gumanitarnogo universiteta. Seriya 4: Pedagogika. Psihologiya: 2014, №4 (35), PP. 9-22.

6. Pleshakov V. A. Teoriya kibersocializacii cheloveka [Theory of cybersocialization of the person]. Moscow: MPGU, «Homo Cyberus», 2011, P. 24.

7. https://www.euro.who.int/предотвращение самоубийств. глобальная императива /

8. http://www.euro.who.int/ru/publications/abstracts/european-health-report-2012/

9. http://sartraccc.ru/Pub/kvashis(9-03-13).html

The author:

Dutkin Maxim Petrovich, candidate of philosophical sciences, associate Professor of neurology and psychiatry, Medical Institute M. K. Ammosov NEFU , Yakutsk, Republic Sakha (Yakutia), Russia.

F.A. Platonov, V.B. Ignatiev

GENDER ASPECTS OF HISTORICAL MIGRATION AS A FACTOR OF ETHNO-SOCIAL TRANSFORMATIONS ON THE MIDDLE LENA (STATEMENT OF THE QUESTION)

ABSTRACT

The article considers discussion issues of the Yakuts (Sakha) ethnogenesis. Comparing the results of the latest genetic studies with linguistic data, as well as with existing literature on the history, ethnography and social anthropology of the Sakha people, the authors discuss the little-studied aspects of global ethno-social transformations in the middle Lena, which led to the formation of a peculiar gene pool of modern Sakha.

Keywords: Y-chromosome, mtDNA, Yakuts, population, ethnogenesis, migration of pastoralists, ethno-social transformations.

The ethnic history of population of Yakutia, in particular the origin of the Yakuts (Sakha), one of the numerous populations of the north-east of Eurasia, remains among the most controversial issues in Russian historiography. Note that in the existing literature there are different concepts about ethnogenesis of the Yakuts, among which two hypotheses are distinguished with most argumentation. Thus, various versions of the «southern» origin suggest long migrations of the ancestors of the Yakuts from the south (Central Asia, Southern Siberia) to Vilyui and the middle Lena, where separate groups of migrants mixed together [8,9,10,11,22,23,28 , 29]]. In line with the «autochthonous» theory, is opposite, supported the concept of a mix of the alien southern substratum with the predominance of the aboriginal population of Yakutia, which resulted in the formation of a modern Yakut ethnos [2, 31]. Mainly on language affiliation, important elements of material and spiritual culture of the Sakha people to the shared roots of the Turkic world is justified domination of turkic-speaking tribes in their ethnogenesis, occurs with the participation tungus and mongolian groups. For instance, according to the concept of G.V. Xenophontov [19], the Yakuts are a people of ethnically mixed origin, which included three «waves» of turkic-speaking immigrants from the Angara and the Baikal area. According to his assumption, the gradual penetration of ancestors of the Yakuts into the territory of their modern settlement, first «deer» Yakuts, later - Yakut cattlemen, lasted from the I to XII century AD. The multi-component cohort of the ancestors of the Yakuts is also argued by the data of comparative linguistics [5,28,34] and numerous archaeological artifacts [4,12,26]. Today, researchers are inclined to a compromise approach, according to which the basis for formation of the Yakut population is temporally separated migration flows of people from south of Siberia to the north along the Lena river, who entered into close ethno-cultural contacts with various autochthonous tribes [22]. At the same time, there are also significant disagreements over the expected geographical outlets, the chronological linkage of migrations, their logistics and route, the ethnic composition of the migrants, and others.

It is noteworthy that new horizons in the study of existing lacunae in ethnography of the Yakuts (Sakha) are associated with the development of molecular genetic studies characterized by high representativeness of the results. Thus, in the light of the new data on the genetic characteristics of human populations identified by the DNA marker technique, there is interesting hypothesis of formation of the Sakha people on basis of mixing of the region indigenous male population with the newly arrived, predominantly female population from the south.

Objectively, the starting point for the relevant reflection is the fact of the interrelation between historical migrations and the gene pool of the modern peoples of Yakutia [36]. As is known, there are basic paired (autosomal chromosomes, 22 pairs), mitochondrial DNA (mtDNA), sex X and Y chromosomes. In this case, if the Y chromosome determines the male gender and is passed from father to son, then mtDNA is present in both men and women, but is transmitted only from mother to all children, regardless of their gender. The DNA markers (paired chromosomes) characterize the community as a whole, without distinguishing the genetic contribution of each of the sexes. However, by the types (characteristics) of polymorphism (diversity) of DNA, one can evaluate certain events that occurred during the historical development of a given population. Thus, the reliability of the presence of genetic traces of migrations in gene pool of the population provides a basis for historical reconstruction of the ethnogenesis model of any nation.

The genetic history of population is most often considered according to the structural features of mtDNA and Y chromosome. Polymorphisms of mtDNA and Y-chromosome, transmitted from generation to generation along only one of the parental lines, allow (theoretically) to determine the origin of the population separately for the female and male lines. The variety markers of mtDNA and Y-chromosome is determined by the factors of microevolution (migration, selection, mutations). This approach is of particular importance in case of a small population size, its low settlement density, severe geographical and natural climatic conditions of residence, i.e. is fully consistent with the study of genetic history of the Yakuts. For example, analysis of haplotypes of the Y chromosome revealed motifs specific only for the Yakut population. A comparative study of the Yakuts mtDNA and other turkic-mongolian-tungus-speaking populations revealed the genetic relationship of the Yakuts on the maternal line (mtDNA) with the South Siberian Turkic-speaking Tuvinians and Altaians [36,37]. Studies in genetic archeology [17,36] also allowed to date the general male ancestor of the sample 17 marker haplotypes (total 14) of the line N1c1, revealed by the results of testing human remains from burials in the territory of Yakutia [39]. The date of

the common male ancestor at a mutation rate of 0.002 per marker per generation: 42 generations from the average date of burial. When taking into account the last value, the date of the common ancestor of the buried people corresponds to the date of the common ancestor of the Yakuts, tested in our time. Thus, dating [1.36] of the common ancestor of the Yakuts of the line N1c1, when the rates of mutations are reduced to one value, gives the middle of the first millennium A.D.

Specific for the Yakut men N3-chromosome forms a separate branch, which emerged 1540 ± 580 years ago [36]. In other words, it turns out that the Yakut men separated in the middle of the 1st millennium A.D. It is known that the population consists of representatives of individual genera and belonging to it is most often recognized by the male line. Even if agrees with the opinion that some groups or tribes of nomadic pastoralists came to the middle Lena from somewhere in the south, their ancestral Y-chromosome, which belongs to the so-called northern variant, they could already have in specified period, respectively, the Yakuts ancestors, probably, and earlier lived in the North. Immediately we stipulate that the attachment of the time of divergence to this territory does not yet have convincing evidence.

In gross, the results of biogenetic research in the comparative historical context make it necessary to further search for new knowledge related to the problem of the origin of Sakha people. If we proceed from the thesis of their addition as a result of the mixing of different ethnic groups over a long historical period, then in the light of the identified genetic profile of the Yakut population, a method of retrospective analysis is obtained, allowing to reactivate individual ideas of existing concepts and make non-standard interpretations of a vast historiographic information. In this article, a thematic discussion is offered to the little explored aspects of historical migration of the ancestors of Yakuts, characterized by a small number and low density of settlement, and their impact on the process of global ethno-social transformations in region.

In this context, the general problems of the «demographic explosion», which has long attracted the interest of researchers, is noteworthy, but it still has no proper explanation. Thus, according to calculations by B.O. Dolgikh, specially studying the question of the number of Yakuts, in the middle of the XVII century, there were 28.4 thousand people, both sexes [14]; a century later, in the middle of the XVIII century, their total number was approximately 69 thousand people [18], and at the end of the XIX century - 221.4 thousand people [25]. Note that throughout the history of human communities, a significant increase in population was achieved only because of cardinal changes in the way of life support (gathering, hunting, fishing, cattle breeding, farming) and the introduction of technological innovations. Applied to the Yakuts S.A. Tokarev pointed that when they were formed as a single community of heterogeneous components with predominance of the autochthonous element, «one of the most significant aspects was the transition of fishing-hunting-reindeer breeding tribes to breeding of horse and cattle» [31]. The decisive role of economic factors in demographic processes was noted by G.P. Basharin, substantially bearing in mind the relationship between the change of landmarks in the dominant type of economy (the transition from breeding horses to the predominant content of cattle) and population growth [6]. Of course, such a transition dramatically increases the volume and quality of consumed products and their supplies, which directly affects the dynamics of the number of individual families and genera, and the population as a whole.

At the same time, demographic shifts, due to the specific nature of the process of population reproduction, usually take a long time and are not rapid. Accordingly, the comprehensive basis for the demographic development of the Yakuts was laid down even during the formation of the early cattle-breeding society, represented by the kulun-atakh archeological culture [12]. The diverse nature of the Yakut mtDNA indicates that the growth of the number of bearers of cattle breeding culture was due both to natural growth and the mechanical movement of the Turkic-speaking population of South Siberia, in which a significant place was occupied by women. Immediate impetus for formation of the gender profile of migration could be significant disparities in demographic structure of the population - sex, age, marriage, aggravated by high child and female death rate. Sustainable women's migrations could be supported by a generalized exchange of marriage partners, in which women were «changed» only in one direction (for example, a son could marry a representative of the same group from which his father took his wife, and the daughter could not to marry a representative of the same group). In this context, is of interest the material about the system of terms of kinship and the Yakuts' property, which is distinguished by the differentiation of the categories of patrilateral kinship. The matrilateral line of kinship is represented by one term «taai», with the help of which it is modified in the form of a base: taai-balys, tay-ini, etc., i.e. all related by mother. In addition, the term «kylyn» is a bilateral term for kinship in marriage in Turkic languages, in the Yakut language it means, first of all, the relatives of the wife. According to experts, this is due to the earlier separation of the Turkic-speaking Yakut nucleus from its ethnic background [7].

As a replica of migrations stimulated among other reasons by the need to search for marital partners, one can also take the Yakut proverb: «Uluu doydu ospoostaah, aan doydu aattiktaah, kueh dalai olomnooh, hara tia ilyktaah» (a large country has a road uphill, the land inhabited by people - mountain pass, deep, wide river - ford, dense forest - paved trail). Note that the excellent knowledge of diverse landscapes (large orographic objects and river systems, taiga) and, accordingly, the ability to navigate in large physical and geographical spaces, is evidence not only of the vibrant migration movement of the ancestors of the Yakuts, but also their active involvement in the Eurasian circle of ethno-cultural interactions .

The gender-migration component of development of the human potential of the pastoral population may be indicated by the system of social norms of demographic behavior, which is implicit in many attitudes, associations and metaphors. For example, these are ancient parables associated with the approved matrimonial behavior: «yu chugaha, uruu uraaga orduk» (it's better when the water is close, and the relatives are far away); «kyys ogo - omuk anala» (the destiny of daughter is another tribe / people), as well as with the censure of marital ties within its community: «teltgehattitten tiinnneebikke, kurdugutten bultaabikka dyli» (like a man who hunted in his own yard).

In the cultural tradition, the Yakuts cannot help attracting attention to the woman as a «temporary» person in the father's house and «stranger» in the home of her husband's parents. At the same time, it is with the figure of a woman that not only the cattle-breeding economy itself is associated, but also its life purpose, prescribed by the family

and the social environment. All this is contained in the formula of parental blessing when a girl who marries leaves home: «inniger uuruulen, canniger seetilen» (drive cattle in front, lead horses behind). In this connection N.V. Emelianov rightly observes: «First of all, the wife is a worker. Female labor ... was the most debilitating, hard work. Indeed, as the proverb says: Dyakhtar oronuttan turan wot otuor dieri tuort uon sanaana sanyyr (a woman, rising from her bed, while she will dissolve the fire, the forty thoughts will change her mind). She works constantly ... at home, looks after cattle, cleans the cowshed, feeds the whole family, shepherds, clothes, nurses children. How can she not change her thoughts!»[16]. The gender reality of the woman as an integral part of cattle breeding and the keeper of home was preserved in social notions of the mother as the basis of the family / household prosperity («dyie - yial yiyetinen»). Presumably, the economic necessity of conducting a large cattle-breeding farm and practiced virilocal exogamy promoted the spread of polygamy «keep as many wives as they can feed», which was preserved by the Yakuts before the XVII century [6,32].

In connection with the above, the question of türkic-speaking Yakuts (Sakha) is reactivated as a result of the integration of ethnically differentiated groups [29]. As you know, an outstanding orientalist-turkologist V.V. Radlov (1837-1918) regarding the Yakut language adhered to the concept of the turkization of the non-türkic language. For a comparatively historical study of the Yakut lexicon, he attracted 1,748 root and indissoluble foundations, of which 32.5% were identified as turkic elements, 25.9% as mongolian, 41.6% as elements of «unknown origin,» and concluded, that the number of mongolisms can be considered equal to one-third of the lexical stock of the Yakut language [40]. E.I. Ubryatova, who shared the opposite opinion, nevertheless believed that he was «somewhat right when he expressed his supposition about the participation of non-türkic elements in the formation of the Yakut language, the phonetics and grammatical structure of the Yakut language bear the imprint of the deep influence of Evenk and one of mongolian languages «[35].

Without going into the subtleties of the theoretical discussion that continues to the present time [20], we only note the contribution of women to the creation of a single Yakut ethnos, aware of its linguistic, ethnic and territorial community, and the formation of the Yakut language itself. Widely recognized and needs no proof of the fact that the construction and reproduction of linguistic and ethnic identity is greatly influenced by the primary socialization of human - language acquisition, learning social and cultural norms, acquisition of generic skills, etc., necessary for its life at small and large social groups. The mother woman, being the central figure in the economy and home life, was the most important agent of primary socialization, choosing the language of child-rearing and, accordingly, determining their linguistic and ethno-cultural identity. Naturally, the first language, assimilated by the child in the process of primary socialization, which is simultaneously an instrument of this socialization, was the language of his mother. It is no accident that in many languages of the world's people there is such a concept as «mother tongue», represented in the Yakut language as «iye tyl» (mother language) and «terebut tyl» (born tongue). Accordingly, with the migration of turkic women from the south, the progressive distribution of kulun-atakh cattle breeding culture and the further development of the traditional Yakut economy as a combination of sedentary pastoralism and shepherding are directly related.

But there is one question: why do the Yakuts have a predominantly dominant carrier of the N1c1 line? It seems that the answer to this question can be found by referring to the concept of so-called «bottle neck» in population genetics. In accordance with it, the Yakut ancestors' population, supposedly on the way from Baikal to Central Yakutia, passed through this «neck», but it turned out that N1c1 carriers mostly passed through it. The version that seems appropriate the modern genetic portrait of the Yakut men was formed, mainly due to the reconciliation of their biological features and factors (the spread of previously unknown diseases in Northeast Asia), conditionally called «Western civilization» [33]. The results of the last genochronological dating of the ancestors of the Yakuts have made it possible to clarify this basic scheme. According to E.Crubezy, «From the 17th to the 19th centuries, the epidemics of smallpox and measles, caused by contact with Russian settlers, devastated the Yakuts and their neighbors ...» [39]. A specific period of the smallpox epidemic is given, 1650-1653, which, he believes, has profoundly affected the DNA characteristics of the indigenous peoples of Yakutia, including the Even and Evenk [1]. This phenomenon, if there was a place, could determine the effect of the «bottle neck». Equally, we can assume, and that the ancestors of the Yakuts by the XVI century already adapted to smallpox and measles, and in a broad sense to factors conventionally called «Western civilization».

Then another question arises: Why through the «bottle neck» were only men, and women - not? It can be answered only by admitting that the Yakut gene pool was constantly replenished by mtDNA from neighboring regions, mainly from Southern Siberia. Derenko and Malyarchuk indicate the colonization of the earliest (beginning of I thousand) by the Yakuts of the area of the middle Lena [13]. As they write, the modern population of Siberia is characterized by one of the most frequent group in Northern Eurasia (from Northeast Asia to Eastern Europe) group HG16. In the gene pools of ethnic communities in Southern and Eastern Siberia, its frequency varies from 2% in Shorians to 55.6% in Yakuts; for the Koryaks and Evens - about 30%. It is noteworthy that the group of HG12 (ancestral to HG16) is also present in the gene pools of the Altai-Sayan region ethnics, the maximum frequency of which is up to 35% - registered with the Shorians and Tofalars. Recent genetic studies [38] indicate the purely Asian origin of the haplogroup N3 in support of the high incidence of the HG12 group and the presence of the HG16 group in the Altai-Sayan populations [13].

The use of different methods of dating ethnogenesis (archeological, historical, genochronological, glottochronological) should reveal the coincident period of formation of the Yakut population only if integrity of the gene pool and language identity of the people are preserved to some extent. The approximate coincidence of time formation of population according to two methods (glottochronological and genochronological) and lack of confirmation of others (archaeological and historical) do not provide an opportunity to unambiguously define the «core» and «periphery» of a multi-unit ethnos. Despite this, it can be assumed that in the course of migrations, which could represent the infiltration of small groups into local communities, and later have a more massive character, factors of profound ethno-social transformations that determined a qualitative leap in demographic development of the Yakut population were formed. With reference

to the problems of the article, the most important of them are changes in the ethno-demographic characteristics of the region population and the economic orientations caused by them. The place of these transformations can be identified as region of the middle Lena, where they could occur during the XIII-XIV centuries, which is generally confirmed by the wide diversity of mtDNA of the Yakut population, some of which are part of the gene pool of neighboring peoples living predominantly in Southern Siberia. Undoubtedly, the above material requires additional arguments and reinforcements in detail with other data, but still provides enough grounds for continuing the interdisciplinary discussion on various aspects of historical migration, the colonization of the region by pastoral communities and the formation of the language, identity and culture of the modern Yakuts (Sakha).

The work was carried out within the framework of the Ministry of Education and Science of the Russian Federation №17.7344.2017/VU и AAAA-F17-117030110062-0.

REFERENCES

1. Adamov D. Ob osnovnykh gaplogruppakh Y-khromosomy tungusoman'chzhurskikh narodov [About the main haplogroups of the Y-chromosome of the Tungus-Manchurian peoples] http://rjgg.molgen.org/index.php/RJGGRE/article/view/29. The Russian Journal of Genetic Genealogy (russkayaversiya). Vol.1, №2 (2009).The Russian Journal of Genetic Genealogy. http://rjgg.molgen.org/.

2. Alekseev A.N. Drevnyaya Yakutiya: zheleznyj vek I ehpokha srednevekov'ya [Ancient Yakutia: the Iron Age and the Middle Ages] Novosibirsk, 1996.

3. Alekseev A.N. Proiskhozhdenie yakutskogo naroda po arkheologicheskim dannym [The origin of the Yakut people according to archeological data] Irkutsk, 2002.

4. Alekseev A.N. Osnovnye ehtapy proniknoveniya tyurkskikh ehtnicheskikh grupp na Srednyuyu Lenu [The main stages of the penetration of turkic ethnic groups into the Middle Lena] Arkheologiya Severo-Vostochnoj Azii: astroarkheologiya, paleometrologiya: sb. nauch. tr. [Archeology of Northeast Asia: astroarcheology, palaeometrology: coll. Sci. Tr.] Novosibirsk, 1996, pp.57-164.

5. Antonov N.K. Istoricheskaya leksika yakutskogo yazyka [Historical lexicon of the Yakut language] Yakutsk, 1971.

6. Basharin G.P. Istoriya agrarnykh otnoshenij v YAkutii. T.1. Agrarnye otnosheniya s drevnikh vremen do 1770-khgodov [The history of agrarian relations in Yakutia. T.1. Agrarian relations from ancient times to the 1770s] Moscow, 2003.

7. Burykin A.A. Sistema terminov rodstva yakutov v sinkhronnom, sravnitel'no-istoricheskom i areal'nom aspektakh [System of terms of kinship of the Yakuts in synchronous, comparative-historical and areal aspects] Algebra rodstva [Algebra of kinship] Vol. 5. PSP, 2000, pp.213-242.

8. Gogolev A.I. Lektsii po istoricheskoj ehtnografi i yakutov: uch. posobie[Lectures on the historical ethnography of the Yakuts: textbook] Yakutsk, 1978.

9. Gogolev A.I. Istoricheskaya ehtnografiya yakutov [Historical ethnography of the Yakuts] Yakutsk, 1980.

10. Gogolev A.I. Istoricheskaya ehtnografiya yakutov (voprosy proiskhozhdeniya) [Historical ethnography of the Yakuts (issues of origin)] Yakutsk, 1986.

11. Gogolev A.I. Yakuty: problem ehtnogeneza i formirovaniya kul'tury [Yakuts: problems of ethnogenesis and formation of culture] Yakutsk, 1993.

12. Gogolev A.I. Arkheologicheskie pamyatniki Yakutii pozdnego srednevekov'ya (XIV-XVIII vv.) [Archaeological monuments of Yakutia of the late Middle Ages (XIV-XVIII c.)] Irkutsk, 1990.

13. Derenko M.V. MalyarchukB.A. Geneticheskaya istoriya korennogo naseleniya Severnoj Azii [Genetic history of the indigenous population of North Asia] Nature. 2002. 10. pp.69-76.

14. Dolgikh B.O. Rodovoj I plemennoj sostav narodov Sibiri v XVII v. [The tribal and tribal composition of the peoples of Siberia in the XVII century] Moscow, 1960. pp.542-544, 615-617.

15. D'yachkovsky F.N. Vasilij Vasil'evich Radlov (1837-1918) [Vasily Vasilyevich Radlov (1837-1918)] Yakutskij yazyk v zarubezhnoj tyurkologii [The Yakut language in foreign Turkology] Yakutsk. 2005. p.11.

16. Emelyanov N.V. Yakutskie poslovitsy I pogovorki [Yakut proverbs and sayings] Yakutsk, 1962, 68 p.

17. Klesov A.A. Pervyj primer opredeleniya vremeni zhizni obshhego predka po iskopaemym gaplotipam [The first example of determining the lifetime of a common ancestor in fossil haplotypes] Vestnik Rossijskoj Akademii DNK-genealogii [Bulletin of the Russian Academy of DNA Genealogy] T.3. 2010.№3 (March) Michael Temosh's Storefront http: // stores.lulu./temosh.

18. Kabuzan V.M. Troitsky S.M. Dvizhenie naseleniya Sibiri v XVIII v.[The movement of the population of Siberia in the XVIII century] Sibir' XVII-XVIII vv. [Siberia of the XVII-XVIII centuries] Novosibirsk, 1962. 155 p.

19. Ksenofontov V.G. Uraangkhaj-sakhalar: ocherki po drevnej istorii yakutov [Uraanghai-sahalar: essays on the ancient history of the Yakuts] Irkutsk, 1937. P.576.

20. Levin G.G. Istoricheskie svyazi yakutskogo yazyka s drevnetyurkskimi yazykami VII-IX vv. (v sravnitel'no-sopostavitel'nom aspekte s vostochno-tyurkskimi i mongolskimi yazykami) [Historical relations of the Yakut language with the ancient Turkic languages of the 7th-9th centuries. (In a comparatively comparative aspect with the East Turkic and Mongolian languages)] Yakutsk, 2013.

21. Lindenau Ya.I. Opisanie narodov Sibiri (pervaya polovina XVIII veka). Istoriko-ehtnograficheskie materialy o narodakh Sibirii Severo-Vostoka [Description of the peoples of Siberia (the first half of the XVIII century). Historical and ethnographic materials about the peoples of Siberia and the Northeast] Magadan, 1983.

22. Mir drevnikh yakutov: opyt mezh distsiplinarnykh issledovanij (po materialam sakha-frantsuzskoj arkheologicheskoj ehkspeditsii [The world of the ancient Yakuts: the experience of interdisciplinary research (based on the materials of the Saha-French archaeological expedition] Yakutsk, 2012.

23. Okladnikov A.P. Istoriya Yakutskoj ASSR. T.1. Yakutiya do prisoedineniya k Russkomu gosudarstvu [History of the Yakut ASSR. T.1. Yakutia before joining the Russian state] Moscow-Leningrad, 1955.

24. Okladnikov A.P. Neolit i bronzovyj vek Pribajkal'ya [Neolithic and Bronze Age of the Baikal Region] Materialyi issledovaniya po arkheologii SSSR [Materials and Research on USSR Archeology] 1955. №43.

25. Pervaya vseobshhaya perepis' naseleniya Rossijskoj imperii LXXX. Yakutskaya oblast' 1897 g [The first general census of the Russian Empire in 1897 LXXX. The Yakut region] St. Petersburg, 1904, pp. 48-49.

26. Bravina R.I. Pogrebal'nyj obryad

yakutov kak istoriko-ehtnograficheski jistochnik (XVII-XIX vv.): avtoref. dis. … kand. ist.nauk [Funeral rite of the Yakuts as a historical and ethnographic source (XVII-XIX centuries.): Abstract. Dis. ... cand. History Scientific] Leningrad, 1983.

27. Seroshevsky V.L. Yakuty. Opyt ehtnograficheskogo issledovaniya. 2-e izd. [The Yakuts. Experience of ethnographic research. 2nd ed.] Moscow, 1993, 736 p.

28. Sidorov E.S. Etyudy po sravnitel'no-istoricheskoj leksikologii yakutskogo yazyka [Studies on the comparative-historical lexicology of the Yakut language] Sovetskaya tyurkologiya [Soviet Turkology] 1985, N. 3, pp.53-63.

29. Sleptsov P.A. Proiskhozhdenie i razvitie yakutskogo yazyka [Origin and development of the Yakut language] Yakuty (Sakha), Seriya «Narodyi kul'tury Yakuts (Sakha) [Series «Peoples and Cultures] Moscow, 2012, pp.107-111.

30. Tokarev S.A. Ocherk istorii yakutskogo naroda [Essay on the history of the Yakut people], Moscow, 1940.

31. Tokarev S.A. Proiskhozhdenie yakutskoj narodnosti [Origin of the Yakut people] Kratkie soobshheniya Instituta istorii material'noj kul'tury AN SSSR [Brief Communications of the Institute of the History of Material Culture of the USSR Academy of Sciences] 1941, V.9, 229 p.

32. Tokarev S.A. Obshhestvennyj stroj yakutov XVII-XVIII vv. [Social system of the Yakuts XVII-XVIII centuries] Yakutsk, 1945.

33. Tyurin A.M. K voprosu o genokhronologicheskom datirovanii predkov yakutov [To the question of the genochronological dating of the ancestors of the Yakuts] http://new.chronologia.org/turin/.

34. Ubryatova E.I. Yakutskij yazyk v ego otnoshenii k drugim tyurkskim yazykam, a takzhe k yazykam mongol'skim I tunguso-man'chzhurskim [Yakut language in its relation to other Turkic languages, as well as to the languages of Mongolian and Tungus-Manchurian] Moscow, 1960.

35. Ubryatova E.I. Ocherk istorii izucheniya yakutskogo yazyka [Essay on the history of the study of the Yakut language] Yakutsk, 1945.

36. Fedorova S.A. Geneticheskie portrety narodov Respubliki Sakha (Yakutiya) [Genetic portraits of the peoples of the Republic of Sakha (Yakutia)] Yakutsk: Publishing House of the Yants SB RAS, 2008. -235 p.

37. Tarskaya L.A. Gogolev A.I. El'chinova G.I. Egorova A.G. Limborskaya S.A. Ehtnicheskaya genomika yakutov (naroda sakha) [Ethnic genomics of the Yakuts (Sakha people)] Moscow. Science, 2009, 271 p.

38. Ilumae AM. Reidla M. Järve M. et al. Human Y Chromosome Haplogroup N: A Non-trivial Time-Resolved Phylogeography that Cuts in Language Families / [et al.] // The American journal of Human Genetics. - 2016. july 7, 99, 163-173,

39. Crubezy E. Amory S. Keyser C. Bouakaze C. Bodner M. Gibert M. Röck A. Parson W. Alexeev A. Ludes B. Human evolution in Siberia: from frozen bodies to ancient DNA BMC Evolutionary Biology, 2010, 10-25. Http://www.biomedcentral.com//1471-2148/10/25.

40. Radloff W. Diejakutische Spracheinihrem Verhaeltnissezuden Tuerksprachen Abteilunghistor. -filol. -V.VIII, N7, St.-Petersburg, 1908.

The authors:

Platonov Fedor Alekseevich - Doctor of Medical Sciences, Chief Researcher Research Institute of Health M.K. Ammosov NEFU, Yakutsk, Russia;

Ignatieva Vanda Borisovna - Candidate of History, Head sector of ethnosociology of the Institute of Humanitarian Studies and Problems of Indigenous Peoples of the North of the SB RAS, Yakutsk, Russia.

CLINICAL CASE

S.N. Alekseeva (Ogotoeva), N.A. Afanasieva, K.I. Burnasheva

THE OUTCOME OF PRENATALLY DIAGNOSED CONGENITAL HEART DISEASE – AORTIC ARCH DOUBLING

ABSTRACT

The article is devoted to contemporary diagnostics of rare developmental anomaly of cardiovascular system – aortic arch doubling. The clinical case of early diagnostics of aortic arch doubling during the period of screening of pregnant woman in term of 22nd gestation week is considered. No actual frequency of the pathology is known, as 90 % of cases can be symptomatic. Among patients with CHD hospitalized in the cardiosurgical clinics a vascular ring is registered less than at 1 %. Approximately 50 % of these patients have trachea congenital anomaly such as absence of membranous area in tracheal cartilages. As a result, cartilages make a complete ring that aggravates tracheal stenosis. When esophagus considerably compressed in the first days of life it can be diagnosed as esophageal atresia. Swallowing problem is not constant, weakening in some cases, even disappearing and appearing again. Since birth the patient G. in a clinical picture had dominant trachea narrowing manifested with mixed stridor. Symptoms of dysphagia appeared on 4-5th months of life. No hemodynamic abnormalities at the patient were observed. The computer tomography data were proved to be relevant after the operative intervention. When analyzing the follow up study the newborn's arrested physical development was revealed, whereas psychomotor development was normal. Within the year there was obstruction of respiratory ways, also symptoms of dysphagia. The early diagnosis of the congenital heart disease subjected to correct tactics of the patient management since the birth, accelerating the process of surgical intervention as well as reducing the risk of life-threatening complications.

Keywords: a newborn, congenital heart disease, aortic arch doubling, dysphagia, breath

INTRODUCTION

Aortic arch doubling (AAD) is the rare anomaly at which aorta covers trachea and esophagus like a ring, it making up 1 % from number of all CHD [2]. Prenatally the diagnosis is revealed at 0,01 % of all surveyed. At the same time, frequency of operations concerning vascular ring among the population makes up 0,0013 %. Thus, for 90 % the pathology can proceed without symptoms [1].

As an isolated defect the aortic arch anomalies are noted in the formation of vascular ring along esophagus and trachea, causing the compression of the above-stated bodies. There are two types AAD such as functional aortic arch doubling and aortic arch doubling with left arch atresia, the latter noted as the rare pathology. At all these anomalies there are no hemodynamic abnormalities, this feature being the main distinction from other congenital heart diseases and great vessels [4, 5]. Cardiac tones are pure, noise is absent. The symptoms depend on compression of abnormally passing aorta and its branches to esophagus, trachea and recurrent nerve. They are manifested as difficulties in breathing and swallowing, phonation disturbance, sometimes they can be absent or present depending on a case. Dysphagia is one of characteristic signs. Approximately 50 % of these patients have the congenital anomaly of trachea such as absence of membranous area in tracheal cartilages. As the result cartilages make the complete ring that aggravates trachea stenosis [3, 5]. Considerable narrowing of trachea is revealed more often in the mixture with stridor. Concomitant severe tracheomalacia aggravates the prognosis. Difficulty in the diagnostics is caused not only by lower incidence rate, but also by lack of objective information on the pathology in periodical press [3].

MATERIALS AND METHODS

Clinical follow-up study of the patient with CHD, AAD in the neonatal pathology unit №1 (NPU №1) in 2016 in the Prenatal centre SAE RS (Y) «RHN№1-NCM».

RESULTS OF RESEARCH

The patient G. at the five-day age was hospitalized in NPU №1 with complaints on noisy strident breath at crying.

According to the anamnesis the child's mother is 31 years old, 5th pregnancy, toxicosis and ARVI at first trimester. The childbirth at term, 3 medical abortions, chlamydial and cytomegalovirus infections. On the second prenatal investigation (20 weeks of pregnancy) CHD AAD was diagnosed at the fetus. Trisomy 21, 18, 13 syndromes out of the amniotic fluid were excluded after the DNA testing. The second childbirth, at term, cephalic presentation. The newborn was a live boy, in a severe state with Apgar 7/9, full-sized, sanitation of upper airways in the maternity hall and further was taken to the intensive therapy department. Physical, morphofunctional maturity corresponded his gestation age (weight 3300g, height 51 cm, head circumference 34 cm, breast circumference 33 cm). In the neonatal pathology unit saturation decrease on 74 at rest was noted. When crying at birth inspiratory stridor was marked. In the first days of life moist rales were listened at auscultation . On phenotype the child had some abnormalities: relative disproportion due to slightly truncated limbs, ocular hypertelorism, wide philtrum, microgenia, short neck, four-finger fold on both palms. In the neurologic status a little reduction of muscular tone and depletion of inborn reflex are revealed. 1st stage of the investigation included electrocardiogram, ECHO cardiogram, X-ray of thoracic organs in direct projection, x-ray computer tomography of lungs with contrast.

The electrocardiogram was conducted on the second day of life, sinus rhythm with heart rate 143 beats per minute. Electric cardiac axis is rejected to the right. Signs of overstrain (hypertrophy) of the right ventricle. Infringement of repolarization processes.

The X-ray of thoracic organs at birth revealed pulmonary fields of mild transparency at the expense of hypoventilation, detected mostly in medial parts of both sides. Few structures in lung markings. Roots of lungs are not differentiated. Cardiac shadow is of typical size and form. Upper mediastinal widening is noted. Pulmonary-pleural sinuses are free. Diaphragm contours are even and accurate. Slight pneumaticity on the part of abdominal cavity organs. In dynamics, for the third days of life hypoventilation on the right was remaining.

The ECHO CG data did not exclude CHD and recommended RCT. It revealed interatrial septum aneurysm with shunting d=0,38. Functioning arterial channel (d=0,18 cm). Dilatation of the

right atrium (2,0 cm), right ventricle cavity (1,1 cm), pulmonary trunk (0,9 cm). Additional trabecular in the left ventricular cavity. EF - 71 %. Double aortic arch is not excluded.

According to the RCT of lungs aortic arch doubling is revealed. Aneurismal outpouching of distal part of the left aortic arch is marked, aortal diverticula is not excluded and the clinical diagnosis CHD is disclosed. Aortic arch doubling. Interatrial septum aneurysm with shunting. Functioning arterial channel. Impaired circulation of 1 stage. Respiratory insufficiency of 0-I stages.

The NPU №1 was supervising the case. Jaundice syndrome began on the third day, the maximum rate was 235 mkmol/l in 7 days. The child was on demand chest feeding at all stages, the weight value with positive dynamics (growth on 208 g for 1 week). In act of breastfeeding no difficulties in swallowing were noted. Stridor cry remained. The symptomatic treatment was carried out. In the hospital the boy was examined by the geneticist, cardiologist, oculist and the neurologist. After the correspondence consultation on neonatal cardiology (14.00.009) for performing highly technological aid the child was hospitalized in the Scientific institute of cardiovasculatory pathology named after E.N. Meshalkin, Novosibirsk.

When admitted in the scientific institute there were complaints to atony, dyspnea, hyperhidrosis. According to the multispiral computer tomography the diagnosis aortic arch doubling was proved, in addition, dominant left aortal arch, 2,2x3,8 mm trachea constriction, the diagnosis CHD. Aortic arch doubling with esophagus and trachea compression: dominant left aortic arch. Distal segment obstruction of the right aortic arch. Interatrial septum aneurysm. Patent foramen ovale.

On 18th day of life the patient was operated by conducting a section of aortic arch with separation of the vascular ring and trachea and esophagus decompression. Ligation with transecting patent ductus arteriosus. The postoperative period was critical due to respiratory insufficiency, ALV was used within 18 hours. Antibacterial therapy was carried out including Cephalosporin and Meropenem, diuretics, broncholytics, infusion-transfusion therapy, physiotherapy, massage. At 1 month and 11 days the child was discharged in a state of moderate severity, with preservation of stridor breath, slight dyspnea at rest, tube feeding as a result of breastfeeding refusal, frequent vomiting provoked by cough.

The follow-up data: at one year disharmonious development and hypotrophy of 2 stage was noted at the child's physical development. According to L.T.Zhurba, E.M.Mastjukova's psychomotor assessment (1981) the total score was 27 regarded as age norm. At one-year-old age stridor breath remained at rest, dysphagia was periodically observed. The child had twice pneumonia, ARVI. Preventive vaccinations were cancelled till 18 months.

CONCLUSION

Rare cardiovascular abnormalities require precise attention at their diagnostics. Even when CHD diagnosed, due to absence of characteristic clinical symptoms the diagnostics can be incomplete, thereafter resulting in serious consequences. Qualitative prenatal diagnostics promotes the earlier diagnosis of rare developmental anomalies in the neonatal period and leads more favorable prognosis for the disease. According to radiological and ultrasonic research all the patients with the syndrome of trachea and esophagus compression particularly the patients with signs of aortic arch anomaly were shown the RCT data for acknowledgement or exception of that diagnosis.

REFERENCES:

1. Arakelyan V.S. Ivanov A.A. Makarenko V.N. Problemy diagnostiki vrojdennoi deformatsii dugi aorty [Issues of diagnostics of aortal arch congenital abnormalities] Detskie bolezni serdtsa i sosudov [Children's cardiovascular diseases]. 2010, №3, pp. 31 - 37.

2. Arakelyan V.S. Gidaspov N.A. Kulichkov P.P. Dvojnaja duga aorty s formirovaniem sosudistogo kol'tsa i razvitiem sindroma kompressii trakhei i pischevoda: osobennosti klinicheskoi kartiny, diagnostiki i khirurgisheskoi taktiki [Aortal arch doubling with formation of vascular ring and development of a syndrome of trachea and esophagus compression: characteristics of clinical picture, diagnostics and surgical tactics] Grudnaya i serdechno-sosudistaya khirurgiya [Chest and cardiovascular surgery]. 2016, №5, pp. 299 - 302.

3. Bokeriya L.A. Arakelyan V.V. Vrojdennye anomalii dugi aorty. Diagnostika, taktika lecheniya [Congenital anomalies of aortal arch. Diagnostics, management] Grudnaya i serdechno-sosudistaya khirurgiya [Chest and cardiovascular surgery]. 2012, №4, pp. 14 - 19.

4. Gidaspov N.A. Taktika i neposredstvennye resul'taty khirurgicheskogo lecheniya patsientov s anomaliyami dugi aorty pri ikh sochetanii s drugimi zabolevaniyami grudnoi aorty i ee vetvei. Avtoref. kand … med. nauk [Management and short-term results of surgical treatment of patients with aortal arch anomalies at their combination to other diseases of chest aorta and its branches: thesis of cand… medical sciences] 14.00.44. Moscow, 2009, pp.24.

5. Krivchenya D.Y. Krivchenya A.K. Slepov T.D. Vnutrigrudinnye kompressii dykhatel'nykh putei, obuslovlennye dvoinoi dugoi aorty, u detei [Intrasternal compressions of respiratory ways caused by double aortal arch at children. Vrachebnoe delo [Medical practice]. 2006, №5, pp. 30 - 36.

Authors:

1. Sargylana Nikolaevna Alekseeva (Ogotoeva), senior lecturer of the department of pediatrics and children's surgery MI NEFU, Yakutsk, Republic Sakha (Yakutia), Russia sargylanao@mail.ru,

2. Natalia Aleksandrovna Afanasieva, neonatologist of the neonatal pathology unit №1 Perinatal center SAE RS (Y) «RHN№1-NCM », Yakutsk, Republic Sakha (Yakutia), Russia familyafanas@mail.ru,

3. Karina Ilichna Burnasheva, 5 year-course student of Pediatric Department, Medical institute NEFU named after M.K.Ammosov, Yakutsk, Republic Sakha (Yakutia), Russia karivin2015@mail.ru.

METHODS OF DIAGNOSIS AND TREATMENT

V.N. Yadrikhinskaya, T.N. Aleksandrova, I.I. Mulina, A.N. Sannikova, S.N. Parfenova, A.M. Popova, I.E. Soloveva

TREATMENT OF CHRONIC MYELOID THERAPY WITH TYROSINE KINASE INHIBITORS: DRUG TOXICTY AND RESISTANCE TO THERAPY

ABSTRACT

The study was conducted to assess the incidence of tyrosine kinase inhibitors toxicity and resistance to first-line therapy of chronic myeloid leukemia. The results demonstrated that indications to prescription of the second line tyrosine kinase inhibitors are mostly due to significant non-hematologic toxicity. Side effects of mild and moderate degree are represented by general weakness, peripheral edema, headaches, arthralgia. Episodes of hematological toxicity of mild and moderate degree decreased with the prolongation of therapy and don't require treatment withdrawal. Hematological toxicity of the third degree, more often presented by isolated thrombocytopenia, required the drug withdrawal for no longer than 14 days, followed by the resumption of therapy. Study demonstrated cases of development of secondary resistance to imatinib. Optimal response to therapy requires regular clinical and laboratory monitoring for early detection of drug intolerance and resistance to first-line therapy.

Keywords: chronic myeloid leukemia, tyrosine kinase inhibitors, toxicity, resistance.

Introduction

Chronic myelogenous leukemia (CML) is the first oncohematological disease, in which specific changes in chromosomes resulting activation of proto-oncogenes have been described. For many years CML was considered as an incurable and fatal disease with an average life expectancy of about 4 years after diagnosis [6]. Only bone marrow transplantation allowed achieving a long-term remission in 18-20% of patients with chronic phase of CML [8].

Modern understanding of the mechanisms underlying this disease and progress of medical technologies allow using pathogenetical diagnosis and therapy of diseases. The appearance of inhibitors of tyrosine kinase (specific protein) which play a key role in the development of CML, fundamentally changed the tactics of its treatment, making it pathogenetically specific. This allowed to achieve hematological, cytogenetic, molecular remission, increase the overall survival by several times, improve the quality of life and reduce the annual morbidity with the application of the first line tyrosine kinase inhibitor (TKI) – imatinib mesylate (IM)[3].

Currently, three TKI are registered in Russian Federation for treatment of CML: imatinib, nilotinib and dasatinib. IM is the first drug with pathogenetic orientation. It reduces the activation of numerous effector molecules that transmit intracellular stimuli by inhibiting phosphorylation and, thus, prevents subsequent events that induce leukemia transformation. In international randomized IRIS study imatinib demonstrated a significant advantage over a combination of interferon with low doses of cytarabine. Patients with CML in chronic phase showed good tolerability and a high level of complete cytogenetic response (87% of cases) and a major molecular response (39%) [8].

However, subsequently besides high efficacy imatinib demonstrated wide spectrum of side effects, which worsen life quality of patients. Long-term therapy CML with TKI based continuous exposure of drug to the tumor clone, which is not always possible in patients with therapy intolerance (grade III-IV toxicity, long-term grade II toxicity). Involuntary interruptions in drug administration lead to a decrease of effectiveness and may contribute to the disease progression [5]. The development of side effects leads to a decrease in quality of life and compliance, which also affects the efficacy of treatment. According to the literature, the proportion of patients who do not achieve a complete cytogenetic response (CCyR) during 1 year of treatment is 34-35%. In general, the need for a transition from imatinib to second-line TKI therapy is seen in 40-45% of patients with CML [2].

The purpose of the study was to assess the incidence of toxicity and resistance to tyrosine kinase inhibitors.

MATERIALS AND METHODS

The study included 33 patients diagnosed with CML (58,3% women and 41,7% men, mean age 49.6 ± 15.78) receiving therapy with TKI and undergoing regular cytogenetic/molecular monitoring. In 100% of cases, the diagnosis was confirmed by cytogenetic and/or molecular research. The duration of the disease is on the average 7.32 ± 3.64 (from 1 to 18 years).

A retrospective analysis of the patient's medical records for the toxicity and resistance to TKI was carried out. Data taken into account include: patients' complaints, objective examination data, indicators of full blood count, biochemistry, bone marrow examination, instrumental studies and conclusions of specialists consultations. The toxicity of regimens was assessed by the NCI CTCAE scale, proposed by the National Cancer Institute. Imatinib intolerance was defined in patients with chronic CML phase as: non-hematologic toxicity ≥3rd degree, or grade 4 hematologic toxicity lasting more than 7 days, or any non-hematologic toxicity of the 2nd degree, lasting more than 39 days [7].

Dynamics of the response to therapy was assessed based on the data of a clinical blood test, morphological and cytogenetic analysis of the bone marrow and the expression level of the BCR-ABL gene according to polymerase chain reaction (PCR). Laboratory tests were performed according to the terms described in the federal clinical guidelines for the diagnosis and treatment of CML [1].

RESEARCH RESULTS

At the time of investigation, 16 patients (44.4%) are administered with imatinib, 8 patients (22.2%) – nilotinib and 9 patients (25%) - dasatinib. All patients started a ITK therapy with imatinib, in most cases they get therapy in primary care unit. Treatment of patients began with a starting dose of 400-800 mg / day, depending on

the phase in the onset of the disease. In the absence of response to therapy or loss of complete hematologic and / or cytogenetic remission in the process, the dose was increased to 600-800 mg / day. If there were evidence of disease progression or serious side effects, the patients were transferred to other drugs (nilotinib, dasatinib). Pretreatment with hydroxyurea therapy was reported in 7 patients (21.2%), with busulfan in 1 (3.0%). In the onset of the disease, before the treatment with imatinib, two patients underwent chemotherapy according to the protocols for management of blast crisis. The median time from the diagnosis of the disease to the initiation of therapy in patients diagnosed before the era of tyrosine kinases was 7 years (from 4 to 10 years). Since 2005 all patients after diagnosis are included in federal register and receive treatment with imatinib with program «7 high-cost nosologies».

Serious adverse events requiring withdrawal of the drug and transfer to the second-line therapy were detected in 10 patients (30.3%), of which due to non-hematological toxicity in 9 patients (27.3%) and severe hematologic toxicity in 1 (3%). Severe non-hematologic toxicity is manifested by dyspeptic syndrome with prolonged vomiting and diarrhea in 4 (12%) cases, toxic dermatitis - in 2 (6%), significant edema with no response to supportive therapy - in 1 (3%) and cardiotoxicity - in 1 (3%) patients. The most common manifestations of non-hematological toxicity of imatinib are presented in table 1.

Initiation of therapy with imatinib was accompanied by hematologic toxicity of various severity in 13 patients (39.4%). Hematological toxicity of the 1st degree was registered in 5 patients (15.2%), with isolated anemia with a hemoglobin level less than 100 g/l and leukopenia below 3.0 * 109/l being more common. Hematological toxicity of the 2nd degree was registered in 5 (15.2%) patients, including 2-lined cytopenia in 3 (9%) and 1-lined – in 2 (6%). Severe 3rd degree hematological toxicity in 3 patients (9%) manifested by isolated thrombocytopenia (platelet count less than 50 * 10 9/l), in 1 patient by leukopenia (leukocyte level 2 - 1 * 109/L).

During imatinib therapy, 6 patients (18.2%) developed secondary resistance to drug as progression to advanced phases in 5 cases (15.2%) and loss of previously achieved major molecular response (MMR) in 1 (3%). Loss of response in most cases occurred due to irregular intake of the drug. The average duration of therapy with imatinib before the development of secondary resistance was 48.5 ± 19.57 months (from 24 to 72). Progression of the disease has required a course of cytoreductive therapy with hydroxyurea in 1 patient (3%) and a course of chemotherapy with cytarabine in minimal doses in 1 (3%). After loss of the previously achieved response to therapy, 4 patients (12.1%) were transferred to 2nd line TKI, 2 (6.1%) were continued high doses of imatinib.

By 18 months of treatment, 7 patients (21.2%) had not achieved MMR of which 2 (6%) had subsequently lost hematologic, cytogenetic, molecular responses and therefore had been administered with 2nd line of TKI; 3 patients (9%) were transferred to second-line therapy due to drug intolerance; and 2 patients (6%) were continued imatinib therapy with regular cytogenetic / molecular control and dynamics.

The results of this study has established that the most frequent cause of imatinib withdrawal and prescribing 2nd line TKI was drug intolerance due to the development of severe non-hematological toxicity.

As a second-line therapy, 11 patients (33.3%) received nilotinib, 5 patients (15%) received dasatinib. Therapy with 2nd line TKI was accompanied with nonhematoligal toxicity presented with general weakness, periorbital edema, arthralgia as well as imatinib therapy. Nilotinib therapy was complicated by dermatitis in 3 (27%) patients, dyspeptic disorders in 4 (36%), with diarrhea in 1 (9%) and severe abdominal pain in 1 (9%), cardiotoxicity in 1 (9%). Secondary resistance to nilotinib was developed in 3 (6%) patients, including progression of the disease in 1 (3%) and MMR loss in 2 (6%). During follow-up 4 patients (36%) were transferred to 3rd line therapy - dasatinib, due to non-hematologic toxicity (27.3%) and secondary resistance (8.7%).

DISCUSSION

All side effects noted during TKI therapy are reflected in the drugs instructions. The side effects of imatinib were mostly mild or moderate (grade 1 and grade 2) and include fluid retention, nausea, vomiting, fatigue, headaches, joint pain, rash. Particular importance of these side effects is acquired due to the need for a constant intake of drugs ITK. Even mild side effects persistent for a long time can lead to a decrease in adherence to treatment (compliance) – irregular admission, or a decrease in the dose of the drug by patients, which leads to worsening of treatment efficacy. According to the literature, imatinib intolerance is established in 32% of cases, which is an indication for prescribing another TKI, as the profile of non-hematological toxicity of drugs is different and the cross-over intolerance is minimal. In our study, intolerance to imatinib therapy was found in 27.3% of cases, which coincides with the literature data. As the analysis showed, at translating into 2nd line TKI the severity of symptoms decreases. Intolerance to both imatinib and nilotinib was noted in only two patients (6%), who were subsequently transferred to dasatinib with satisfactory tolerability.

Hematological toxicity of the 3rd degree required temporary discontinuation of the drug, for no more than 14 days, with the subsequent resumption of therapy in the previous dose. The manifestations of hematological toxicity decreased with the prolongation of therapy. In one case, prolonged thrombocytopenia with hemorrhagic syndrome required the transition to dasatinib.

Another problem of TKI therapy is the presence of primary and secondary resistance to imatinib. A study of the causes of resistance to imatinib showed that a significant (up to 10 times) increase in the expression of the BCR-ABL gene appears in a number of patients, and the amplification of the gene is found in some cells. In addition, resistance may occur as a result of an irregular intake of the drug. In our study the most patients who developed secondary resistance to imatinib reported irregular drug intake. In some cases adverse drug events can

The most common manifestations of nonhematological toxicity of imatinib

Non-hematological toxicity	Prevalence, % (absolute)
General weakness	63,0 (21)
Peripheral edema	51,5 (17)
Headaches	39,4 (13)
Arthralgia	33,3 (11)
Dyspepsia	24,0 (8)
with vomiting and diarrhea	15,0 (5)
Dermatitis	12,1 (4)
Dysphagia	9,0 (3)

lead to irregular drug intake.

CONCLUSION

The study showed that the need for switching from imatinib to the 2nd line therapy is required in 51.5% of patients. In most cases this requirement is caused by significant non-hematologic toxicity. However, the side effects due to imatinib decreased after administration of the 2nd generation TKI. Cases of cross-over intolerance to all drugs have not been reported. 21.2% of patients had not achieved MMR during recommended time. Careful monitoring of therapy efficacy and safety will help for early detection of drug intolerance and the timely appointment of the second-line therapy, which allows achieving optimal response to treatment, improving the quality of life of patients. Transfer of patients to the 2nd line TKI is complicated by the high cost of drugs and requires the inclusion of nilotinib, dasatinib in the federal program of «7 high-cost diseases».

REFERENCES:

1. Abdulkadyrov K.M., Shuvaev V.A., Martynkevich I.S. Dazatinib: 10 let primeneniya v mirovoy klinicheskoy praktike [Dasatinib: ten years of clinical practice worldwide]. Onkogematologiya [Oncohematology]. Moscow, 2016, №1, V.11, p.24-33.

2. Shuvaev V. A., Fominykh M. S., Martynkevich I. S. [et al.]. Korrektsiya neytropenii i trombotsitopenii, obuslovlennykh terapiey ingibitorami tirozinkinaz pri khronicheskom mieloleykoze [Tyrosine kinase inhibitors therapy related neutropenia and thrombocythopenia correction in CML patients]. Onkogematologiya [Oncohematology]. Moscow, 2016, №4, Vol.8, P.7-12.

3. Savelyeva M.I., Samoylova O.S., Samarina I.N. [et al.]. Otsenka nezhelatel'nykh lekarstvennykh reaktsiy targetnoy terapii u patsientov s khronicheskim mieloleykozom [Assessment of adverse drug effects of targeted therapy in patients with chronic myeloid leukemia]. Kremlevskaya meditsina. Klinicheskiy vestnik [The Kremlin medicine. Clinical bulletin]. Moscow, 2012, №2, P.52-55.

4. Vinogradova O. Yu., Kulikov S.M., S.M. Kutsev. Problemy organizatsii lecheniya khronicheskogo mieloleykoza v Rossii [Problems of the organization of chronic myeloid leukemia therapy in the Russian Federation] Klinicheskaya onkogematologiya [Clinical oncohematology]. Moscow, 2011, №4, Vol.4, P.292-297.

5. Abdulkadyrov K.M., Abdullaev A.O., Avdeeva L.B. [et al.] Federal'nye klinicheskie rekomendatsii po terapii khronicheskogo mieloleykoza [Federal clinical recommendations for diagnosis and treatment of chronic myeloid leukemia] Vestnik gematologii [The bulletin of hematology]. Moscow, 2013, №3, V.9, P.4-43.

6. Drug treatment is superior to allografting as first-line therapy in chronic myeloid leukemia / R. Hehlmann, U. Berger, M. Pfirrmann [et al.]// Blood. – 2007. - №11. – Vol.109. – P.4686–92.

7. Dasatinib induces notable hematolgic and cytogenetic responces in chronic phase CML after failure of imatinib/ A. Hochhaus, M. Hagop Kantarjian., M. Baccarani// Blood. – 2007. – Vol.109. – P.2303-2309.

8. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia / S.G. O'Brien, F. Guilhot, R. Larson R [et al.] // N Engl J Med. – 2003. – Vol. 348. – P.994-1004.

Authors:

1. Yadrikhinskaya Vera Nikolaevna –candidate for medical sciences, M.K. Ammosov North-Eastern federal university, Institute of medicine, associate professor at the department «Hospital therapy, occupational diseases and clinical pharmacology» 677000, Yakutsk, Ojunsky street 27 yadrvera@mail.ru

2. Aleksandrova Tuiara Nikonovna – postgraduate student M.K. Ammosov North-Eastern federal university, Institute of medicine, department «Internal diseases and general medicine» 677000, Yakutsk, Ojunsky street 27 alexandrova_tuyara@mail.ru

3. Mulina Inna Ivanovna – leading visiting hematologist of Ministry of Healthcare of Republic of Sakha (Yakutia), head of department of hematology of Republican hospital №1 «National center of medicine», 677019, Yakutsk, Sergelyakhskoe shosse 4

4. Sannikova Anna Nikolaevna – hematologist, department of hematology of National center of medicine, 677019, Yakutsk, Sergelyakhskoe shosse 4

5. Parfenova Svetlana Nikolaevna – hematologist, department of hematology of National center of medicine, 677019, Yakutsk, Sergelyakhskoe shosse 4

6. Popova Alina Mikhaylovna – hematologist, department of hematology of National center of medicine, 677019, Yakutsk, Sergelyakhskoe shosse 4

7. Soloveva Irina Eremeevna - hematologist, department of hematology of National center of medicine, 677019, Yakutsk, Sergelyakhskoe shosse 4.