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Comparative Evaluation of Antioxidant Activity of Cytoflavin in Various Doses in the Conditions of Cold stress

ABSTRACT

The article reports results of study of the cytoflavin effect in doses of 50 mg / kg and 100 mg / kg on the antioxidant status of rats at chronic cold exposure.

It was established that the studied preparation prevented from stress-induced activity of lipid peroxidation in serum of the animals, exposed to cold. The effect is expressed in less formation of peroxidation products and in the prolonged conservation of a high level of antioxidant system components activity. During the comparative pharmacological analysis it was established that cytoflavin produced a direct antioxidant effect according to a dose during cold exposure on the organism of the experimental animals.

Keywords: antioxidants, cytoflavin, cold exposure, lipid peroxidation, experiment.

INTRODUCTION

Preservation of health and efficiency of people living and working in the conditions of the extreme north is one of the actual directions of medicine. In the zone of high latitudes, which occupy 1/3 of the territory of our country, a person meets with numerous unfavorable factors and temperature is the most important one among them [3, 6, 8, 9]. Prolonged exposure of a low temperature on the human organism may cause the development of such phenomena as syndrome of arctic hypoxia, syndrome of arctic tension, cold hypoxia, cold–associated symptoms [10]. Cold exposure induces the development of critical condition accompanied by exhaustion of energy and other reserves, reduction of tissue metabolism, forming proliferative and dystrophic disorders in all organs [5]. Stage development of consequences of cold exposure leads to polyorganic insufficiency, hypoxia, development of late cold hemolysis, collapse, disturbance of activity of coagulation system, function of the liver and the kidneys [2, 4].

It is known that in the base of any kind of hypoxia there is insufficiency of the main energy forming system of mitochondrial oxidative phosphorylation, conditioned by considerable decrease of oxygen delivery to the tissues or inhibition of oxidative enzymes [1, 11]. At present in the clinical practice compounds of succinic acid, having antioxidant and cytoprotective properties, are used as pharmacological active substances with a wide range of biological activity. Cytoflavin is a balanced complex consisting of two coenzymes vitamins – riboflavin – mononucleotide (vitamin B_2) and nicotinamide (vitamin PP).

Taking into consideration the above mentioned data **the aim** of the investigation is the study of cytoflavin effect in doses of 50 mg/kg and 100 mg/kg on the intensity of lipid peroxidation (LPO) and the condition of antioxidant system (AOS) in the conditions of cold exposure.

MATERIALS AND METHODS

To study the effect of cytoflavin in doses 50 mg/kg and 100 mg/kg on the organism of the experimental animals (white rats-males) cold model of the experiment was made [1]. In the experiment 4 groups of animals with the weight of 200g took part. There were 30 rats in each group: 1- intact group, the animals were in standard conditions of a vivarium; 2 – control group, the animals were exposed to the prolonged cooling in the climatic chamber "Fentron" (Germany) at the temperature -15°C during 3 hours daily within 21 days; 3- experimental group, before cooling the animals were made intraperitoneal introduction of cytoflavin in the dose of 50 mg/kg during 21 days; 4 – experimental group, before cooling intraperitoneal introduction of cytoflavin in the dose of 100 mg/kg was made to the animals during 21 days. The investigation was conducted simultaneously in all groups during 21 days, slaughter of the animals was made by means of decapitation on the 7^{th}, 14^{th}, 21^{th} days of the experiment. The intensity of LPO processes was estimated during examination of the content of lipid hydroperoxides, dien conjugates (according to methods, worked out by I.D. Stal'naja), malonic dialdehyde (according to coloured reaction with thiobarbital acid) and the main components of AOS (ceruloplasmin – according to methods of V.G. Kolb, V.S. Kamyshnikov, vitamin E according to methods of R.Zh. Kiselevich, S.I. Skvarko, catalase and glucose-6-phosphate dehydrogenase according to methods in modification of Ye.A. Borodin) in the rats' serum. Statistical processing of biochemical data was conducted by means of parametrical method with the use of "t" Student criterion.

RESULTS AND DISCUSSION

In the conditions of the prolonged cold exposure during the experiment a reliable increase of the content of dien conjugates (DC) in blood by 38-54% regarding intact animals was observed. Introduction of cytoflavin in the dose of 100 mg/kg in the conditions of cold model promotes a stable reliable decrease of DC content in the blood of the experimental animals during all days of the experiment on the average by 25% in comparison with the control. During the introduction of cytoflavin in the dose of 50 mg/kg considerably less expressed decrease of this index was observed at the end of the second (by 18%) and the third weeks of the experiment (by 4%).

In the control group of animals a reliable accumulation of lipid hydroperoxides (LHP) in the blood by 27%, 40%, 24%, on the 7^{th}, 14^{th}, and 21^{st} days of the experiments was observed

correspondingly regarding intact rats. In the experimental group of animals receiving cytoflavin in the dose 50 mg/kg before cold exposure some decrease of LHP in the serum by 14%, 10%, 5%, was observed on the on the 7th, 14th, and 21st days of the experiment correspondingly and these differences of index were not reliable. The increase of cytoflavin dose to 100 mg/kg led to more pronounced reliable decrease of LHP in the serum during all days of the experiments in comparison with the control group average by 12%-21%, the best result was received by the end of the second week of the experiment, on the 21st day of experiment the level of LHP content in the blood of experimental animals is comparable with analogous index in the intact group.

Thus, by the end of the experiment LHP content in the serum in the group of animals receiving cytoflavin in the dose of 100 mg/kg unlike experimental animals, receiving cytoflavin in the dose 50 mg/kg, became equal with the initial LHP content in the serum of the animals of the intact group. It shows the absolute stabilization of LPO processes.

A reliable increase of malonic dialdehyde (MDA) content by 60-73% in the blood was observed during the experiment in the conditions of cold exposure on the experimental animals. In case of cytoflavin introduction in different doses the the content of MDA in the blood was reliably lower, that in the control animals on the 7th and 14th days of the experiment. Antioxidant effect is more pronounced in cytoflavin in the dose of 100 mg/kg during all days of the experiment (the decrease of MDA content made up 32%-34% regarding the control group), the level of index, against the background of cytoflavin introduction in the of 100 mg/kg on the 21st day of the experiment is comparable with the level of index of the intact group.

The pronounced decrease of concentration of ceruloplasmin by 32-34% in plasma was marked as a result of cold exposure on the organism of the laboratory animals. Against the background of the intraperitoneal introduction of cytoflavin in the dose of 100 mg/kg before the cold exposure the content of ceruloplasmin in plasma inereases by 23%, 32% on the 7th and 14th days of the experiment correspondingly regarding the control and it corresponds to the level of ceruloplasmin in the animals of the intact group by the end of the animals of the intact group by the end of the third week. Cytoflavin introduction in the dose of 50 mg/kg leads to small increase of ceruloplasmin content in plasma by 19%, 7% and 20% on the 7th, 14th and 21st days of the experiment correspondingly regarding the control. Thus, more pronounced effect of normalization of ceruloplasmin level is observed during cytoflavin introduction in the dose of 100 mg/kg.

Against the background of cytoflavin in the dose of 100 mg/kg a reliable increase of vitamin E content by 16% and 24% is marked on the 7th and 14th days of the experiment correspondingly regarding the control group. Cytoflavin in the dose of 50 mg/kg affected considerably less the level of this index (by 2%, 9% and 1%) on the 7th, 14th and 21 days of the

experiment correspondingly, these differences regarding the control group were not authentic. Thus, there is a direct dependence of vitamin E content on the dose of preparation, but in the groups receiving cytoflavin in the dose of 100 mg/kg the effect is achieved and it allows to suppose stimulating effect of this dose of preparation on the intensified production of endogenous vitamin E, it may be a significant factor in prophylaxis of the cold stress.

Cold exposure causes (by 19-17%) the decrease of GL-6-PhDH activity in the blood of laboratory animals in comparison with the intact group. The partial normalization of enzyme activity is observed during all days of the experiment (by 6-7%) against the background of cytoflavin introduction in the dose of 100 mg/kg. Cytoflavin in the dose of 50 mg/kg leads to less pronounced effect partially normalizing GL-6-PhDH activity by the 7th day of the experiment to 7%. By the end of the second week the level of GL-6-PhDH activity is lower that the level of the control group index by 4% and by the 21st day of the experiment GL-6-PhDH activity during cytoflavin introduction in the dose of 50 mg/kg corresponds to the level of the control group.

Thus, cytoflavin in the dose of 100 mg/kg in comparison with cytoflavin in the dose of 50 mg/kg gives more pronounced effect on normalization of GL-6-PhDH activity during its decrease against the background of cold exposure in the control group of animals.

A considerable decrease of catalase activity from (16%, to 27%) regarding group of the intact animals takes place during the experiment in the conditions of cold exposure. Cytoflavin in the dose of 100 mg/kg prevents from the decrease of catalase activity in the blood-partially after the first week of low temperature action (by 8%). In this case level of the intact group is not achieved. After the second week and by the end of the third week of cold exposure the enzyme activity increased by 21-44% in comparison with the control group correspondingly. Effect of cytoflavin introduction in the dose of 50 mg/kg is less pronounced on the 7th and 14th days of the experiment, catalase activity increased by 4-5% correspondingly and on the 21st day of the experiment the level of enzyme activity corresponds to the control group.

As a whole, the examination of LPO products content in the blood, content and activity of AOS components in the conditions of cold exposure and influence on these indices of cytoflavin in the dose of 50 and 100 mg/kg allows to establish antioxidant effect which is more pronounced in the dose of 100 mg/kg.

CONCLUSIONS

1. The possibility of the cold stress correction by means of introduction of preparation "Cytoflavin" which contains succinic acid is confirmed experimentally for the first time.
2. Intraperitoneal introduction of cytoflavin to the laboratory animals (rats) decreases the intensity of LPO processes biomembranes induced by the prolonged cold exposure normalizing stationary level of peroxidation products against the background of a reliable increase of activity of the main AOS components (ceruloplasmin and vitamin E).
3. Statistically significant differences of changes of indices of LPO processes and components of AOS depending on the dose of cytoflavin and the duration of its application are determined (direct dose dependence – in case of application of cytoflavin greater dose, the antioxidant effect is more pronounced).
4. The results of the investigation give the grounds to recommend cytoflavin as an antioxidant as well as regulator of adaptation reactions of an organism at a low temperature.

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Table 1

Content of LPO products in the rats' blood in the conditions of the prolonged cold stress against the background of applying cytoflavin in the dose of 50 and 100 mg/kg

Indices	Group / Periods of experiment	*Group1* intact n = 30	*Group 2* cold (control) n = 30	*Group 3* Cytoflavin in the dose of 50 mg/kg + cold n = 30	*Group 4* Cytoflavin in the dose of 100 mg/kg + cold n = 30
Dien conjugate (nmole/ml)	the 7th day	35,2± 4,3	48,7 ± 3,3* $P_{1,2}$< 0,05	36,1 ± 1,1** $P_{2,3}$ < 0,01	36,8 ± 1,0** $P_{2,4}$ < 0,01
	the 14th day	35,4 ± 3,0	49,2 ± 2,6* $P_{1,2}$< 0,01	40,4 ± 2,7 $P_{2,3}$ > 0,05	36,9 ± 1,1** $P_{2,4}$<0,01
	the 21th day	31,2 ± 2,6	48,1 ± 3,4* $P_{1,2}$ < 0,01	46,3 ± 3,4 $P_{2,3}$ > 0,05	36,6 ± 0,7** $P_{2,4}$ < 0,05
Hydroperoxides (nmole/ml)	the 7th day	26,0 ± 1,8	33,2 ± 1,1* $P_{1,2}$ < 0,01	28,8 ± 2,0 $P_{2,3}$ > 0,05	29,3 ± 1,1** $P_{2,4}$ < 0,05
	the 14th day	25,0 ± 2,7	35,2 ± 1,2* $P_{1,2}$< 0,01	32,0 ± 1,3 $P_{2,3}$ > 0,05	27,9 ± 1,1** $P_{2,4}$ < 0,01
	the 21th day	28,6 ± 1,5	35,6 ± 1,1* $P_{1,2}$ < 0,01	34,1± 1,6 $P_{2,3}$ > 0,05	28,4 ± 1,0** $P_{2,4}$ < 0,01
Malonic dialdehyde (nmole/ml)	the 7th day	3,8 ± 0,1	6,1 ± 0,2* $P_{1,2}$ < 0,001	4,3 ± 0,2** $P_{2,3}$ < 0,001	4,2 ± 0,1** $P_{2,4}$ < 0,001
	the 14th day	3,8 ± 0,2	6,6 ± 0,4* $P_{1,2}$ < 0,001	4,1 ± 0,1** $P_{2,3}$ < 0,001	4,4 ± 0,3** $P_{2,4}$ < 0,01
	the 21th day	4,4 ± 0,3	5,6 ± 0,4* $P_{1,2}$ < 0,05	4,7 ± 0,2 $P_{2,3}$ > 0,05	4,5 ± 0,2** $P_{2,4}$ < 0,05

Notes: * and ** – differences, reliable regarding the intact group* and the control group of animals **

Table 2

The content of AOS components in the rats' blood in the conditions of the prolonged cold stress against the background of application of cytoflavin in the dose of 50 and 100 mg/kg

Indices	Group / Periods of experiment	*Group1* intact n = 30	*Group 2* cold (control) n = 30	*Group 3* Cytoflavin in the dose of 50 mg/kg + cold n = 30	*Group 4* Cytoflavin in the dose of 100 mg/kg + cold n = 30
Ceruloplasmin (mkg/ml)	the 7th day	30,0 ± 1,9	20,5 ± 1,8* $P_{1,2} < 0,01$	24,4 ± 1,8 $P_{2,3} > 0,05$	25,4 ± 0,9** $P_{2,4} < 0,05$
	the 14th day	28,8 ± 1,4	19,1 ± 1,2* $P_{1,2} < 0,01$	20,5 ± 1,5 $P_{2,3} > 0,05$	25,4 ± 1,4** $P_{2,4} < 0,05$
	the 21th day	26,8 ± 1,4	20,3 ± 1,0* $P_{1,2} < 0,01$	24,5 ± 2,0 $P_{2,3} > 0,05$	26,1 ± 1,7** $P_{2,4} < 0,05$
Vitamin E (mkg/ml)	the 7th day	48,7 ± 3,6	37,3 ± 1,5* $P_{1,2} < 0,05$	38,4 ± 1,4 $P_{2,3} > 0,05$	43,5 ± 1,7** $P_{2,4} < 0,05$
	the 14th day	47,5 ± 2,2	34,0 ± 1,6* $P_{1,2} < 0,01$	37,1 ± 1,0 $P_{2,3} > 0,05$	42,2 ± 1,0** $P_{2,4} < 0,01$
	the 21th day	45,8 ± 2,0	38,0 ± 1,8* $P_{1,2} < 0,05$	37,8 ± 2,9 $P_{2,3} > 0,05$	44,4± 1,8** $P_{2,4} < 0,05$
GL-6-PhDH (mcmoleNADFH $л^{-1}c^{-1}$)	the 7th day	6,9 ± 0,2	5,6 ± 0,2* $P_{1,2} < 0,01$	6,0 ± 0,2 $P_{2,3} > 0,05$	6,0 ± 0,3 $P_{2,4} > 0,05$
	the 14th day	6,8 ± 0,2	5,9 ± 0,2* $P_{1,2} < 0,05$	5,7 ± 0,3 $P_{2,3} > 0,05$	6,3 ± 0,1 $P_{2,4} > 0,05$
	the 21th day	6,7 ± 0,3	5,6 ± 0,2* $P_{1,2} < 0,05$	5,6 ± 0,3 $P_{2,3} > 0,05$	6,0 ± 0,2 $P_{2,4} > 0,05$
Catalase (mcmole H_2O_2 $г^{-1}c^{-1}$)	the 7th day	93,0 ± 2,7	78,6 ± 5,1* $P_{1,2} < 0,05$	82,4 ± 3,1 $P_{2,3} > 0,05$	85,0 ± 3,8 $P_{2,4} > 0,05$
	the 14th day	95,2 ± 3,2	72,8 ± 5,9* $P_{1,2} < 0,05$	77,0 ± 3,8 $P_{2,3} > 0,05$	88,8 ± 5,0 $P_{2,4} > 0,05$
	the 21th day	97,0 ± 3,5	71,0 ± 4,2* $P_{1,2} < 0,05$	72,8 ± 3,2 $P_{2,3} > 0,05$	81,4 ± 4,2 $P_{2,4} > 0,05$

Notes: * and ** – differences, reliable regarding the intact group* and the control group of animals **

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THE ANALYSIS OF STRUCTURE OF CHD AMONG NEWBORNS OF RS(Y) ACCORDING TO DATA IN 2002-2004 AND 2011-2013

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ABSTRACT

Growth of registration of CD, including CHD, in recent years, and a tendency to increase in difficult CHD and the critical CHD demanding the high-tech cardiac help in the period of a neonatality and at infancy in the Russian Federation, the leading role of CHD when forming invalidization among children, formed the basis for carrying out the comparative analysis of frequency and structure of congenital heart diseases and large vessels among newborn children in RS (Y) in 2002-2004 and 2011-2013. Research was conducted on the basis of the Perinatal Center State Budgetary Institution RS (Y) RH№1 NCM among live-born newborns. CHD were registered according to the nomenclature headings Q20-Q28 (ICD10). The indicator of frequency was made on 1.000, the live born. According to research growth of frequency of CHD is observed among newborns in comparison with 2002-2004 by 4.7 times.

Keywords: the congenital heart diseases (CHD), congenital anomalies of development of the large vessels, difficult CHD, CHD frequency in RS (Y), CHD structure in RS (Y).

INTRODUCTION

In structure of children's incidence, disability and infantile mortality congenital developmental anomalies, (CD) which meet at 4,0-6,0% of newborns are of all great importance, making more than 20,0% in structure of infantile mortality [1,4]. In structure of congenital developmental anomalies the congenital heart diseases (CHD) and large vessels are high on the list (22% of all CD) and their frequency of birth rate worldwide makes 8-14 cases on 1000 newborns [2]. Frequency of occurrence of CHD among the live-born makes 0.7 to 1000 newborns. In 40% of cases of CHD is the reason of perinatal losses and in 60% of death on the first year of life [5,9]. Birth rate of children with heart diseases makes in the Russian Federation from 3.2 to 8.0 to 1000 newborns and tends to growth [6]. The researchers conducted in the USA and Great Britain, showed that at a natural current of CHD by the end of the 1st year more than 70% of children die, in North America this pathology is the cause of death of 37% of babies, and

in Western Europe – 45% [3,10]. Actuality of this problem is caused not only by their big prevalence, but a tendency to increase in proportion of heavier patients, combined CHD with a frequent failure on the first year of life [7] these data are provided without CHD among dead born and abortions.

Population of RS(Y) according to Goskomstat of Russia makes 955 580 people (2013) [8]. Distinctive feature of Yakutia from other regions of Russia - extremely low population density at the huge territoryб occupied by the republic. It makes — 0.3 people/sq.km (2013). It is one of the lowest among subjects of the Russian Federation. Republic of Sakha (Y) (RS(Y)) steadily is a part of the few regions of Russia in which the natural increase of the population remains. Natural reproduction of the population grew in 2012 in comparison with 2010 by 7,8% (2012 - 8,3 to 1000 population; 2011 – 8,3; 2010-7,7). (to data of Territorial body of Federal State Statistics Service (TO FSGS)). According to TO FSGS, during 2002-2004 the average value of birth rate of urban and country people on RS (Y) made 15,0 to 1.000 newborns; average value infant mortality 14,0 to 1.000. During 2010-2012 the city and country people made an average value of birth rate 17,2; in comparison with 2002-2004, it grew by 2,0 to 1.000. The average value of infantile mortality taking into account new criteria 1) made 7,7 to 1.000 been born the live; in comparison for 2002-2004, an average value of infantile mortality decreased almost by 2 times (by 1,8).

In structure of the reasons of perinatal mortality the specific weight of congenital anomalies of development – by 1,5 times significantly increased: 2012 - 23,9% (56 cases), 2011 - 15,7% (22 cases), 2010 - 16,3% (22 cases). Leaders in structure of congenital developmental anomalies are multiple developmental anomalies (33,9%), heart diseases and the central nervous system (21,4% -each). / the Report of the minister of HS about states of health of the population of RS (Y) 2012/. The condition of disability along with demographic indicators is one of the main characteristics of public health. The main reasons for an invalidization of children in RS (Y) are the congenital developmental anomalies (CDA) of which 48,3% make anomalies of system of blood circulation (the Report of the minister of HS about states of health of the population of RS (Y) 2012). According to the existing order MH Russian Federation No. 268 of September 10, 1998 "About monitoring of congenital developmental anomalies at children" and to No. 392 order MH Russian Federation of 02.11.1999. among all heart diseases and large vessels of obligatory registration and to the account only congenital anomalies of large arteries and "a syndrome of a left-side hypoplasia of heart" are subject, thus at the moment in RS (Y) there is no uniform full monitoring of CHD in nosological forms, including among newborns though primary incidence of CD of bodies of blood circulation, is generally formed by incidence of CHD among newborns. Thus, insufficiently full data on frequency and CHD structure among

newborns in RS (Y), their essential contribution in structure of perinatal and infantile mortality; growth of registration of CD, including CHD, in recent years, and a tendency to increase in difficult CHD and the critical CHD demanding the high-tech cardiac help in the period of a neonatality and at infancy in the Russian Federation, the leading role of CHD when forming invalidization among children, formed the basis for carrying out the comparative analysis of frequency and structure of congenital heart diseases and large vessels at newborn children in RS (Y) for 2002-2004 and 2011-2013.

Work purpose: to study and carry out the comparative analysis of structure and frequency of the congenital heart diseases (CHD) and large vessels among newborns in RS (Y) according to the Perinatal Center State Budgetary Institution in RS (Y) RH No. 1 NCM for the periods 2002-2004 and 2011-2013.

MATERIALS AND RESEARCH METHODS

Research was conducted on the basis of the Perinatal Center State Budgetary Institution in RS (Y) RH№1 NCM among live-born newborns: department of pathology of newborns (DPN), department of nursing of the prematurely born (DNPB), infectious department of newborns (IDN). On time research is conditionally divided into 2 periods: 2002-2004 – the period A and 2011-2013– period B CHD were registered according to the nomenclature headings Q20-Q28 "Congenital anomalies of system of blood circulation'' of the XVII class "Congenital Anomalies [Developmental Anomalies], deformations and Chromosomal Violations" of the International statistical classification of diseases and the problems connected with health (the 10th revision) (ICD10) as primary documentation are used: stationary magazines (form No. 010u пр MH USSR 04.10.1980 No. 1030); statistical cards of the inpatient (form No. 066/u-02 пр MH Russian Federation 30.12.2002 No. 413). Nosological diagnoses of CHD are confirmed with data of an echocardiography of heart with a dopplerography of vessels (EHO-KG with DG), electrocardiograms (ECG), roentgenograms, computer tomograms in angio regime, angiographic researches. The indicator of frequency counted on 1.000, been born the live.

RESULTS AND DISCUSSION

The comparative analysis of structure of CHD according to the Perinatal center State Budgetary Institution RS (Y) RH№1 NCM) for 2002-2004 (the period A) and 2011-2013 (the period B) is carried out. For 2002-2004 (the period A) the analysis of 186 clinical records of newborns with "CHD" diagnoses was carried out. In total it is processed: in OPN 70, in DNPB 56, in IDN 60 stories of diseases of children. For 2011-2013 (the period B) all 899 cases of CHD, among the newborns who have been born alive are registered. In total it is processed: in OPN 433, in DNPB 266, in IDN of 200 statistical cards. In total 1.085 stationary cards were processed. The comparative analysis of frequency of CHD for 2002-2004 and 2011-2013 was

carried out. According to our data, CHD frequency among newborns made 0,19 to 1.000 live-born during 2002-2004 (the period) and 0,9 to 1.000 live-born during 2011-2013 (the period B); т.о. growth of frequency of CHD among newborns in comparison with the period A by 4,7 times is observed. Results of research are presented in table.№1

Table 1

Comparative characteristic of the CHD nosological forms in 2002-2004 and 2011-2013

Form CHD ICD 10	A (2002-2004) - 186		B (2011-2013) - 899		Comparison with A	
	number/frequency	%	number/frequency	%	frequency	%
Q21.0-21.1, Q21.8 VSD, ASD, OOW +.FAC, VSPA	137/ 0,14	73,66	779/0,78	86,65	+ by 5,6	+ to 12,99
Q25.0 OAC	8/0,008	4,30	51/0,05	5,67	+ by 6,25	+ to1,37
Q25.1 Ao Ko	0		21/0,02	2,34		
Q22.1 VSPA	12/ 0,01	6,45	В сочет Q21.0-21.8			
Q22.0 APA	2/0,002	1,08	7/0,007	0,78	+ by 3,5	
Q21.3 T. Fallo	4/0,004.	2,15	10/0,01	1,11	+ by 2,5	- to 1,04
Q21.0 AVC	1/0,001	0,54	10/0,01	1,11	+ by 10 p	+by 2 p
Q26.2-26.3 TADPV, PADPV	1/5/0,006	0,54/2,69/3,23	3/1/0,004	0,33/0,11/0,44		
Q25. Stenosis of LA	4/0,004	2,15	4/0,004	0,45	0	- to 1,7
Q20.3 TMV	2/0,002	1,08	4/0,004	0,45	+ by 2p	- to 0,63
Q20.1 DOMV from RV	1/0,001	0,54	2/0,002	0, 22	+by 2p	0
Q20.4 SV	0		1/0.001	0,11		
Q22.8 Displasia of the TV Q22.5 Ebstein's desease	1/0,001	0,54	4/1/0,005	0,45/0,11	+ by 5 p	0
Q22.6 Atresia of the TV	1/0,001	0,54	1/0,001	0,11	0	0
Q20.0 GAT	2/0,002	1,08	0			
Q23.4 Atresia of the MV	4/0,004	2,15	0			

Q24.5 Anomaly of develop. of CA	1/0,001	0,54	0			

According to the obtained data (table1) among all revealed CHD the leading place on frequency was taken by group of the septal defects/ ventricular septal defect (VSD), atrial septal defect (ASD), the open oval window (OOW) / in combination with the functioning an arterial channel (FAC), the valvate stenosis of a pulmonary trunk (VSPA) which made 0.14 in A and 0.78 period in the period of B. In comparison with the period A group frequency of the septal defects in combination with FAC, VSPA grew with 0.14 to 0.78, i.e. by 5,6 times. Defects of large vessels / the isolated open arterial channel (OAC), Coarctation of the aorta, or aortic narrowing (abbreviated as CoA[1]), the abnormal drainage of pulmonary veins (ADPV), a stenosis of a pulmonary artery (LA stenosis) / came with a frequency of 0,02 and 0,08 in the periods A and B, from them CD of large arteries – 0,008 and 0,07, CD of large arteries (PDA, CoA) unambiguously prevail in the period of B. In structure of CD of large arteries (PDA, CoA, LA stenosis) in both periods isolated PDA most often met – 8/0,008 and 51/0,05, the increase in frequency of PDA is probably connected with diagnostics improvement. CoA frequency made 0.02 (21cases), all cases are diagnosed in the period of B. The received results can be explained with improvement of beam methods of diagnostics CoA since this pathology in 100% of cases is confirmed with results of RCT with a contrast angio research. The stenosis of LA met identical frequency of 0,004. In structure of CD of large veins of ADLV met with frequency of 0,006 (total / 1 and partial / 5) in A period and 0,004 (total / 3 and partial / 1); but for the period B total ADLV (ADPV) - 3 cases that can speak about "weighting" of this CD and about improvement X-ray contrast methods of diagnostics. Frequency of a tetrad of Fallo (T. Fallo) made 0,004 (4 cases) during A and 0.01 (10 cases) for the period B; the increase in frequency of T. Fallo by 2,5 times is observed. More often the share of anomaly of Ebstein became registered– 4 cases and other congenital anomalies of the tricuspidal valve (congenital anom. TV) – 1 case that made 0,005 in comparison with the period A - 0,001; growth of frequency of this pathology by 5 times is observed. According to our data, the increase in frequency of the revealed general atrioventricular channel (G. FVC) by 10 times (0,01 period B) in comparison with the period A (0,001) is observed. Frequency of valvate CHD decreased: with 14/0,01 to 8/0,008, at the expense of isolated VSPA (12 cases in the period A, in the period B weren't registered). The atresia of the tricuspidal valve (atresia of the TV) as a part of a syndrome of a hypoplasia of the right compartments of heart came to light equally (1 case - each), it is observed increase in frequency of an atresia of the LA valve (APA) - 7/0,007 with the period A – 2/0,002. Frequency of the transposition of the main vessels (TMV) made 0,002 (the period A) and 0,004 (the period

B). Frequency of a double outlet of the main vessels from the right ventricle (DOMV from RV) 0,001 (the period A) and 0,002 (the period B). In the period A the syndrome of a hypoplasia of the left compartments of heart with an atresia of the mitral valve (atresia of the MV) met the frequency of 0,004 (4 cases), in the period In this CHD wasn't observed. As in the period A 1 case (frequency 0,001) anomalies of development of coronary arteries (anomaly of develop. of CA): coronary-pulmonary fistula. In total difficult and combined CHD were registered with a frequency of 0,03 (32 cases) in A and 0,04 period (42 cases) in the period B.

The comparative analysis of structure of CHD was carried out in periods 2002-2004 and 2011-2013. According to the presented data table.№1 in CHD structure traditionally leading place was taken by a group share of the septal defects (VSD, ASD, VSD+ASD, open company), in combination with FAC, VSPA which made 73,66% (137/frequency 0,14) in the period A and 86,65% (779/frequency 0,78) in the period B. In comparison with the period A the share of the septal defects in combination with FAC in structure of revealed CHD grew from 73,66% to 86.65% (for 12,99%). Defects of large vessels (isolated PDA, CoA, LA, ADLV stenosis) made only 9,68% (18) and 8,90% (80) of all revealed cases of CHD. In CD group of large vessels CD of large arteries in the period In – 95% (76 cases unambiguously prevail: PDA, CoA and LA stenosis); whereas in the period A it made 66,66% (12 cases: PDA, LA stenosis). In structure of CD of large arteries in the period A first place was won by isolated PDA – 8 of 12 cases (66,66%), CoA didn't happen, LA stenosis - 4 cases from 12 (33,34%). In the period B as isolated PDA – 51 of 76 cases (67,10%) most often met, on the second place met CoA – 21 cases from 76 (27,63%), on the third place LA stenosis - 4 cases from 76 (5,26%). Received results: CoA identification which occupied one of leading places in structure of CD of large arteries in the period B, can be explained with considerable improvement of quality of diagnostics, including active use of beam, X-ray contrast methods of research in recent years. CHD of large veins (all cases-ADLV): in ADLV structure in the period A unambiguously partial ADLV of 83,33% (5 of 6 cases) whereas in the period B the increase in a share of total ADLV – 75% (3 of 4 cases) was observed, and a share partial prevailed made 25% that can speak about "weighting" of this CD, and as improvement of X-ray contrast methods of diagnostics. T. Fallo's share made 2,15% (4) during A (186) and 1,11% (10) during B (10) from all revealed CHD (899). Some reduction of a share of T. Fallo, for 1,04% is observed. In structure of all CHD in recent years, but increase in its frequency (0,004 and 0,01). The share of anomaly of Ebstein and other congenital anomalies of TV made 0,54% (1 case) in the period A and 0,56% (5) in the period B. Share of groups of valvate CHD (VSPA, APA): in the period A made 7,53%-14 cases (VSPA-12, a LA valve atresia - 2); in the period B made 0,78%-7 cases, all cases were made by an atresia of the LA valve isolated by VSPA didn't come to light. Reduction of a share of valvate

CHD by 7%, twice, in the period B, at the expense of VSPA was observed. 0,54% fell to the share of G. AVC (1) in the period A and 1,11% (10) of all cases of CHD in the period B, e.i. the increase in a share of AVK in structure of all CHD twice in the last years (and increase in frequency by 10 times) was observed. The share of TMV made 1,08% (2) in the period A and 0,45% (4) in the period of B. Difficult defects made 12,37% (23 cases) of CHD total in the period A and 4,67% (46) of all quantity of revealed CHD in the period of B According to our data in structure of difficult defects in nosological forms the increase in a share of such CHD was observed as T. Fallo (for 4,55%), APA (for 6,52%), T.ADPV (for 2,17%) in the period of 2011-2013, in comparison with 2002-2004. The share of G.AVC in structure of difficult defects increased by 5 times (!), a share of anomaly of Ebstein twice in the period of 2011-2013, in comparison with 2002-2004. TMV share (8,7%) and DOMV from RV (4,35%) remained without changes. Reduction of a share of a stenosis of LA in structure of difficult CHD-for 8,69% in recent years, in comparison with 2002-2004 was observed. Other defects (the SV, the Atresia of the TV (syndrome of a hypoplasia of the right compartments), the Atresia of the MV (syndrome of a hypoplasia of the left compartments) were registered 1 time in 3 years. The lethality in the period A made 3,22% (6 cases) of total number of cases of CHD and was generally formed due to difficult defects of 66,67% (4 cases) from all cases of a lethality (6). The lethality in the period made 1,22% (11 cases), from total of children with CHD (899) and was formed due to difficult defects (5), obstructive damages of an aorta (4), a combination of the septalny defects with Edwards's syndrome (2).

CONCLUSIONS

According to our data, CHD frequency among newborns made 0.19 (186) to 1.000 live-born during A and 0,9 (899) on 1.000 live-born for the period B; i.e. growth of frequency of CHD among newborns in comparison with the period A by 4,7 times is observed. In CHD structure the leading place was taken by a group of the septal defects (VSD, ASD, VSD+ASD, OOW), in combination with FAC, VSPA which made 73,66% (137/frequency 0,14) in the period A and 86,65% (779/frequency 0,78) in the period B. In comparison with the period A the share of the septal defects in combination with FAC in structure of revealed CHD grew from 73,66% to 86.65% (for 12,99%), and on frequency with 0,14 to 0,78, i.e. by 5,6 times.

Defects of large vessels: isolated PDA, CoA, ADLV, a stenosis of LA came with a frequency of 0,02 (9,68% of all CHD) and 0,08 (8,90% of all CHD) in the periods A and B, from them CD of large arteries – 0,008 and 0,07, CD of large arteries (PDA, CoA) unambiguously prevail in the period of B. Difficult and combined CHD were registered with a frequency of 0,02 (23 cases) in A and 0,05 period (46 cases) in B period and made 12,37% in the period A and

4,67% in the period B from all quantity of revealed CHD. In structure of difficult defects in nosological forms, in comparison with the period A, the increase in a share and frequency of such CHD as it is APA (for 6,52%, frequencies in 3,5 t), by T. Fallo (for 4,55%, frequencies in 2.5 t), T. ADPV (for 2,17%, frequencies in 3 t), G.AVC (shares by 5 times, frequencies by 10 times), Ebstein's anomalies (shares twice, frequencies in 4 t). TMV share: 8,7% and DOMV from RV: 4,35% remained without changes for both periods, frequency increased twice in comparison with A. Reduction of a share of a stenosis of LA in structure of difficult CHD - by 8,69% was observed, frequency remained without changes in recent years, in comparison with the period A other defects (the SV, atresia of the TV, atresia of the MV) were registered 1 time in 3 years. Lethality reduction from 3.22% of the period A to 1,22% of the period (for 2%) was observed.

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Effect of Systemic Retinoids on Proteins Oxidative Modification during the Treatment of Patients with Acne in Dynamics

T.V. Kopytova, E.V. Kotkova, N.A. Dobrotina

ABSTRACT

32 patients with acne were surveyed to study changes in total protein oxidative modification of blood. Along with the generally accepted clinical and laboratory findings in patients electrophoresis of serum proteins by the severity of oxidative stress on the content of carbonyl derivatives (in spontaneous oxidative modification of proteins) was determined.

It is proved that the treatment of acne patients with systemic retinoids is accompanied by oxidative modification of serum proteins. The consequence of these processes can be aggravating oxidative stress and increased body harmful effects caused by free radicals in tissues.

Considering not sufficient study of the effects of systemic retinoid therapy, the treatment of acne should be strictly controlled, and in the selection of the dosage form should be dominated by the principles of more bioavailability and maximum effective dosage.

Keywords: acne, oxidative modification of proteins, reactive oxygen species, protein electrophoresis, isotretinoin.

INTRODUCTION

Acne (syn: vulgaris) - extremely common worldwide chronic skin disease that affects both teenagers and adults. Different forms of acne occur in 80% of adolescents in puberty, thus, 20% of patients revealed severe illness accompanied by the formation of deep scars, virtually no effective treatment [9,10]. Besides long-term physical effects, severe acne cause psychological suffering, causing disruption of social adaptation and the development of depression. This dermatosis characterized by the severity of the inflammatory process, damaging the connective tissue with metabolic disorders of the skin and subcutaneous tissue, causes a change in the microbial landscape.

In the etiology and pathogenesis of inflammatory processes of the skin, acne have different value system interrelated factors: - the accumulation of DHT in the sebaceous glands; - Family history; - Change in the skin metabolism and other systems; - Seborrhea; - Follicular hyperkeratosis; - Violations of immune homeostasis, functions of the endocrine glands and the gastrointestinal tract; - Colonization of microorganisms; - Environmental factors and others [10,11].

Metabolic processes in the body during normal operation of hemostasis systems are accompanied by the formation of free radicals and reactive oxygen species. The content of free radicals at the physiological level is controlled with balanced work of pro- and antioxidant systems. Imbalance due to the activation of prooxidant system leads to an intensification of a free-radical process [7] and of the oxidative stress. Under these conditions a carbonyl compound having a cytotoxic effect [3,13].

Under pathological conditions effective traps generated active oxygen species are lipids, nucleic acids, proteins. The presence of pronounced peroxide oxidation of these substrates have been shown in patients with severe chronic dermatoses [5,12] and, in particular, acne [1]. However, oxidative modification of proteins (OMB) number of authors is regarded as one of the early and reliable markers [14].

Currently being sought therapy protocol based torpidly occurring acne. In the treatment of severe forms of the disease are increasingly using the system, the active ingredient isotretinoin, a chemical analog of vitamin A. These drugs are known for their cytotoxicity and even teratogenic. [2,6,8] Therefore, control of the state and destructive oxidative processes in proteins for the treatment of inflammatory processes of the skin with isotretinoin may be important in the selection of the dose and type of drug.

The purpose of the research is to study changes in the general oxidative modification of blood proteins in normal and acne treatment with systemic retinoids dynamics.

MATERIALS AND METHODS

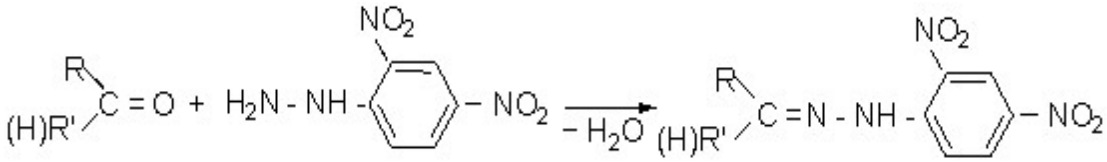
We examined 32 patients with acne. The average age of the surveyed was 21,3 ± 3,7 years. In the patient treating drugs with isotretinoin (aknekutan and roaccutane) were used.

Therapy with aknekutan or roakkutan prescribed for long term (average rate - 4-9 months). For each patient, the dose is calculated individually depending on the weight and shape of acne.

Roaccutan is used in Russia for over 20 years in capsules of 10 mg and 20 mg. Aknekutan appeared in Russia in 2010 and produced by innovative technology Lidose, developed and patented in Belgium. Product produced in capsules of 8 mg and 16 mg.

22 patients were treated with aknekutan, 10 with roakkutan. To treatment were excluded patients with dysfunction of the gastrointestinal tract, liver and lipid metabolism. The control group consisted of 20 healthy subjects of comparable age with no signs of cutaneous pathology. 3 surveys were conducted of patients: the first before treatment with systemic retinoids, the second - after 1 month, the third - after 2 months of treatment. During each assessment the study of serum protein fractions by electrophoresis was performed to determine the degree of spontaneous OMB on the level of carbonyl derivatives [3]. The basis of our method is the

definition of serum amounts of 2,4-dinitrophenylhydrazone of oxidized amino acid residues, which are formed as a result of oxidative processes in the protein molecule (Fig. 1).



Carbonyl derived protein

2,4-dinitro-phenylhydrazine

2,4-dinitrophenylhydrazone

Fig. 1. Reaction of carbonyl derivatives protein (aldehydes and ketones) with 2,4-dinitrophenylhydrazine

Absorbance formed by aldehyde and ketone-dinitro phenylhydrazone was recorded on SF-56 spectrophotometer (Spectrum Lomo, Russia) at wavelengths of 270 nm (aldehyde derivatives of neutral character), 430 nm (aldehyde derivatives main character), 370 nm (ketone derivatives neutrality), 530 nm (ketone derivatives main character).]

For data processing program Microsoft Office Excel 2010 was used.

RESULTS AND DISCUSSION

To characterize the protein homeostasis in patients with acne, we performed a serum protein electrophoresis. In the dynamics of treatment we revealed Dysproteinemia characterized by a statistically significant increase in α2 and β-globulin (Table).

Table

Indicators of electrophoretic separation of serum proteins at norm and acne (M ± m), %

		Albumins	α_1	α_2	β	ϒ
Before treatment (n=32)		54,21±0,65	3,78±0,07*	10,12±0,17*	12,21±0,47*	19,65±0,67
aknekutan	After 1 month	55,09±0,99	3,97±0,15	10,48±0,48*	11,94±0,42	18,51±0,58
	After 2 m-s	57,95±1,85	3,44±0,22*	9,13±0,39	10,98±0,75	18,49±1,25
roakkutan	After 1 month	58,00±2,6	3,78±0,17*	10,26±0,74	10,29±0,59	17,11±1,86
	After 2 m-s	51,58±0,99	4,17±0,43	11,18±0,99*	12,39±0,47*	20,66±1,45

*- statistically significant differences with the control group ($p < 0.05$)

Taking into account the available literature data, it indicates not only acute, but also on the severity of dermal manifestations. Note that hypergammaglobulinemia is not detected and it may indicate a possible immunodeficiency. Upon repeated dynamic examination of patients after

30 and 60 days, the ratio of protein fractions in serum was normalized. Thus, patients had acute-phase inflammatory response.

To modify the content of oxidative modification of proteins (aldehyde and ketone groups) we can predetermine the degree of cell damage under oxidative stress, as well as the reserve capacity of the organism to peroxidation. In the study of spontaneous OMB in the serum of patients we found a significant increase in the level of aldehyde groups neutrality of 1.5 times and ketone groups neutrality of 1.6 times in patients with acne relative to the control group. The level of ketone main character groups significantly reduced of 4.2-fold (Fig. 2).

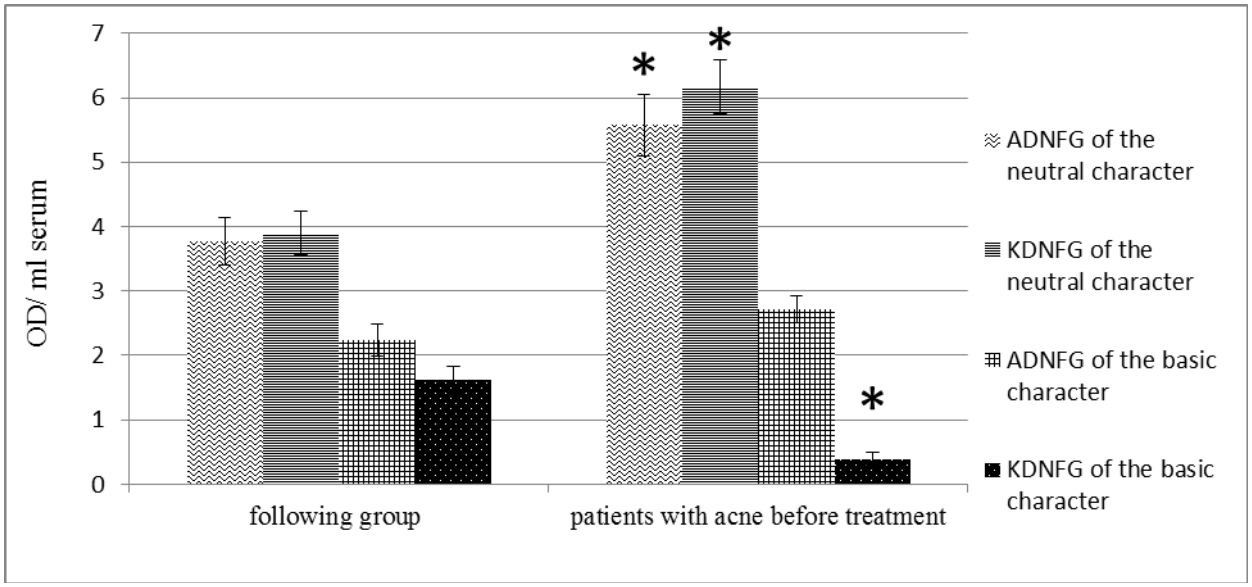


Fig. 2. The level of carbonyl derivatives of proteins in blood serum of the control group and patients with acne

* - statistically significant differences with the control group ($p < 0.05$)

ADNFG - aldehyde-dinitrophenylhydrazone

KDNFG - ketone-dinitrophenylhydrazone

Increasing the level of aldehydic and ketonic groups in patients with acne indicates that for inflammatory processes and in the conditions of oxidative stress different tissue damage occurs, including the cellular level. Reduction of ketone main character groups happens probably due to the process of intensive destruction of oxidized amino acid residues of the protein.

Treatment of acne with isotretinoin leads to normalization of the increased activity of the sebaceous glands, but its toxicity can lead to excessive formation of free radicals and the inability of the antioxidant system to neutralize them [4,7]. This was confirmed by an increase in serum levels of carbonyl derivatives during the second examination of patients. After a month of treatment with aknekutan the level of ketone groups increased by 1.3 times, and by 1.2 times for the treatment with roakkutan, compared with those before treatment (Fig. 3).

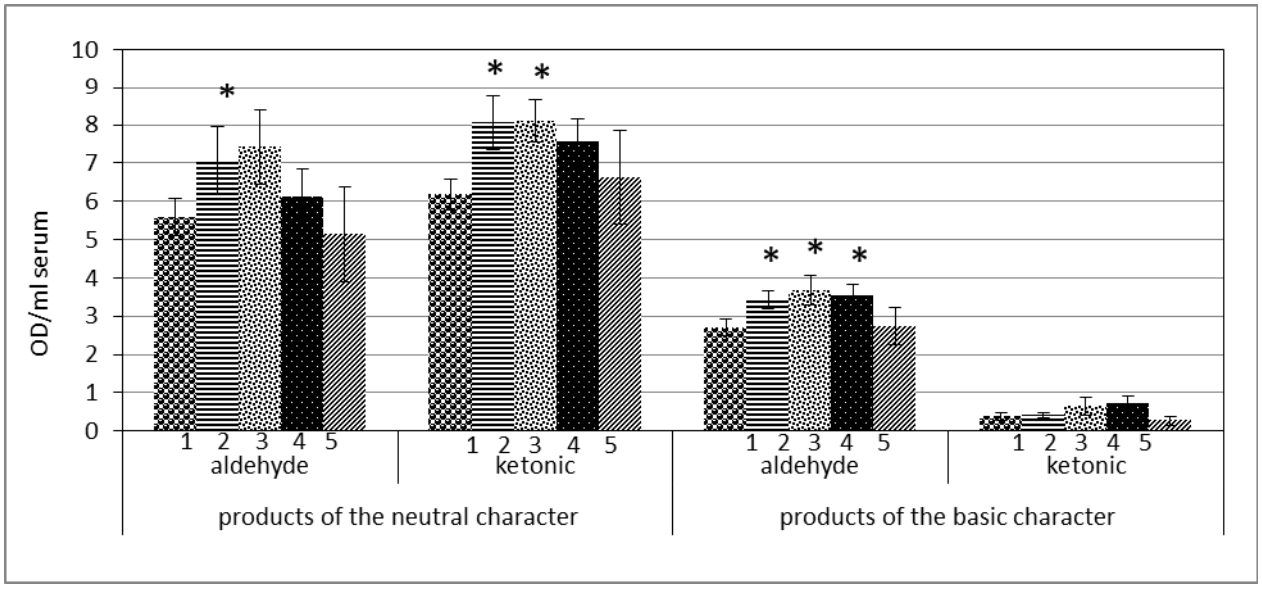


Fig. 3. The level of carbonyl derivatives for the oxidative modification of protein before the treatment with Isotretinoin (1), for the treatment with aknekutan after 1 month (2), after 2 months (3), for the treatment with roakkutan after 1 month (4), after 2 months (5).

* - statistically significant differences to before treatment ($p < 0.05$)]

At the final examination in the course of the treatment with aknekutan still celebrated slightly elevated levels of ketone groups. In the other hand, the result of the treatment with roakkutan leads to indicators reducing to the level specified in the beginning of therapy. None of the tested parameters were observed normalization parameters.

When comparing the level of aldehyde groups statistically significant increase ADNFG neutrality, both before and during the treatment relative to the control group. ADNFG a basic level significantly increased (average 1.3 times) a month after treatment with both drugs. In the third survey studied indices significantly reduced as a result of treatment with roakkutan and the treatment with aknekutan remain high.

RESULTS

It is proved that the treatment of acne patients with systemic retinoids is accompanied by oxidative modification of serum proteins. The consequence of these processes can be aggravating oxidative stress and increased body harmful effects caused by free radicals in tissues.

Considering not sufficient study of the effects of systemic retinoid therapy, the treatment of acne should be stemic retinoid therapy; the treatment of acne should be strictly controlled, and in the selection of the dosage form should be dominated by the principles of more bioavailability and maximum effective dosage.

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Features of the Functional State of Vascular Endothelium in Elderly Patients after Splenectomy

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ABSTRACT

We studied functional state of arterial wall endothelium in elderly patients after splenectomy due to trauma of spleen in close post-operational period. Data showed that antithrombotic features of endothelium has changed heterogeneously, i.e. intensification of fibrinolytic activity due to low thromboresistance of endothelium, which is accompanied by reduced tissue plasminogen activator (tPA) in vascular wall and reduced secretion of it to bloodstream. This data suggests that certain biologically active substances are secreted by spleen, which facilitates release of tPA from endothelium, which in turn can lead to intravascular thrombus formation in these group of patients.

Keywords: splenectomy, functional state of arterial wall endothelium, elderly patients.

INTRODUCTION

Splenic rupture with abdominal trauma occurs in 23 - 40% of the victims [2,4,6]. The structure of the spleen, the fragility of its parenchyma cause significant bleeding even at small lesions of the capsule and make it impossible to achieve reliable hemostasis, owing to surgical treatment of the damaged organ in most cases ends with splenectomy [2]. However, it is proved that the spleen belongs to a number of important functions, the main of which - participation in hematopoiesis and immune status of the body [4]. It is noted that in patients who underwent splenectomy, there were disorders in the coagulation system. They appear as the development of hemorrhage and thromboembolism. However, if the application of autolientransplantation in pediatric patients, young and middle age does not cause doubts, but in elderly patients application of this method is controversial enough.

The purpose of the study - to examine the state of vascular endothelium in elderly patients after splenectomy performed about her injury in the immediate postoperative period.

MATERIALS AND METHODS

Studies of endothelial function of the vascular wall were performed in 21 elderly patients (study group 1) after surgery on a damaged spleen in the immediate postoperative period in the third - the fifth postoperative day. Comparison group consisted of relatively healthy elderly patients in the number of 19 persons (control group 2) and patients young and middle age in an amount of 19 people after splenectomy performed on the injured spleen (control group 3). All patients (elderly and young and middle age) had isolated splenic injury, light amount of blood loss, all patients underwent splenectomy. Study of the state of vascular endothelium of patients operated on the spleen was performed using functional cuff test, proposed by V.P.Baluda et al. (1992) [5]. The principle of the antithrombogenic properties of vessel walls based on the creation of a three-minute local ischemia caused by overlaying a sphygmomanometer cuff on the arm of the subject and creating pressure in it exceeds systolic 10 mmHg. This leads to the release of the vascular endothelium in the blood of healthy people prostotseklina, nitric oxide, endothelin and other natural antiplatelet agents (antithrombin III, tissue plasminogen activator). This study provides an examination of antiplatelet, anticoagulant and fibrinolytic activity of vascular endothelium. To characterize the functional state of the vascular endothelium, we used indexes of vascular wall thromboresistance, characterizing it antiagregatine, anticoagulant and fibrinolytic activity [5]. The test results attributed to positive in the event that after the creation of local ischemia observed increase in activity of more than 25%

from the data obtained before creating ischemia and activity of fibrinolysis activators and increased by 30% or more of the data obtained prior to the establishment of ischemia. It is proved that patients with these characteristics are not subject to intravascular thrombus formation [1]. In patients with increased anticoagulant activity and the growth activity of activators of fibrinolysis by 15-30% after local ischemia of the extremities possibility of thrombotic complications with additional exposure of the body to extreme factors considered doubtful. With a slight strengthening of the anticoagulant and fibrinolytic activity, as well as an increase in the activity of fibrinolysis to 15-20% results cuff test is considered negative, these patients are attributed to thrombotic dangerous [1].

Statistical data processing was performed using a nonparametric method U-test test Mann - Whitney (software package Statistica 6.0.). In this case, we calculated the main probabilistic characteristics of random variables: the average value; lower (25%) and the upper (75%) Quartile that have accuracy of not less than 95% ($p<0.05$).

RESULTS AND DISCUSSION

Results of the study of the functional state of the vascular endothelium in relatively healthy elderly patients are presented in Table. 1 The data presented in Table 1, it is seen that after the occlusion test in healthy elderly non-stabilized blood clotting time increased by 88.0%, the activity of antithrombin III – 45,1%, in euglobulin fibrinolysis - 17, 1%, and the activity of tissue plasminogen activator - by 25,5%. Indicators antithrombogenic activity of vascular endothelial thus correspond to the data of healthy persons, established by other authors [3,4,5].

Table 1

Some indicators of the hemostatic system in relatively healthy older people before and after the occlusion test (M ± m)

Indicators	The results of the comparison group (n = 19)	
	tosample	afterthetest
The clotting time of blood unstabilized, min	7,5 ± 0,3	14,1 ± 0,3*
Activity of antithrombinIII, %	86,3 ± 0,4	125,2 ± 0,1*
Euglobulinfibrinolysis,min	180,6 ± 0,2	154,2 ± 0,2*
The activity of plasminogen activators, mm^2	66,4 ± 0,3	83,2 ± 0,1*

Note: * - a sign of the significance of differences compared with the data before the occlusion test ($p <0,05$)

Occlusion test results obtained in the group of patients after splenectomy in patients young and middle age in the immediate postoperative period showed that the clotting time of a non-stabilized blood increased by 67.7%, the activity of antithrombin III - 41.5%, euglobulin fibrinolysis - 111, 6%, and the activity of plasminogen activators - by 13.3%, indicating that the stored anticoagulant activity of vascular endothelium. At the same time relative to the comparison group of relatively healthy elderly showed some decrease in the fibrinolytic activity of the vascular wall.

Occlusion test results obtained in patients after splenectomy in elderly in the immediate postoperative period, are presented in table 2.

Table 2

Some hemostatic parameters in elderly patients after splenectomy in the immediate postoperative period before and after the occlusion test (M ± m)

Indicators	The results of the comparison group (n = 21)	
	tosample	afterthetest
The clotting time of blood unstabilized, min	6,0 ± 0,3	9,0 ± 0,3*
Activity of antithrombinIII, %	82 ± 0,4	102,0 ± 0,2*
Euglobulinfibrinolysis,min	182,1 ± 0,4	140,1 ± 0,2*
The activity of plasminogen activators, mm^2	67,4 ± 0,3	74,4 ± 0,2*

Analyzing the results, it can be noted that in the group of elderly patients after splenectomy marked increase in blood clotting time of a non-stabilized 60% in the comparison group - by 88,0%, ($p < 0,05$), the activity of antithrombin III - 38% in the comparison group increase this figure was 45,1% ($p > 0,05$). Euglobulin fibrinolysis by 23,4% in the comparison group - by 25,5% ($p < 0,05$). Activity of plasminogen activators by 13,2% in the comparison group - by 25,3% ($p < 0,05$).

Thus, in the immediate postoperative period, removal of the spleen leads to changes in the functional state of the vascular endothelium, is evident in vascular endothelium thromboresistance.

For indices that characterize the antithrombogenic activity of the vascular endothelium, are presented in table 3.

Table 3

Indicators antithrombogenic activity of the vascular wall of patients operated with the trauma of the spleen, in the immediate postoperative period (M ± m)

Indicators	Resultsinthebands		
	main group	1 comparisongroup	2 comparisongroup
The index of vessels total thromboresistance	1,67 ± 0,4*	1,84 ± 0,3	1,88 ± 0,3
Index anticoagulant activity	1,42 ± 0,1	1,43 ± 0,3	1,45 ± 0,2
Index of fibrinolytic activity	2,11 ± 0,2*	1,21 ± 0,3	1,17 ± 0,1

CONCLUSION

Thus, obtained in the study data suggest that in the elderly patients operated at a trauma of the spleen, in the immediate postoperative period after splenectomy antithrombogenic properties of vascular endothelial are changed inhomogeneously: amid falling thromboresistance of vascular endothelial fibrinolytic activity has increased, accompanied, however, by decrease of tissue plasminogen activator reserves in the vascular wall and decrease of its secretion into the bloodstream. These data suggest that the spleen tissue produced bioactive substances which promote the release into the blood stream of produced in the endothelium of tissue plasminogen

activator, which in turn may lead to the development of intravascular thrombus formation in these patients.

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Syndrome of Amyotrophic Lateral Sclerosis at Vilyui Encephalomyelitis

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ABSTRACT

The review presents clinical polymorphism of Vilyui encephalomyelitis, variability and characteristics of the disease, when it is accompanied by the syndrome of amyotrophic lateral sclerosis. Diagnostic criteria and work-up in the differential diagnosis of Vilyui encephalomyelitis and classic amyotrophic lateral sclerosis are described.

Keywords: Vilyui encephalomyelitis (VEM), amyotrophic lateral sclerosis (ALS), a clinical polymorphism, bulbar palsy, pseudobulbar palsy.

Vilyui encephalomyelitis (VEM) is a severe progressive inflammatory disease of the Central Nervous System, with diffuse panencephalitis spreading of the pathological process, with often fatal outcome within a few months to 5-6 years or profound disability of the patient and affects mainly the aboriginal population of Yakutia.

The disease lies in the necrotic and inflammation processes, mainly in the gray matter of the brain. Pathologic studies the necrotic and inflammatory changes of the meninges or their consequences were detected in all patients with acute, subacute and chronic VEM. Micronecrotic lesions and inflammatory response to these lesions are widely spreading in the cerebral cortex, basal ganglia, cerebellum and brainstem. The inflammatory reaction manifested acutely with acute micronecrotic brain tissue lesions and continuing during the prolonged subacute phase are distinguishing features of VEM, but not short like usually in acute viral encephalitis [1, 2, 22].

VEM problem remains relevant to this day on the background extinction VEM epidemic that began in the 50th of the last century in Viliuisk areas [3, 13, 19]. But significant reduction in incidence in recent years does not guarantee that the epidemic Viliuisk encephalomyelitis will not flare up with renewed vigour, while still remain unresolved until the end of the etiology and pathogenesis of the disease and consequently not as specific tests for its detection and etiotropic treatment. Vilyui encephalomyelitis is the disease calling the relentless universal scientific interest in it, both in Russia and in the World, as evidenced by numerous publications in Russian and foreign literature. An evidence of this are the words spoken by the professor, laureate of the Nobel Prize in Physiology and Medicine in 1976 Member of the National Academy USA of D. Carleton Gajdusek: «Every neurologist in Europe and the United States knows about Viliuisk encephalomyelitis from our publications in journals «Brain» and «Science», of our lectures, and from the chapter on Vilyui encephalomyelitis of the textbook Richard Johnson on Infectious Diseases of the nervous system. In 2014 a group of authors headed by L.G. Goldfarb (National Institute of Neurological Disorders and Stroke, Bethesda, Maryland, USA) – N.M. Renwick (Rockefeller University, New York), V.A. Vladimirtsev and F.A. Platonov (Institute of Health NEFU), prepared for the publication of a joint monograph "Viliuisk encephalomyelitis", which is dedicated to the memory of Procopius, A. Petrov, who was a pioneer-discoverer of the Viliuisk encephalomyelitis, "the most loyal and consistent knight science", by definition of D.C.

Gajdusek. This monograph summarizes all known data on the study of this disease for more than 60 years, highlighted the pathogenesis of the disease. The release of the monograph is the result of long-term and comprehensive study of this deadly disease. In addition, it will help practitioners - neurologists in the differential diagnosis of a large variety of inflammatory and neurodegenerative diseases of the nervous system, as well as for the medical examination of new cases and patients with chronic disease.

As the result of development of the VEM as the panencephalitis, most patients receive a combination of pyramidal, extrapyramidal and cerebellar disorders, which for a post mortem examination corresponds to lesions in the subcortical gray matter formations: a black substance, own nuclei of the pons, the inferior olive, reticular formation of the pons, medulla and cerebellum. As a result of diffuse lesions of these structures, the disease is accompanied by a wide clinical polymorphism and thus quite often - the development of the syndrome of Amyotrophic Lateral Sclerosis in the acute [16] and the terminal stages of the disease [12,14,15,18]. Syndrome of Amyotrophic Lateral Sclerosis is caused by destruction of the gray matter of the spinal cord in the anterior horn and the intermedial part.

Amyotrophic Lateral Sclerosis (ALS) is a severe neurodegenerative disease, which is accompanied by the electoral defeat of the Central and peripheral motor neurons, rapidly progressive course with the inevitable death. Despite the study of this fatal disease since the late Nineteenth Century, the etiopathogenesis of ALS, as well as VEM, to date, remains poorly understood [6].

Recent observations of the occurrence of cases of VEM and epidemiological studies of ALS, conducted in Yakutia, show a significant decline an epidemic VEM over the last 20-year period on the one hand, and a tendency to increase the incidence of ALS in the Sakha Republic, on the other hand [5]. However, given the significant number of patients with chronic forms of VEM, living in the different republican regions, the increasing migration of the indigenous population, both inside the country and outside it, and the Russian Federation does not exclude the possibility of the spread of the disease around the World. The clinical polymorphism and heterogeneity of VEM in the subacute and chronic phases of the disease, rare new typical cases of the disease at the present time, clinically weakly expressed latent current forms, the absence of specific laboratory diagnostic tests, as in VEM and ALS, can present certain difficulties in the practice of physician-neurologist. The VEM clinical polymorphism is described in the works of P. A. Petrov [15], A.N. Shapoval [20], A.I. Vladimirtsev [8], and others researchers.

A.I. Vladimirtsev included syndrome ALS in one of the 8 chronic forms proposed VEM classification [8]:

1. Dementive-paretic;
2. Spastic-paretic;
3. Syndrome protracted infectious psychosis;
4. Syndrome of amyotrophic lateral sclerosis;
5. Cerebellar
6. Parkinsonoid;
7. Diencephalic;
8. Pseudoneuroasthenic.

P.A. Petrov (1987) divided the chronic form with a slow long over, after acute and subacute forms of VEM on [15]:

1. Chronic panencephalomyelitis;

2. Protracted illness;
3. Amyotrophic Lateral Sclerosis;
In his dissertation P.A. Petrov notes that the syndrome of ALS clinic of VEM, increasing the severity of the disease, leading to rapid progression and irreversible fatal [16].

In our days with the diagnosis of IEM in the first place, you need to follow the diagnostic criteria that have been processed in accordance with the recommendation of the world Health Organization [9] and finalized in [10].

In accordance with the diagnostic criteria can be set definite, probable and possible (doubtful) VEM.

Definite VEM installed in the presence of typical manifestations in patients with the following three forms:
A. The acute form (rapidly progressive), with the course of the disease less than 12 months, which is characterized by:
1. Prolonged fever (7 days or more);
2. Symptoms of viral meningoencephalitis with lymphocytic pleocytosis and steady increase in the concentration of protein in the cerebrospinal fluid;
3. Signs of pyramidal system;
4. Pathological examination: lymphocytic infiltration of the meninges with multiple foci of micronecrosis and perivascular infiltrates in the gray matter of the brain and spinal cord;
B. Subacute form (slowly progressive) over the disease from 1 to 6 years:
1. The clinical picture of a slow progression: progressive dementia, dysarthria, signs of pyramidal and extrapyramidal systems;
2. In clinical and laboratory studies: lymphocytic pleocytosis and increase in the concentration of protein in the cerebrospinal fluid; detection of oligoclonal immunoglobulin of cerebrospinal fluid;
3. MRI \ CT images of the brain: diffuse atrophy of the brain;
4 * Pathological examination: Micronecrotic foci, inflammatory changes in the brain parenchyma, perivascular infiltrates and diffuse loss of neurons;
5. Documentary meningoencephalitis history;
* To validate definite VEM morphological study is desirable, although the presence of the above clinical signs is sufficient.
B. The chronic form, with disease duration of more than 6 years with long periods of stabilization of symptoms:
1. The clinical picture observed cognitive impairments of varying severity, dysarthria, signs of pyramidal and extrapyramidal systems;
2. In clinical and laboratory studies:
* oligoclonal immunoglobulin in spinal fluid;
3. MRI / CT images of the brain: diffuse atrophy of the brain.
4. ** Pathological examination: hardening and sometimes residual inflammatory infiltrates in the meninges, the presence in the brain parenchyma microcysts replacing micronecrotic foci, diffuse brain atrophy, gliosis, neuronal loss.
5. Documentary meningoencephalitis in history;
* Intrathecal production of oligoclonal IgG can be observed during the 3 decades after the onset of the disease. Oligoclonal IgG production is stopped when the inflammatory process "burn out"

at the late phase of the disease with the stabilization of the clinical picture and the development of fibrosis / atrophy of brain structures and minimal residual inflammation.

** To validate definite VEM morphological study, it is desirable, although the presence of the above clinical signs is sufficient.

The diagnosis of "probable VEM" can be set, if the disease has not yet developed to the typical picture of the disease, or the patient is not fully examined.

The diagnosis of "possible (doubtful or hypothetical) VEM" is set if there are serious grounds for suspecting the presence of another disease.

However, the above diagnostic criteria VEM unable to provide all the possible variations and combinations of symptoms. Therefore, in the diagnosis, it is necessary to take into account the available medical records, the various manifestations of the disease and paraclinical data of the study. For example: in all forms to set a definite diagnosis VEM is desirable to have documented evidence of meningoencephalitis, which is in a number of reasons specific to the territory of Yakutia, can not be performed in all cases, because of the remoteness of the district centers of medical districts and obstetric points, so and due to the weather conditions encountered. But the mention of about resent neuroinfections (except the patient) can be collected from his relatives, medical personnel and others witnesses this transfered illness and to make the data in the medical records.

According to the above criteria in a database on 01.01.2014, were included 356 cases with reliable VEM, of which the living are now 110 patients with spastic-paretic, dementive-paretic, and psychotic forms of the disease and 41 patients with various forms of VEM, including the syndrome of Lateral Amyotrophic Sclerosis.

Substantial diagnostic difficulties arising due to the clinical polymorphism of VEM may occur in the chronic phase of the disease. As is known, Viliuisk encephalomyelitis, as Amyotrophic Lateral Sclerosis, may give bulbar and pseudobulbar developing syndromes and muscle atrophy. Speech disorders and swallowing occur in patients with VEM and ALS due to the combined spastic bulbar and pseudobulbar syndromes in lesions of supranuclear and nuclear caudal group of cranial nerves. Patients are also observed dysphonia, drooling, impaired chewing and swallowing, increased facial reflexes, weakness and atrophy of the muscles of the tongue and soft palate, inappropriate laughter, uncontrollable crying loud, etc. Neurodegenerative disruptions of the motor neurons of anterior horns of spinal cord cause of muscle atrophy.

V.A. Vladimirtsev also described damage to the peripheral motor neuron in the global electromyogram (EMG) in the terminal phase of each of the clinical forms of VEM. He developed the technique of parallel conducting global and stimulation EMG allowed us to identify signs of dysfunction of the peripheral spinal neurons in 164 patients VEM, which is used to predict the development of more severe spinal amyotrophic syndromes, including ALS, in some VEM cases [4]. Follow-up studies TY Nikolaeva [11] showed that the syndrome of Amyotrophic Lateral Sclerosis is observed in the later stages of the VEM and more often in the terminal stage, in the context of existing symptoms of the pyramidal and extrapyramidal systems. Clinical similarity of chronic VEM with classic ALS may occur in cases of development without the typical acute onset. Therefore differential diagnosis syndrome ALS of VEM with a gradual disease onset even in a stable epidemic VEM focus is very difficult. Although P.A. Petrov observed the development of the syndrome of ALS, as in the subacute and chronic stages of the disease [16]. In his dissertation, he gives a description of two clinical cases: in the first case, the patient signs of bulbar nuclei appeared after 9 months after undergoing prolonged fever for 10

days and drowsiness. Later joined by symptoms of both central and peripheral motor neuron doing fatal outcome within 25 months from the onset of the disease. Such an onset and course of the disease was observed even in 4 patients. In the second described case, when bulbar syndrome developed in the acute period of the woman during the same long hectic 10-day period as 1 if the patient has developed dysphonia and dysarthria. After stabilization, she went back to work, but after a year the state has gotten progressively worse: bulbar symptoms increased, symptoms of pseudobulbar palsy joined, pyramidal and extrapyramidal symptoms, atrophy and fibrillation in the muscles of the arms and shoulder girdle and intellectual impairment, transformed into dementia. Fatal outcome was 29 months from the onset of the disease. Bulbar syndrome that develops in the acute period of VEM, P.A. Petrov still observed in 3 patients.

Among the patients included in the database VEM, dysarthria observed in 87% of cases, dysphagia in 5% of cases, and muscle atrophy in 17% of cases. As can be seen, slurred speech and muscle atrophy occur quite often. In the differential diagnosis between the VEM, which is accompanied by the syndrome of Amyotrophic Lateral Sclerosis and ALS classic, you need to consider the development of intellectual decline, extrapyramidal and cerebellar symptoms in Viliuisk encephalomyelitis, which is not characteristic of ALS. Also one of the distinguishing features may be unusually long duration for syndrome ALS of VEM sometimes (13 years in one such case for example according to our observations). The main manifestations of chronic phase VEM: intellectual impairment, personality change, often psychopathological conditions, movement disorders in the form of spastic paresis predominantly of the lower limbs, impairment of the function of the cranial nerves, bulbar and pseudobulbar disorders, decreased visual acuity, concentric narrowing of the visual field, expressed endocrine and autonomic disorders sometimes small muscle atrophy.

In the differential diagnosis of Amyotrophic Lateral Sclerosis can also help detect intrathecal production of oligoclonal IgG, which is stably present in the 3 decades after the onset of the disease. [17, 21] This technique is implemented in practice of Yakut neurologists from 2011 in the differential diagnosis between inflammatory and neurodegenerative disease of the brain. Tapping on electrophoregram cerebrospinal fluid of individual bands corresponding to clones of immunoglobulins assessed as positive (Fig. 1 (electrophoretogram)).

Imaging on magnetic resonance and computed tomography of the brain during VEM discover communicating hydrocephalus, increased lateral and third ventricles, diffuse atrophy of the cortex, mainly in the fronto-parietal-temporal areas [8] (Fig. 2 CT images)

Thus, in the differential diagnosis between VEM ALS syndrome and classic ALS, careful history taking to identify acute and subacute inflammatory period, the first appearance of symptoms at the onset of the disease, to assess the epidemiological situation in the place of residence at the time of disease and currently hold tracking the migration of the patient. In identifying patients with suspected or ALS VEM, it needs to carry out a full clinical examination with the use of neuroimaging techniques and definitions oligoclonal IgG in the cerebrospinal fluid.

The authors of this article hope that it will help to find the differential diagnostic criteria in the diagnosis of serious diseases and the development of therapeutic approaches for the optimal management of patients.

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Fig.1. Electrophoregram IgG of serum and CSF of patients with oligoclonal IgG and IgG without oligoclonal

1. - patients with oligoclonal IgG

2. - patients without oligoclonal IgG

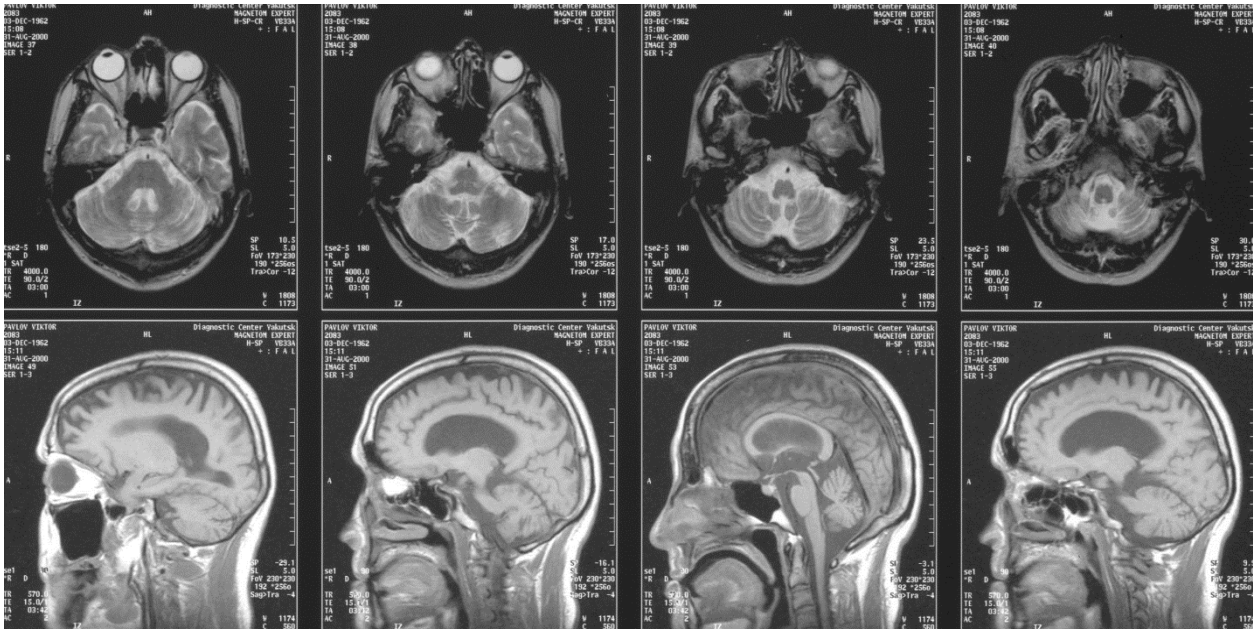

Fig. 2. CT scan of a patient with chronic VEM. Pronounced normal pressure hydrocephalus, cortical atrophy of the brain and cerebellum (V.A. Vladimirtsev 2013)

Long-Term Results of Coronary Artery Bypass Grafting with Extracorporeal Circulation and on Beating Heart in CHD Patients with Diabetes

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ABSTRACT

We compared long-term results for coronary artery bypass grafting in 195 patients with associated diabetes, 108 (55%) patients underwent coronary artery bypass grafting (CABG) with cardiopulmonary bypass (CPB) and 87 (45%) patients underwent off – pump coronary artery bypass grafting (off – pump CABG). Mean follow-up was 56 ±11 months. (≈4.6 years). Five-year survival and the "freedom" of recurrent angina pectoris in patients with diabetes who underwent CABG with CPB and off – pump CABG comparable. We have not received significant differences when compared to the five-year incidence of the myocardial infarction and re-revascularization between the groups. The benefits observed in patients after off – pump CABG, when comparing the frequency of "large" cardiovascular complications between the two groups.

Keywords: diabetes mellitus, coronary artery bypass grafting, cardiopulmonary bypass, coronary artery disease.

INTRODUCTION

In our days the prevalence of diabetes among patients undergoing myocardial revascularization is quite high and the various data confirm that it reaches 35% [1]. It is known that the presence of diabetes is associated with lower long-term survival after CABG. This tendency has been demonstrated by large-scale studies [2, 7]. In turn, it is known that the CPB is an independent risk factor for the development of some postoperative complications. Patel N.C. et al. concluded that the CPB is an independent risk factor for postoperative neurological complications. [8]. A lot of researches have indicated that the increased the frequency of neurological complications, the development of the syndrome of "small" cardiac output and renal failure in the immediate postoperative period during CABG with CPB compared with off – pump CABG. [3, 8, 9, 10]. The benefit of off – pump CABG in the immediate postoperative period recognizes a number of investigators. It is not a lot of studies with evaluating long-term complications in diabetic patients undergoing CABG by CPB and off – pump CABG and their results are contradictory. The aim of our study was a comparative evaluation of long-term complications in diabetic patients undergoing CABG with CPB and off – pump CABG.

MATERIALS AND METHODS

As a comparison of the two groups of patients shows - 108 (55%) diabetic patients underwent CABG with CPB and 87 (45%) diabetic patients underwent off – pump CABG. All patients were operated in the Bakoulev Scientific Center for Cardiovascular Surgery in the period from 2006 to 2008. Mean follow-up was 56 ±11 months. (≈4.6 years). The duration of the maximum period of observation was 70.6 ±8 months. (≈6 years), the minimum period of observation - 13 ±2 months. (≈1 year). First planned postoperative examination was performed one year after surgery. Later, watching the patients included in the study. The course of the disease was evaluated based on interviews and examinations, as well as on the results of telephone interviews with the patients in conjunction with their official receive extracts and advice of the doctors are treating patients in their place of residence. We evaluated the patient's complaints, physical examination results, reflecting the dynamics of the postoperative course, and the frequency held during the observation period of cardiovascular events. We compared the five-year mortality, the offensive "big" cardiovascular events (death, nonfatal myocardial infarction (MI), nonfatal stroke, repeat revascularization) and the incidence of recurrent angina. Baselines clinical characteristics of 2 groups compared patients were comparable (Table. 1). The patients did not differ significantly by gender, age, risk factors and associated health conditions. However, diabetic patients after CABG with CPB, compared with diabetic patients after off – pump CABG, more often had a history of myocardial infarction and percutaneous coronary intervention, and often suffered from atrial fibrillation and cerebrovascular atherosclerosis.

Statistical evaluation of the results was performed using the software package Statistica 6.0. For characteristics with a normal distribution when comparing between groups used the t-student test. If not normal distribution characteristics for comparison of two groups used non-parametric U criterion of Mann-Whitney. Differences were considered statistically significant at $p<0.05$. When processing survey data we used survival analysis using the Kaplan-Meier methods and the survival tables, when comparing actuarial curves used tests GEHA-Wilcoxon test and the F-Cox.

RESULTS AND DISCUSSION

Over the five-year period of observation in the total group of patients with diabetes (n = 195) due to various reasons 25 patients died (13%). In the group after CABG with CPB cumulative five-year survival rate at 1 year was 98.2% (Std. Error - 0.000), after 2 years - 95.5% (Std. Error - 0.002), after 3 years - 93.5% (Std. Error. - 0.007) after 4 years - 89.8% (Std. Error - 0.01) after 5 years - 88% (Std. Error. - 0.035) after 6 years - 87% (Std . Error - 0.047). Among patients after off-pump CABG cumulative five-year survival rate at 1 year was 98.8% (Std. Error - 0.000), after 2 years - 96.5% (Std. Error - 0.005), after 3 years - 93.1% (Std. Error. - 0.015), after 4 years - 88.5% (Std. Error - 0.041), after 5 years - 87.4% (Std. Error. - 0.035) after 6 years

- 87% (Std . Error - 0.051). Construction of the survival curves between treatment groups showed no statistically significant differences (p = 0.5) (Fig. 1).

Next, we had a five-year evaluated cumulative survival after CABG without the development of the "big" post-operative complications (death, myocardial infarction, stroke, and myocardial re-revascularization). All among diabetic patients was - 94 (48.2%) events. In the group CABG with CPB – 55 events, and the group off-pump CABG - 39 events. We received no significant differences in the incidence of myocardial infarction and need for repeat revascularization. However, the incidence of stroke over the observation period was significantly higher in the group CABG with CPB (Table. 2). Among diabetic patients after CABG with CPB cumulative survival without the development of the "big" cardiovascular events at 1 year amounted to 93.52% (Std. Error - 0.000), after 2 years - 83.3% (Std. Error - 0.004) 3 years - 69.4% (Std. Error. - 0.016), after 4 years - 59.3% (Std. Error - 0.028), after 5 years - 53.7% (Std. Error. - 0.037) 6 years - 49.1% (Std. Error - 0.046). Among patients after off-pump CABG cumulative survival without the development of the "big" cardiovascular events at 1 year amounted to 94.2% (Std. Error - 0.000), after 2 years - 87.4% (Std. Error - 0.011) through 3 years - 74.7% (Std. Error. - 0.015), after 4 years - 64.4% (Std. Error - 0.026), after 5 years - 57.3% (Std. Error. - 0.035) through 6 years - 55.2% (Std. Error - 0.044). Comparison of actuarial curves showed a statistically significant difference between groups (p = 0.04) (Fig. 2). There is the least amount of cardiovascular events during 5 years of observation among diabetic patients in the group with off-pump CABG. This difference is mainly ensured by the greater frequency of stroke in the group CABG with CPB, compared with the group off-pump CABG (p = 0.035). The other cardiovascular events, despite some quantitative predominance in the group CABG with CPB, significant differences between the groups did not reach. Over the five-year period of observation of patients studied was registered 45 (23%) cases of proven recurrent angina pectoris: one in the group with diabetes - 24 (22%) patients, in the control group without diabetes - 21 (24%). Among diabetic patients undergoing CABG with CPB, the five-year survival rate without recurrent angina pectoris was over 1 year - 96.3% (Std. Error - 0.001), after 2 years - 90.7% (Std. Error - 0.020) 3 years - 85.2% (Std. Error. - 00.27), after 4 years - 79.6% (Std. Error - 0.034), after 5 years - 78.7% (Std. Error. - 0,039), after 6 years - 77.8% (Std. Error - 0.046). Among diabetic patients undergoing off-pump CABG, the five-year survival rate without recurrent angina at 1 year was 97.7% (Std. Error - 0.005), after 2 years - 90.8% (Std. Error - 0.015), after 3 years - 86.2% (Std. Error. - 0.022), after 4 years - 80.5% (Std. Error - 0.036), after 5 years - 77% (Std. Error. - 0.036) after 6 years - 75 9% (Std. Error - 0.040). We found no significant differences between the groups (Fig. 3). Thus, we have not received any evidence of

the benefits of CABG procedures (with CPB or off-pump) in reducing the frequency of five recurrent angina pectoris.

The study Marcheix B. and Eynden FV (2008) evaluated the effect of diabetes on long-term survival in patients after off – pump CABG were obtained with comparable results in terms of the frequency of myocardial infarction and mortality among patients with diabetes and without. Itself diabetes was a potential risk factor for long-term myocardial infarction and congestive heart failure [5].

In the study Fukui T. et al. included 602 patients with coronary heart disease after off-pump CABG, of which 50% had diabetes; the freedom from cardiac death was 97.7% at 5 years follow-up. Freedom from the onset of the combined endpoint (death, myocardial infarction and re-revascularization) was 83.8%. This made it possible to conclude on acceptable results of off – pump CABG on the incidence of death and cardiovascular events. [4].

The study Matsuura K. et al. (2009) showed that holding off-pump CABG is recommended for most patients with poorly controlled diabetes (for glycosylated hemoglobin level greater than 6.5%) [6].

The results of our study are consistent with the opinion of most researchers indicating the comparable or even superior long-term results after the off-pump CABG. We found no significant differences in the five-year survival and freedom from recurrent angina in the two groups. The survival without the development of "large" cardiovascular events (death, stroke, repeat revascularization) after 5 years of observations was higher in the group off - pump CABG ($p=0.04$). The accuracy of the differences was due to a higher incidence of strokes occurred during the specified period of time in the group CABG with CPB. In turn, the reason for the increased incidence of stroke in the group CABG with CPB may be related to the initial clinical characteristics, patients in this group more often suffered cerebrovascular atherosclerosis and chronic atrial fibrillation, which could play a role in the development of stroke.

CONCLUSION

The five-year survival and freedom from recurrent angina pectoris in diabetic patients underwent CABG with CPB and off-pump are comparable. Significant benefits have been observed in patients after off-pump CABG, when we compared the "big" cardiovascular events between groups. However, in fairness, it should be noted that the decrease in the incidence of the "big" events observed in the group CABG with CPB compared to the group off-pump CABG, was due to significant increase in the incidence of stroke in this group that influenced the final result. We found no significant differences when compared to the five-year incidence of myocardial infarction and re- revascularization.

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Table 1

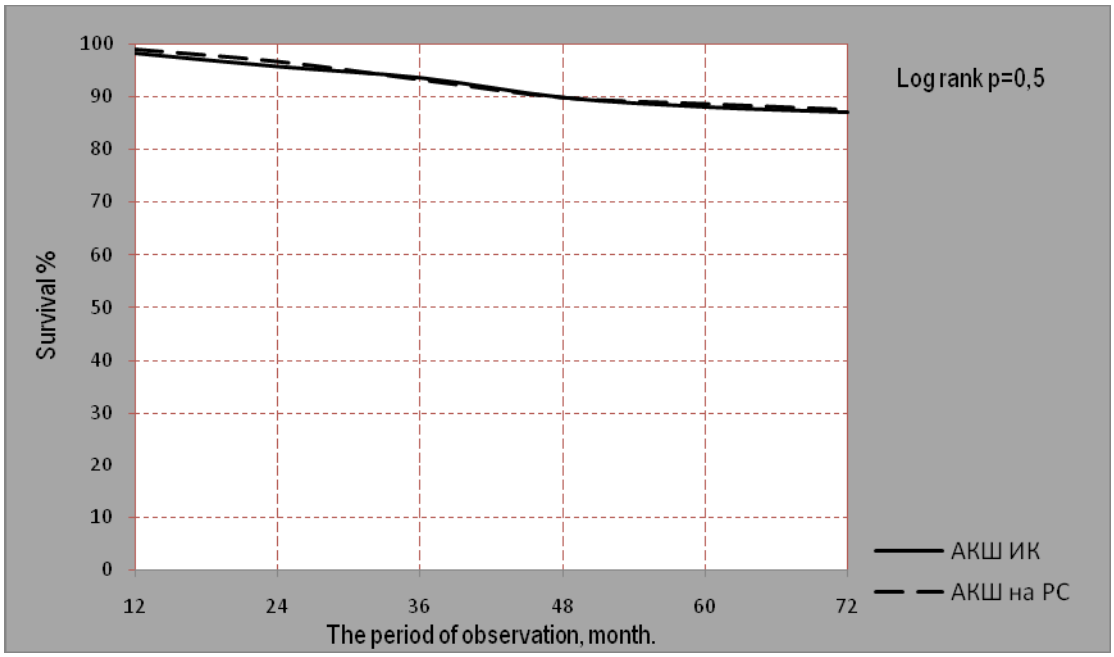
Baseline clinical characteristics of patients with diabetes

	CABG with CPB	Off-pump CABG	p
Age of	53+_5,9	57+5.1	-
Women, %	10 (9%)	12 (14%)	-
Myocardial infarction %	78 (72 %)	43 (49%)	0.01
percutaneous coronary intervention %	13 (12 %)	5 (6 %)	0.01
Chronic atrial fibrillation %	8 (7 %)	2 (2%)	0.001
Smoking %	27 (25 %)	36 (41 %)	-
cerebrovascular atherosclerosis %	20 (18,5%)	9 (10%)	0.02
A history of stroke %	4 (4%)	8 (9%)	-
Atherosclerosis of the lower extremities %	8 (7%)	7(8%)	-
Chronic lung disease %	21 (19%)	11 (13 %)	-
Chronic renal failure %	2 (1,8 %)	2 (2,3 %)	-
Left ventricular ejection fraction	52+_4,9	51+_8,9	-
Insulin-dependent diabetes mellitus type 2 %	16 (15%)	11 (13%)	-
BMI, kg / m2	29+-6,5	29+-5,3	-
Dyslipidemia %	50 (46%)	42 (48%)	-
arterial hypertension %	81 (75%)	76 (87%)	-
Revascularization`s index	2,9	3,0	-
Use of the left internal thoracic artery %	99%	100%	-

Table 2

The development of the "big" of cardiovascular events in diabetic patients after CABG with CPB and off-pump CABG over a five year period of observation

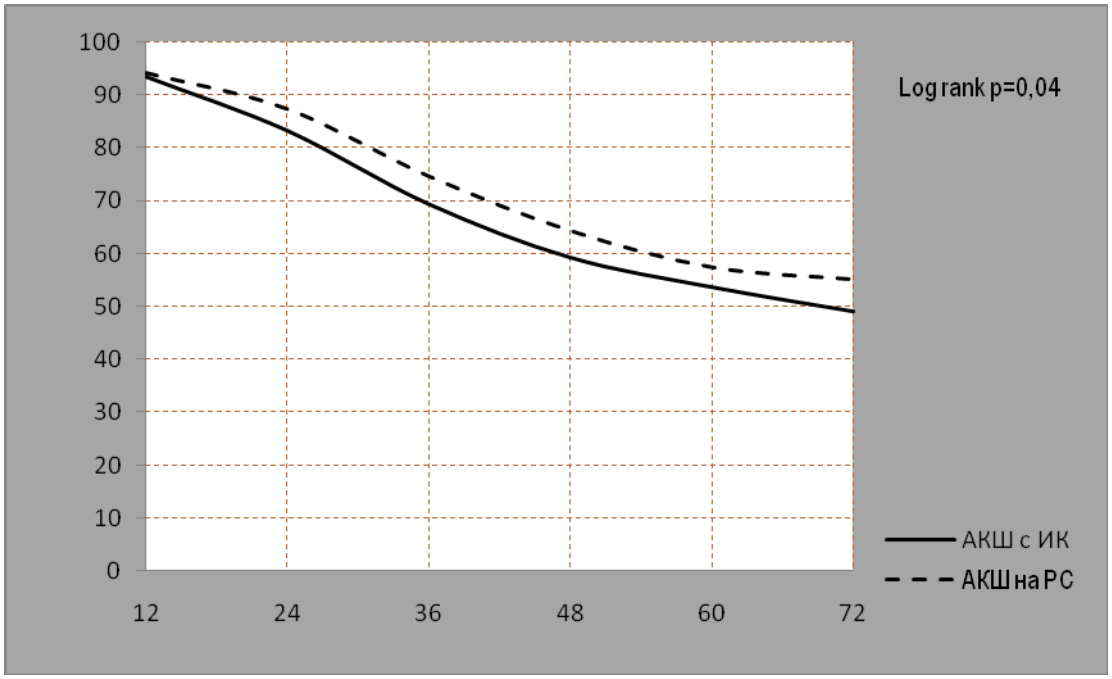
	Total: (n=195)	CABG with CPB (n=108)	Off-pump CABG (n=87)
Mortality	25 (12,8%)	14 (13%)	11 (12,6%)
Myocardial infarction	14 (7,18%)	8 (7,41%)	6 (6,9%)
Stroke	28 (14,4%)	18 (16,7%)	10 (11,5%)*
Re - revascularization	7 (13,8%)	15 (13,9%)	12 (13,8%)
Total:	94 (48,2%)	55 (50,9%)	39 (44,8%)



_____ CABG with CPB

---------- Off-pump CABG

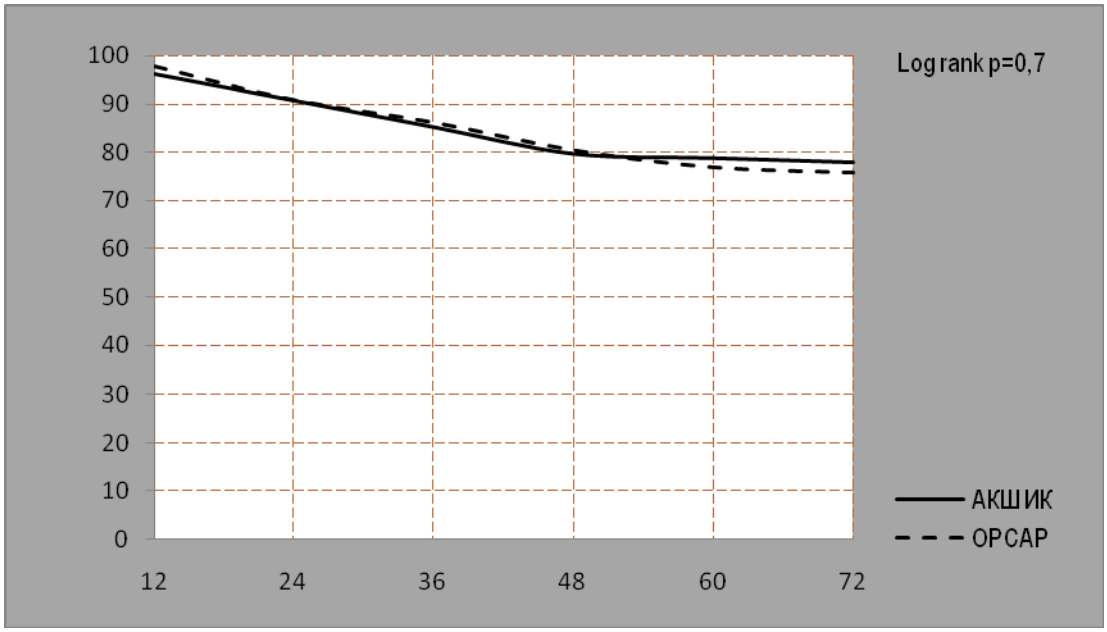
Figure 1. The five-year survival rate of diabetic patients after CABG with CPB and off-pump CABG.



_____ CABG with CPB

---------- Off-pump CABG

Figure 2. Survival without the development of "large" cardiovascular events after CABG in diabetic patients after CABG with CPB and off-pump CABG.



_____ CABG with CPB

---------- Off-pump CABG

Figure 3. Freedom from the recurrent angina pectoris in diabetic patients after CABG with CPB and off-pump CABG.

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Long-Term Results of Treatment of the Proximal Humerus Fractures

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ABSTRACT

The paper presents the analysis of long-term results of treatment of patients with fractures of the proximal humerus - the study of one of the most actual and controversial issues in traumatology. It is revealed that patients with fractures of the proximal humerus in 23% of cases have a reduction in bone density and a high risk of getting re-fractures in the next 10 years. Surgical treatment in up to 85% of cases has a positive long-term outcome.

Keywords: osteoporosis, osteopenia, fracture of the proximal humerus.

Fractures of the proximal humerus according to some authors make up 5% of all fractures of the bones of the skeleton and from 32 to 65% of fractures of the humerus [6, 8], and in 15% they are accompanied by a displacement of fragments [2]. The incidence of such fractures reaches 75-100 cases per 100.000 population per year, with the last 30 years an increase in the morbidity in almost 2 times was marked [7].

In 75% of cases of fractures of the proximal humerus they occur in patients over the age of 60 years, while for women they are in 2-3 times more often than in men [9, 10]. Unsatisfactory results of conservative treatment due to lower bone mineral density in older age groups reach up to 30-40% [4, 5]. Until now question of optimal choice of treatment of fractures of the proximal humerus remains debated [3].

All above mentioned underlines the relevance and explains the growing attention to the pathology of trauma.

Objective: to investigate the frequency of queries of patients with fractures of the proximal humerus in the city Yakutsk, to analyze the long-term results of treatment, to determine the level of bone density and using FRAX index to determine the 10-year probability of obtaining posterior fracture due to lower bone mineral density.

MATERIALS AND METHODS

A retrospective analysis of 164 case histories of patients, had been on outpatient treatment in the trauma station of Yakutsk and hospitalization in trauma and orthopedic department RB№2 TSEMP for 2012-2013, was done. The results of the treatment were assessed using an index scale of the shoulder joint function evaluation by E.A. Askerko and et al. [1]. Due to this scale using 8 parameters of the shoulder joint, the mean clinical index (MCI) is determined, unsatisfactory: MCI = 1.0-2.9; satisfactory: MCI = 3.0-3.9; good: MCI = 4. 0 or higher. X-ray absorptiometry using the GE Lunar iDXA densitometer was performed in 13 patients. Calculation of the FRAX index - method for estimating 10-year risk of fracture.

RESULTS AND DISCUSSION

For the medical care in emergency station in Yakutsk for 2012-2013 in total n - 52568 patients addressed, with diagnosed fracture of the proximal humerus n - 79 (0.16%) patients, including: n - 66 women and n - 16 men. More often fractures of the proximal humerus were in

the age group from 60-64 to 70-74 years n - 38 (48.1%) patients. In autumn and winter the frequency of calls was up to 50.6%, street injury prevailed in n – 53.1% of cases.

In total for 2012-2013 in trauma and orthopedic department RB№2 TSEMP 2972 people were hospitalized, with fractures of the proximal humerus - 85 people, among them women - 67,0% (n-57), men - 32,9% (n-28). More often fractures of the proximal humerus were in the age group from 60-64 to 70-74 years n - 25 (29.4%) patients. In autumn and winter the frequency of calls was up 21.0%, and in the spring and summer of 32.9%. More frequent were street traumas (fall from his own height) in the 85.0% of cases. In 85 patients the diagnosis was established as collateral "Osteoporosis" in 32 (37.6%).

Long-term results of treatment in 2013 were followed up in 16 patients after 1 and 3 months after conducted conservative 50% (n-8), and surgical treatment 50% (n-8). After 1 month results in all the studied patients were unsatisfactory (MCI after operative and conservative treatment 1.375 to 2.125), remained pain and limitation of movement in the shoulder joint. After 3 months after conducted conservative treatment: unsatisfactory - 2 (12.5%), satisfactory - 6 (37.5%). MCI after 3 months of conducted surgery: unsatisfactory -1 (6.2%), satisfactory - 6 (37.5%), good - 1 (6.2%).

According to a conducted survey of patients with X-densitometer Lunar iDXA osteoporosis was confirmed in 5 patients (38.5%), osteopenia in 8 patients (61.5%). FRAX index was calculated in 12 patients, high risk (FRAX index of 12 to 26.6%) was observed in 9 cases, moderate risk in 3 cases (FRAX index from 6.3 to 8.7%).

CONCLUSION

Thus, the frequency of requests for outpatient and inpatient care of patients with fractures of the proximal humerus in 2012 - 2013 amounted - 0.14% - 0.16%, respectively. Women addressed more frequently than men, with a maximum frequency peak of references in age from 60 to 74 years. In autumn and winter the frequency of calls increased. The results of treatment in 1 month in all studied patients were unsatisfactory. After 3 months after surgery, satisfactory and good results were observed in 87.5% of cases (n-7). After 3 months of conducted medical treatment satisfactory results have been observed in 75% of cases (n-6). Decrease in bone mineral density was found in 13 patients, osteoporosis (T-score <-2.5) was detected in 5 patients. From 12 patients, the index FRAX, in 9 (75%) had a higher risk (FRAX index of 12 to 26.6%) of fractures due to lower bone mineral density, in 3 (25%) patients, 10-year absolute fracture risk was defined as moderate (FRAX index from 6.3 to 12%). Stable osteosynthesis gives up to 85% of the positive long-term results of surgical treatment. Early diagnosis of osteoporosis and application of FRAX index can help to carry out prevention and reduce the frequency of recurrent fractures.

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Comparative Evaluation of Different Dressings for Applications on Transplanted Splitting Perforated Autodermotransplants

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ABSTRACT

Objective: Comparative study of effectiveness of different dressings for application on transplanted split perforated autodermotransplants.

Material and methods: Clinical and laboratory evaluation of autodermoplasty made in 108 patients with deep lesions.

Results: It was revealed that good engraftment and epithelialization of autodermotransplants largely depended on the preparation of recipient bed and creation of optimal conditions for healing through use of dressings, rather than on any additional manipulations. Complications in the form of festering wounds with lysis of the transplanted autodermotransplants most often occurred in application of dressings containing no antibiotics.

Conclusion: Rational treatment tactic of burn wounds after autodermoplasty is proposed.

Keywords: burn wound, dressing, autodermotransplant.

INTRODUCTION

In treatment of full-thickness burns, closure of the wound through surgical intervention remains the only effective way. Here the main method is grafting with free split meshed autodermotransplants. After autodermoplasty, the primary goal of wound treatment is to create optimal conditions for engraftment without any complications.

For protecting grafted autodermotransplants, dressing application is the most suitable way. The dressing should protect them from drying and infection, ensure uniform pressure, optimize regeneration, possess anti-adhesive activity, be easily and painlessly removed. In addition, such dressings should be easy to use and access.

For application on autodermotransplants, clinicians use wet-to-dry dressings with antiseptic solutions, waterborne and fat-based ointments, as well as various synthetic and biological wound dressings (4-6, 8, 9, 11, 13, 16-19, 21-23, 25).

The **aim** of the study was to compare the effectiveness of different group dressings when applying them on grafted split meshed autodermotransplants.

MATERIAL AND METHODS

The study is based on the analysis of treatment results for 118 patients (26 women and 92 men) with thermal injuries, aged 18-65 (with the average age at 41.4±0.8 years), treated at Department of thermal injuries, wound and wound infection, Burns Centers at A.V.Vishnevsky Institute of Surgery and State Hospital 36, Moscow. Most observed injuries (70.3%) were caused

by flame. The total affected area made from 5 to 50% of the body surface (in average 25.3±1.1%), with full-thickness burns covering from 1 to 40% of the body surface (in average 11.4±0.7%). All the patients with full-thickness burns underwent tangential escharotomy of pathological granulations followed by autodermoplasty of the wounds on 1-15% of the body surface (in average 6.4±0.7%). Dissection of 0.3-0.4 mm thick split transplants was performed with electrodermatomes. They were processed through the skin mesher with 1:4 expansion ratios. Various dressings were applied to the transplanted skin grafts (Tab. 1).

Table 1

Distribution of the treated patients by groups of dressings used

Group	Dressing	Number of patients
Textile dressings	Gauze dressings with Furacilin solution	25
	Activetex-CHA (with chlorhexidine and hydroxyapatit)	5
Atraumatic dressings	Voskopran	5
	Branolind	5
	Jelonet	5
	Parapran	10
	Urgotul	10
Films	Biodespol-1 (without drugs)	8
	Biodespol-LB (with lidocaine and clorehexidine)	10
Hydrogels	Supresorb X+PHMB (with chlorehexidine and polyhexamethylenbiguanede)	5
Hydrocolloids	Hitoskin-call with epidermial growth factor (EGF)	5
	Hitoskin-call with vascular-endothelial growth factor (VEGF)	5
	Hitoskin-call without medicinal substance(WMS)	5
Synthetic foams (hydrocellular)	Mepilex Transfer	10
Biological dressings from pigskin	Xenoderm	5
Total		118

The contrasted group consisted of the patients treated with Furacilin gauze dressings for the same purpose. The first dressing was applied on the 3^{d}-5^{th} day after the surgery. During the study, all the patients kept on receiving the standard general therapy, including treatment of accompanying pathologies.

The comparative clinical and laboratory evaluation of the dressing effectiveness involved clinical criteria, with the main one being how fast the grafted autodermotransplants healed. We also conducted

a laboratory evaluation, consisting of cytological and microbiological studies. In addition, we studied functional properties of the used dressings, evaluated their safety, acceptability, and patient-friendliness.

The data obtained was processed with the use of standard Excel statistical tools; we calculated the arithmetic average and its standard error. All the data, obtained during the analysis, were systemized in tables.

RESULTS AND DISCUSSION

For application on meshed autodermotransplants, it proved to be the most effective, as well as easiest and cheapest, to use standard **wet-to-dry dressings with Furacilin solution**, with waterborne ointment Levomecol dressings on top to reduce drying. This technique made it possible to leave the dressings on autodermotransplants for five and more days (Fig. 1).

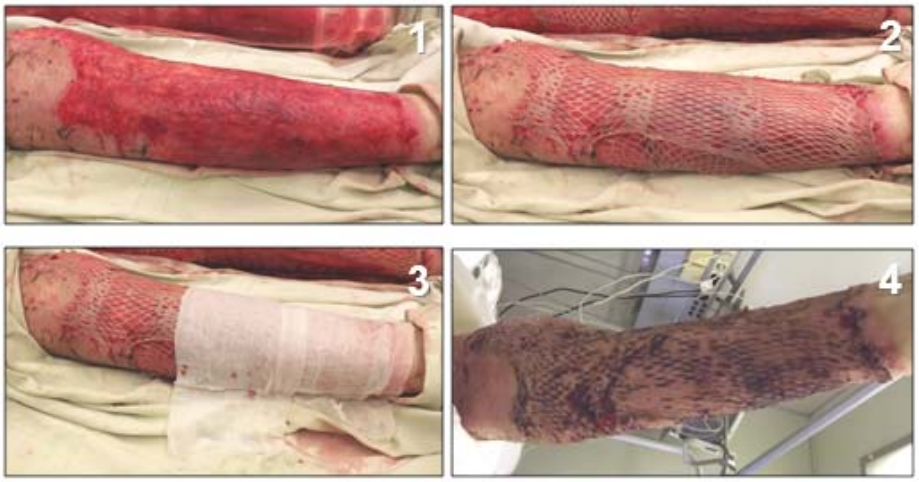

Fig. 1. Use of wet-to-dry dressings with antiseptic solution on autodermotransplants with 1:4 expansion ratio (1- granulating would after surgical treatment, 2- autodermoplasty, 3 - application of dressing, 4- in 9 days after the surgery).

Earlier rebandaging could have led to displacement of non-integrated autodermotransplants, traumatization of newly formed capillaries, capillary trophic insufficiency and formation of hematoma underneath. Festering with areas of partial lysis of transplanted autografts developed in 16% of cases, only. At the same time, in most patients the gauze dressings dried. Removal of such fixed dressings at rebandaging often resulted in traumatizing of the grafted autodermotransplants in the slits. Thus, if there were no fluids, lower layers of the dressings were left on the wound, with only upper ones being changed. The complete epithelialization in the autodermotransplants slits took 10.3±0.4 days, in average, after the surgery.

The use of **atraumatic dressings** for application on autodermotransplants with 1:4 expansion ratio protected the wounds from drying, so rebandaging went without traumatizing. We observed good additional adherence of autodermotransplants on the wound surface when using Branolind, Jelonet,

Urgotul and Parapran dressings. In contrast, Voskopran dressings sometimes failed to adhere and slid over the wound, which caused displacement of autodermotransplants. With all the atraumatic dressings, most patients showed good integration of autodermotransplants and epithelialization in the graft slits in 3-5 days after the surgery (Fig. 2).

Fig. 2. Use of atraumatic 'netlike' dressings on split autodermotransplants (1 – autodermoplasty, 2- application of Urgotul dressings, 3 – in 5 days after the surgery).

However, despite the meshing in atraumatic dressings, we observed local accumulation of traumatic discharge and its festering. All cases of autodermotransplants festering under atraumatic dressings were caused by persistence of hospital strains *S.aureus* and *P.aeruginosa*, as well as the superinfection *Ent.faecalis*. During subsequent bandaging, the use of atraumatic dressings in those patients led to partial autodermotransplants lysis, especially with Voskopran and Parapran dressings (Table 2).

Table 2

Comparative evaluation of dressing's effectiveness for application on autodermotransplants

Parameters	Branolind	Jelonet	Voskopran	Parap[ran	Urgotul
Number of patients in the group	5	5	5	10	10
Effluent accumulation, %	20	20	40	30	30
Frequency of festering with partial lysis of grafted autodermotransplants, %	20	20	40	30	20
Traumatization of autodermotransplants	-	-	-	+/-	-
Period of epithelialization of autodermotransplants with skin cover 1:4 without lysis areas, days	8.6±1.1	9±0.7	9.2±0.8	9.1±0.6	8.3±1

In average, the periods of epithelialization of autodermotransplants with the use of atraumatic dressings were 1-2 days shorter that with gauze dressings with Furacilin solution, and Urgotul and Branolind dressings proved to be particularly effective.

The application of **film dressings** (Biodespol and Biodespol-MS) on autodermotransplants protected the latter from drying and promoted epithelialization, thus resulting in reliably shorter periods of wound healing in comparison with gauze dressings with Furacilin solution (Table 3). However, the frequency of festering and wound autolysis under the films limited their use. At the same time, festering was less frequent under the use of dressings with chlorehexidine (Biodespol-MS).

Table 3

Comparative evaluation of dressings for application on autodermotransplants

Parameter	Biodespol-1	Biodespol-MS
Frequency of festering with partial lysis of grafted autodermotransplants, %	25	20
Period of epithelialization of autodermotransplants with skin cover 1:4, days	7±0.5	7.1±0.9

Hydrogel dressings Suprasorb X+PHMB was also placed right at the surgery on grafted split autodermotransplants with 1:4 expansion ratio, which provided their additional fixation on the wound surface. No festering cases of grafted ADT were revealed. Most observations showed drying and firm fixation of the dressings on the wound. Dry covers provided good engraftment of autodermotransplants and extensive epithelialization in the slits. However, endeavors to remove them, even after soaking, resulted in the graft traumatization, so the dressings were left on the wound until the complete epitelialization, when they detached from the wound on their own. The period of full epitelialization of grafted autodermotransplants with 1:4 expansion ratio averaged to 8.2±0.4 days after the surgery.

In some patients, the use of Hitoskin-call **hydrocolloid dressings** on split autodermotransplants was accompanied by their drying and firm fixation on the wound. Under dry covers, there was good healing of autodermotransplants and their extensive epitelialization in the slits, especially with the use of EGF (epidermal growth factor) dressings (Table 4). However, endeavors to remove the fixed dressings, even after soaking, resulted in the graft traumatization, so the dressings were left on the wound until the complete epitelialization, when they detached from the wound on their own.

Table 4

Comparative evaluation of different Hitoskin-call dressings effectiveness for application on autodermotransplants

Parameter	VEGF	EGF	WMS
Frequency of festering with partial lysis of grafted autodermotransplants, %	60	20	20
Period of epithelialization of meshed autodermotransplants with skin cover 1:4, days after surgery	12.2±1.2	9±1.2	11.6±1.4

At the same time, some patients, treated with the use of Hitoskin-call dressings on the grafted meshed autodermotransplants, developed hypergranulations, increase of traumatic discharge under the dressings, which was of festering nature and resulted in the autodermotransplants lysis. The occurrence of complications was the highest with the use of Hitoskin-call dressings with VEGF, which took the healing more time.

It should be noted that when hydrogel and hydrocolloid dressings were used for application on autodermotransplants located at side and lower surfaces of the body, we observed 'sliding' of the dressings put, which required their additional fixation with gauze bandages. In addition, they were uncomfortable to use in the complex-configuration areas (fingers and toes, joints), also due to the problems with fixing.

With the use of **Mepilex Transfer foam dressings** for application on meshed autodermotransplants, the period of epithelialization was shorter than that in the group treated with gauze dressings. However, in some patients, endeavors to remove the fixed dressings, even after soaking, resulted in the graft traumatization; in 20% of the cases, certain body areas developed festering and lysis of the grafted autodermotransplants (Table 5).

With the use of **textile dressings Activetex-CHA**, containing hydroxyapatit as a reparation promoter, we observed accumulation of traumatic discharge under the dressings and traumatization of the integrated autodermotransplants at rebandaging. At the same time, the period of epithelialization was not shorter than that in the group treated with wet-to-dry dressings with antiseptic solutions (Table 5).

The use of **Xenoderm biological covers** for application on split autodermotransplants was also accompanied by accumulation of traumatic discharge underneath. In 40% of the cases, at the first rebandaging, we found festering and partial lysis of the autodermotransplants under Xenoderm, which was not observed in the contrasted group (Table 5). However, the wound epitelialization period after engraftment was approximately the same.

Therefore, the study did not show additional impact of using different dressings on epitelialization of grafted autodermotransplants. Most often, the complications in the form of wound festering with lysis of the grafted autofermotransplants occurred with the dressings not containing antibacterial medications. This confirmed the published data that during first days skin grafts themselves fail to protect from infection (10, 24), whereas the use of local antiseptics considerably minimizes the number of lyses of grafted autodermotransplants in burn patients (26). This justified the prescription of local antibacterial medications for treatment and prevention. Taking into consideration our previous research data (2), which showed that poly-resistant strains *S.aureus (*37.93% of the cases) and *P.aeruginosa* (27.59%) were the dominant microorganisms responsible for local infectious complications after surgery in burn patients, with others affecting significantly rarer - *S.epidermidis* (10.34%), Gram-positive rods (8.05%), *Acinetobacter spp*. (4.6%), *Candida* gender fungi (4.6%) and other microorganisms (6.85%), as well as the data of studying the microbiological activity of locally applied antimicrobal preparations (3), it is recommended, for application on meshed autodermotransplants, to use dressings with antiseptic solutions, which eliminate the majority of potential infectious agents (for example, Prontosan), unlike Furacilin solution, which is effective against Gram-positive microorganisms, only. At the same time, it is not recommended to use iodium pyron, chlorehexidine and dioxidine solutions for the same purpose, since, according to the published data (2, 20), they are cytotoxic and may affect regeneration negatively.

The analysis of the evaluation results for different dressing effectiveness for application on grafted meshed autodermotransplants showed that all of them are almost identical clinically (Table 5). The epitelialization period was the shortest with the use of dressings creating moist wound environment. However, their effectiveness was neutralized by accumulation of effluent under dressings, and the risk of festering and partial lysis of autodermotransplants (in 20 to 40% of the cases).

Table 5

Comparative evaluation of clinical effectiveness of dressings for application on meshed autodermotransplants

Parameters	Atraumatic 'netlike' dressings	Biodespol films	Hydrogel dressings	Hydrocolloid dressings	Synthetic foams (Mepilex)	Biological cover Xenoderm	Activetex textile dressings	Gauze dressings with Furacilin solution
Effluent accumulation	28.6%	33.3%	20%	35%	30%	40%	20%	20%
Frequency of festering with partial lysis of grafted autodermotransplants	25.7%	22.2%	20%	25%	20%	40%	20%	16%
Traumatization of autodermotransplants	-	-	++	-	+/-	-	+	+
Period of epithelialization of autodermotransplants with skin cover 1:4 (without lysis areas), days	9±0.4	7±0.3*	8.2±0.4*	10.8±0.8	8.7±0.4*	9.8±1	11.8±0.6	10.3±0.4

* $p<0.05$ — in contrast with gauze dressings with Levomecol ointment.

It is obvious that after grafting of split meshed autodermotransplants, the wounds in their slits are still in the 2nd stage of the wound process; given those conditions, it is effective to use the moist method of local treatment, which creates the wound environment optimal for healing. However, in 3-5 days after surgery, i.e. transfer to the 3d stage of the wound process, it is recommended to continue treatment with the dry method, which protects the wound from infections and supports the newly-formed epithelium. Otherwise, the continuing moist environment promotes inflammation, results in excessive wound effluent discharge, secondary infection and autolysis of the healed wound surface.

Taking into consideration the above mentioned, the following tactics of the wound care after autodermoplasty is recommended: after a single use of dressings creating moist wound environment, at the first rebandaging in 3-5 days they should be replaced by gauze wet-to-dry dressings with antiseptic solutions, creating dry wound environment, which, in most cases, prevents development of local festering complications and promotes epitelialization of autodermotransplants in the shortest period possible.

CONCLUSION

The effectiveness of autodermoplasty is closely connected with primary treatment of wounds, as well as thorough surgical processing and hemostasis. Good engraftment and epithelialization of autodermotransplants largely depends on the preparation of recipient bed and creation of optimal conditions for healing through use of dressings, rather than on any additional manipulations. Yet, further search for more efficient dressings to take care after burn wounds in the post-surgery period, especially in patients with vast full-thickness burns, remains one of the promising academic research areas.

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Wobenzym in the Complex Treatment of Pneumonia among Military Personnel Immunized with Pneumococcal Vaccine

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ABSTRACT

The **purpose** of the work: to evaluate the clinical efficacy of preparation Wobenzym inclusion in the complex therapy of pneumonia in previously vaccinated with pneumococcal vaccine "Pneumo-23" and unvaccinated patients.

The method of research. The study included 157 patients with pneumonia, men, soldiers performing military service at the age of 18 to 22 years (19.2 ± 0.19), admitted to the pulmonology department of the military hospital in the period from 2007 to 2010. Depending on the treatment, all patients included in the study were divided into four groups randomly. The 1st main group (MG, n = 46) included patients previously vaccinated with pneumococcal vaccine and treated with standard therapy; in the 2-nd (MGSET) - vaccinated patients (n = 44), who were prescribed in addition Wobenzym; in the third group - the comparative (CG, n = 34) - patients previously non-vaccinated and treated with standard therapy, and the 4th (CGSET) - unvaccinated patients, but additionally treated with medication Wobenzym (n = 33).

Results. It is shown that the inclusion of the preparation Wobenzym in the complex therapy of pneumonia contributed to a more rapid regression of all clinical manifestations of pneumonia and reducing the probability of formation of residual radiological changes of lung tissue. It is found that the inclusion of systemic enzyme therapy drugs in the complex treatment of pneumonia is pathogenetically substantiated.

Keywords: pneumonia, systemic enzyme therapy, Wobenzym.

INTRODUCTION

The problem of diagnosis and treatment of pneumonia continues to be one of the most relevant in the modern health care. Despite the continuous improvement of diagnostic methods and the availability of modern high antibacterial drugs, pneumonia remains a leader in the structure of morbidity and mortality from infectious diseases in developed countries [2, 11]. Remains a high incidence of pneumonia in the Armed Forces of the Russian Federation among the soldiers performing military service [3, 5, 8], despite ongoing treatment and preventive measures, including vaccination of personnel autumn appeals pneumococcal vaccine [1, 10]. Promising to study the possibility of potentiation medication events in patients with pneumonia,

including those previously vaccinated with pneumococcal vaccine, through the use of systemic enzyme therapy. At present, a number of studies have shown that the presence of drugs in systemic enzyme therapy (SET) plant and animal enzymes with different substrate specificity allows for synergistic anti-microbial agents at various stages of treatment of infectious and inflammatory processes affecting the microcirculation disorders and immune disorders [4, 6].

Objective: to evaluate the clinical efficacy of inclusion in the complex therapy of pneumonia preparation Wobenzym in previously vaccinated with pneumococcal vaccine "Pneumo-23" and the non-vaccinated patients.

MATERIALS AND METHODS

The study included 157 patients with pneumonia, men, soldiers performing military service at the age of 18 to 22 years (19,2 ± 0,19), admitted to the pulmonology department of the military hospital in the period from 2007 to 2010. Depending on the treatment, all patients included in the study were divided into four groups randomly. In the 1st main group (MG, n = 46) included patients previously vaccinated with pneumococcal vaccine and treated with standard therapy in the 2 nd (MGSET) - vaccinated patients (n = 44), which was prescribed in addition Wobenzym, a the 3th group - the comparative (CG, n = 34) included patients previously non-vaccinated and treated with standard therapy, and the 4th (CGSET) - unvaccinated patients, but additionally treated with medication Wobenzym (n = 33). Pneumococcal vaccination vaccine "Pneumo-23» (Aventis Pasteur SA, France) soldiers conducted only once, in the first days after the arrival of a military unit, 0.5 ml intramuscularly concurrently with the administration of purified adsorbed tetanus-diphtheria toxoid. The preparation Wobenzym (Mucos Pharma GmbH & Co, Germany) was administered in groups and OGSET SGSET simultaneously with an antibiotic to 3 tablets 3 times a day for 7 days, 30 minutes before a meal. Side effects during treatment with the drug have been identified. All patients received empirical antibiotic treatment with amoxicillin or III generation cephalosporin (ceftriaxone, cefotaxime), or azithromycin, or cephalosporin combined with a macrolide. Select antimicrobial dose and route of administration (intravenous, intramuscular or oral) dependent on the probability of the proposed agent pneumonia and severity of disease. According to the testimony appointed detoxification infusion therapy, bromhexine 48 mg / day, range of physical therapy and physiotherapy. The control group consisted of 20 healthy individuals

The study used classification of pneumonia, proposed by the European Respiratory Society (ERS) in 1995, taking into account the conditions in which the disease has developed, especially infection of lung tissue, as well as state of immunological reactivity of the patient [9, 12].

Inclusion criteria were the presence in the patients of clinical and radiographic evidence of pneumonia. Exclusion criteria were patients with severe pneumonia requiring treatment in the intensive care unit and intensive care, and the presence of comorbidity.

The study used the following diagnostic methods:

- general clinic: general blood, urine, sputum, including Mycobacterium tuberculosis, bacteriological culture of sputum on the microflora and its sensitivity to antibiotics diskodiffuzionnym method;

- biochemical studies: determination of ALT, AST, fibrinogen, C-reactive protein seromucoid, serum glucose, serum total protein.

- instrumental: radiography or fluoroscopy of the chest in a straight line, the left and / or right lateral views in the dynamics of the disease, the study of respiratory function (ERF), an electrocardiogram.

Fluorography of the chest was performed with a scanning digital fluorograph "Proscan 2000". Standard X-ray examinations of the chest cavity - a digital installation DuoDiagnost vertical module Bucca company «Philips» at 100% of the patients on admission and on the 14th day of treatment. In the case of persistent infiltration of X-ray examinations of the chest were added every 10 days until complete resolution of infiltrative changes in the lung tissue. ERF study was carried out with the help of computer spirometer MedGraphics CPFS - D / USB 1, 8 and 14 day hospital treatment.

The analysis of the clinical efficacy of the drug was conducted in Wobenzym study groups on the following criteria: the duration and intensity of the temperature response on a 4-point standardized scale [7], the severity and duration of symptoms of intoxication, the dynamics of clinical symptoms of pneumonia - weakness, malaise, cough severity and number of sputum on a 4-point standardized scale [7], we supplemented with a detailed symptom severity of pleural pain syndrome, physical signs over the zone of destruction of lung tissue, the rate of complications. Consideration was also given laboratory (white blood cell count, erythrocyte sedimentation rate, C-reactive protein, fibrinogen, α2 - globulins) and instrumental data (radiographic infiltration of the lung tissue, lung function) and the duration of antibiotic therapy.

The obtained data were processed using the statistical software Micro-soft Office Excel 2007 and Statistica 6.0 (StatSoft, Inc. 2001). Universal statistical package Statistica 6.0 was used to test the hypothesis of equality of the means for the two different data from general populations using two-sample Student's t-test. For a comparison of the percentages used goodness $\chi^2$of fit

calculated using the package Statistica 6.0.

RESULTS AND DISCUSSION

The main clinical symptoms (cough, chest pain, fever, weakness) and objective signs of pneumonia (shortening of percussion tones over an area of damage to lung tissue and moist finely wheezing) were arrested in MGSET for 3 - 4 days earlier than in MG and in CGSET, and 5 - 6 days faster than in the CG. By the 3 rd day of febrile patients in MGSET was 91% lower in all the examined were cropped symptoms of intoxication, and by the 5th day - and all of the original pathological symptoms. Patients in this group normalization of body temperature occurred two times faster (at 4,2 ± 0,2 days) than in patients with CG ($p<0,05$). If the first third day in patients MGSET and MG statistically determined before the benefits of the vaccination pneumococcal vaccine, in the following 4 days of treatment - inclusion in the complex treatment of pneumonia preparation Wobenzym, and especially in vaccinated patients.

So, if in the 1st study day statistically significant difference between groups MGSET, MG, and CGSET, CG in the number of patients who had chills, chest pain, shortness of breath ($p<0,05$ / χ^2/) attracted attention, then on day 3 – there was a statistically significant difference in the above characteristics between CGSET and CG, MGSET and MG. Regression MGSET cough occurred in 2.4 times faster than MG ($p<0, 05$ / χ^2/). In CGSET since the third day from the beginning of application Wobenzym observed a decrease in cough and expectoration of sputum and their subsequent termination of an average of 8-day, and by the 7th day of treatment in this group was a statistically significant difference on the clinical symptom with ill CG ($p <0,05$ / χ^2/) and MG ($p <0,05$ / χ^2/) In the CG character of the cough within the first 5 days of treatment is not significantly changed, and completely arrested only 14 - the 15th day of treatment.

Duration periods of fever and toxicity were shorter in 1.5 and 1.2 times shorter than MGSET than in MG, 1.8 and 1.3 to CGSET times than CG, 0.9 times and 1.1 MGSET times shorter than CGSET, respectively (Table 1). The decrease in body temperature to the 3rd day of treatment was observed in 91% of patients MGSET and only 79.4% of patients CG. By 4rd day all patients MGSET body temperature to normal one, while the CG to 5-day body temperature dropped from 91.1%, and only on the 7th day - all patients. Low scores were higher in patients CG and CGSET is 1.8 times higher than in MGSET and MG. Patients MG normalized temperature at the 6th day, CGSET - 5-th day and CG - to 7-day treatment. In MGSET temperature normalization occurred two times faster than CG, wherein the average baseline score was higher than the temperature of CGSET and CG. In the course of treatment was observed alignment scoring indicators of temperature reaction between groups MGSET and CGSET. The worst results were

noted in CG: on the 6th day of fever corresponded to 0, 3 points. Normalization auscultation pictures over the affected lung segments in patients MGSET occurred on the average for the 5th, in patients CGSET - to 7-th, and in patients MG and CG - to only 8 - 9 day of treatment, there was a 1, 4 times slower than MGSET.

Length antibacterial therapy did not exceed MGSET 5 - 6 days, dose rate - 10.2 g, while in these MG were 6 - 7 days. and 13.8 g of CGSET - 6 - 8 days. and 15.6 g of CG - 8 - 9 days. 17.9 g and thus the effectiveness of antibiotic therapy in MGSET was the highest, and the average dose rate of antibiotics in this group was less than CG 1.75 fold (Table 1). In MGSET complications of pneumonia (toxic shock, acute respiratory failure) were cropped to 2.1 times faster than MG, and CGSET - 1.5 times faster than CG.

In addition, patients and MGSET and CGSET, unlike the MG and CG celebrated faster regression of initially elevated laboratory parameters of inflammatory activity (leukocytosis, ESR, CRP, seromucoid, content, α2-globulin and fibrinogen), starting from 5th day of the disease. Laboratory parameters in patients of the groups at the end of the course of antibiotic and systemic enzyme therapy (day 8) are presented in Table. 2.

In the analysis of blood parameters at the time of completion of the course of treatment would Wobenzym la showed a trend toward normalization in their groups MGSET, CGSET, approaching normal levels in the MG and store it above the norm in the CG (Table 3).

Violations of ERF in the first day of hospital treatment for obstructive, restrictive or mixed type were found in 52.2% of patients MGSET, 54.3% of patients in the MG, in 84.8% of patients CGSET and 85.2% of patients CG (Table 4).

A statistically significant difference between the above parameters indicative of the effectiveness of vaccination in patients MGSET and MG affecting the severity of pneumonia and the nature of the complications of the disease. However, data on the 8th day of treatment, not only confirmed the benefits of immunization troops organized military groups, but also showed the effectiveness of inclusion in the complex treatment of pneumonia preparation Wobenzym as in vaccinated and non-vaccinated patients. Multimodality treatment involving Wobenzym clearly depends on the recovery of external breathing. Thus, normalization of respiratory function by increasing ventilation mainly by improving bronchial obstruction was observed significantly more frequently in MGSET and CGSET than in the MG and CG. To discharge violations ERF in patients treated with additional medication Wobenzym as the previously vaccinated with pneumococcal vaccine "Pneumo-23" (MGSET group) and non-vaccinated (group CGSET) were detected in 4.5 times less likely than patients administered standard regimen (group MG, CG).

According to X-ray examination of the chest on the 14th day of treatment, complete

resolution of infiltrative changes in MGSET was found in 97.7%, in CGSET - at 93.9%, in the MG - at 93.5% in CG - in 85 3% of patients. Recovery of residual radiological signs in the form of strengthening lung pattern in MGSET noted only in one patient (2.3%), in CGSET - in 6.1% of patients. In the MG in 6.5% of patients were diagnosed with residual radiographic changes in the form of strengthening pulmonary pattern, focal fibrosis and pleural Mooring. In the CG in 14.7% of patients were ascertained recovery with residual changes in the form of the syndrome of pathological disorders lung pattern (interstitial tissue sealing, reinforcement, enrichment, strain, blurred pulmonary pattern), the expansion of the lung root on the affected side and pleural reaction in the form of its thickening .

Time resolution of infiltrative changes in the lungs according to radiographs in patients MGSET was 14,6 ± 1,6 days, length of stay in hospital - 18,1 ± 1,7 days. Similar rates of patients in the groups CGSET, MG and CG totaled respectively: 14,9 ± 1,8 and 19,4 ± 1,5 days; 16,5 ± 1,4 and 20,7 ± 1,2 days; 18,7 ± 1,3 and 24,1 ± 1,6 days. As a result, the inclusion of Wobenzym in the complex treatment of pneumonia al-lowed to reduce the time of treatment in the hospital with a 24,1 ± 1,6 to 18, 1 ± 1,7 days ($p< 0,05$).

CONCLUSION

The inclusion of the drug Wobenzym in the complex therapy of pneumonia contributed to a more rapid regression of all clinical manifestations of the disease. This is confirmed by the reduction in terms of clinical and laboratory recovery by an average of 3 days, febrile period - twice more clear positive dynamics of the X-ray is the 10th day of treatment in 87% of patients and a reduction in the amount of residual radiological manifestations of the 14th day of treatment to 9%. These clinical effects are due, presumably, the achievement of higher concentrations of antibiotic at the site of inflammation in common use with Wobenzym due to improved rheological properties of the blood and microcirculation in the lung tissue. The efficacy of Wobenzym in the treatment of pneumonia is higher in vaccinated patients.

These data suggest justified the inclusion of systemic enzyme therapy drugs in the complex treatment of pneumonia as a pathogenetically valid form of therapy.

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Table 1

Indicators of clinical efficacy of Wobenzym in the treatment of pneumonia

Index (duration, days)	BGSET (n = 44)	BG (n = 46)	CGSET (n = 33)	CG (n = 34)
Fever	3,2 ± 0,3*	5,3 ± 1,1	4,5 ± 0,4**	6,3 ± 0,6
Cough	5,5 ± 1,2	7,7 ± 1,8	7,2 ± 0,6	8,1 ± 1,9
Antimicrobial therapy	6,1 ± 0,4*	6,7 ± 0,6	6,9 ± 0,7**	7,3 ± 0,9
Patient day	11,4 ± 0,7	13,6 ± 1,2	13,2 ± 0,9	17,4 ± 2,2

Note:

* - difference between BGSET and BG significantly, $p < 0,05$;

** - difference between CGSET and CG significantly, $p < 0,05$

Table 2

Laboratory findings in patients studied groups on the 8th day of treatment,%

Index	BGSET (n = 44)	BG (n = 46)	CGSET (n = 33)	CG (n = 34)
Leukocytosis, ($\geq 9{,}0 \times 10^9$/l)	0	2,1; **p =0,042 (χ^2)	0	8,8
Accelerated ESR, (more 10 mm / hr)	2,2; *p =0,001; **p =0,000001; ***p =0,017 (χ^2)	10,8; **p =0,003(χ^2)	15,1; **p =0,032 (χ^2)	29,4
Seromucoid, (more 0, 20 units)	0	0	0	8,8
The presence of CRP	0	2,1; **p =0,009 (χ^2)	0	11,7
The increase in α_2-globulin, (more 6, 9 %)	0	2,1; **p =0,009 (χ^2)	0	11,7
Fibrinosis, (more 11,7 micromoles /l)	0	4,0; **p =0,017 (χ^2)	3,0 **p =0,005 (χ^2)	14,7

Note:

* - differences are statistically significant with respect to CGSET;

** - differences are statistically significant with respect to CG;

*** - differences are statistically significant with respect to BG

Table 3

The peripheral blood of patients studied groups on the 8th day of treatment

Index	Groups of patients			
	BGSET (n = 44)	BG (n = 46)	CGSET (n = 33)	CG (n = 34)
Average Rating:				
leukocytes, × 10^9/l	5,6 ± 0,75	6,7 ± 1,21	6,3 ± 2,44	8,5 ± 1,31
neutrophils stab, %	4,2 ± 1,12	4,7 ± 1,23	4,1 ± 2,08	6,6 ± 0,75
The number of immature forms of leucocytes more 10%	0	2,1; **p =0,042 (χ^2)	0	8,8
The average number of lymphocytes, %	22,6 ± 2,4	21,2 ± 2,9	20,2 ± 2,1	17,2 ± 2,8
Average ESR, mm / hr	15,2 ± 2,3*	17,4 ± 3,6	19,1 ± 4,4	21,4 ± 5,8

Note:

* - difference to those in CG significantly, $p < 0, 05$;

** - the difference is statistically significant with CG

Table 4

The frequency of violations of respiratory function in patients studied groups,%

Groups of patients	The frequency of violations of respiratory function during therapy,%		
	1-е сутки	8-е сутки	14-е сутки
BGSET (n = 44)	52,2; *p =0,005; **p =0,004 (χ^2)	2,2; *p =0,001; **p =0,0000001; ***p =0,0002 (χ^2)	0
BG (n = 46)	54,3; *p =0,009; **p =0,008 (χ^2)	19,5; **p =0,000006 (χ^2)	0
CGSET (n = 33)	84,8	15,1; ***p =0,0000001 (χ^2)	0
CG (n = 34)	85,2	59,9	2,9

Note:

* - differences are statistically significant with respect to CGSET;

** - differences are statistically significant with respect to CG;

*** - differences are statistically significant with respect to BG

Possibilities of Computer Prediction of the Relative Risk of Lethal Outcome in Septic Patients

V.V. Grebenyuk, K.A. Kovtunov, A.A. Nazarov, I.V. Chumachenko

ABSTRACT

The algorithms of actions for the definition of the condition severity and choice of the medical-diagnostic measures in the patients with the biliary sepsis are presented. We take into account the traumatic factor of the operation, the kind of narcosis (endotracheal, local anesthesia) and severity level of the initial condition of the patients. We suggest using this program of the actions in the form of the computer program for the diagnostics of the severity level of a condition of the septic patients, creation of the database and electron archives of results of treatment, and also continuous monitoring of the condition of the patients.

Keywords: sepsis, severity level, program of the actions.

INTRODUCTION

Nowadays, the role of predicting the outcome of surgery in the optimization of therapeutic tactics is very important. The prediction of the outcome of any treatment and diagnostic measures is **operational risk** that includes postoperative complications, including death, caused by an underlying medical condition and accompanying pathology [1-3, 6]. Operational risk consists of the anesthetic and surgical risks; the objective assessment of the severity of patients allows predicting the mortality risk and evaluation of the effectiveness of the treatment [2]. **The purpose** of our research was the creation of a program to determine the degree of severity of patient's condition and the choice of algorithms of treatment and diagnostic measures in patients with surgical sepsis.

THE EXPERIMENTAL PART

In the current study, the authors studied the immediate results of integrated clinical and laboratory examination and treatment for 60 patients with surgical sepsis from age 21 to 93 years (mean age 53 ± 0.7 years), out of which 25 men (35%) and 50 women (65%). All patients were divided into three groups by age: the first consisted of 35 patients from age 21 to 59 years, the second - 25 patients from age 60 to 74 years old, and the third, with 15 patients from age 75 to 93 years old. Causes of surgical sepsis by localization of primary infection: 1) purulent forms of pyelonephritis with urolithiasis (20 patients); 2) spilled purulent-inflammatory diseases of abdominal cavity (30 patients: perforated gangrenous appendicitis - 10, pancreatic necrosis - 10, acute ileus-10); 3) acute purulent cholangitis in benign lesions of biliary ducts - (10 patients).

All patients conducted intensive care and surgical treatment, according to current recommendations for treatment of sepsis. The following surgical interventions were performed: 1) laparotomy, the elimination of infection, sanitation and drainage of abdominal cavity (30 patients), with marsupialisation stuffing bags and cholecystostomy(10 patients); 2) laparoscopic cholecystectomy with holedoholitotomy and common bile duct drainage for A.V.Vishnevsky, Kehr (10 patients); 3) endoscopic papillosphincterotomy or suprapapillary choledochoduodenotomy with mechanical litoextraction and laparoscopic or laparotomic cholecystostomy. (10 patients); 4) Tool kidneys cavity drainage (ureteral stenting, catheterization, percutaneous puncture nephrostomy) for the intensive care of pyelonephritis and sepsis; kidney's decapsulation, excision of the carbuncles, nephrostomy with removing stones from ureter and without that, nephrectomy (20 patients).

All the patients were similar in accompanying pathology (coronary heart disease), the severity of the disease and the prevalence of the disease process (a severe surgical sepsis, confirmed bacteriemia, multiple organ dysfunctions, the presence of primary inflammatory focus). Criteria of organ dysfunction [1] in severe biliary sepsis were: 1) cardiovascular system (systolic BP $\geq$ 90 mmHg or mean BP $\leq$ 70 mmHg during 1 hour and more, despite the correction of hypovolemia), 2) urinary system (diuresis < 0.5 ml/kg/h with adequate volemic filling or increasing creatinine to 2 times the normal value), 3) respiratory system ($p_aO_2/FiO_2 \leq 250$ or bilateral infiltrates on x-ray, or the need for respiratory care), 4) liver (increased bilirubin content above 20 μmol/l within 2 days or increase in transaminases in 2 times and more), 5) coagulative system (the number of platelets less than 100x109/l, or a reduction of 50% relative to the highest value for 3 days), 6) metabolic dysfunction (pH $\leq$ 7.3, lactate plasma in 1.5 times more than normal), 7) Central nervous system is less than 15 points on a scale of Glasgow. Bacteremia was confirmed in 20 patients: S. epidermidis in 4 patients, Pseudomonas aeruginosa in 10 patients, Klebsiela Pneumaniae - in 6 patients.

All indicators were tested for normality, according to criteria of Kolmogorov-Smirnov, Lillieforse, Shapiro-Wilkes. All data does not obey normal distribution law of Gauss. We conducted analysis of variance by rank Kruskal - Wallis test and the median, as well as the correlation analysis using Spearman rank correlation coefficient. The relative risk of death as the ratio of the number of patients who have died to the number of survivors was determined [5]. Statistical processing was performed using the program STATISTICA 6.0 for Windows. The level of significance was set at P 0.05.

RESULTS AND DISCUSSION

According to the statistical analysis of correlative factor proportion traumatic operations, the degree of severity and frequency of recovery or death in patients with surgical sepsis with

different versions of the infection in the abdominal cavity and retroperitoneal space, we have developed a programme of action to determine the severity of the condition and the selection of treatment in patients with surgical sepsis. We took into account the traumatic level of surgery, the type of anesthesia (local anesthesia, endotracheal), and severity of patient's condition. It should be noted that the relative risk of death, in the proposed prediction method, calculated taking into account the patient perform a laparotomy or lumbotomy and eliminate the source of infection in the abdomen and / or retroperitoneal space under endotracheal anesthesia.

To save time, the diagnosis of the severity of septic patients, establishing a database and electronic archives results treat, and continuous monitoring of patients, we offer the use of the programme of action in the form of a computer program [4]. The program is designed to determine the risk of death according to the results of surveys of patients with surgical sepsis. The program performs the following functions: maintenance of charts of patients, conducting the survey maps for each patient, plotting changes survey results and probabilities of death for each patient, getting statistics on patients.

The Program works as follows.

On admission the patient with suspected surgical sepsis, we estimate the severity of the patient's condition on the basis of clinical, laboratory and instrumental data and correlated with the risk of death or recovery. The degree of severity of the patient is determined automatically by the program on the basis of the proposed method of determining the degree of severity of patients with surgical sepsis [5].

According to a degree of severity the practical doctor recommended specific action algorithm based on valid traumatic operations.

This computer program facilitates continuous monitoring of the condition of patients with surgical sepsis based charting: 1) the results of laboratory and instrumental diagnostics; 2) the risk of death at any time of observation; 3) statistical data.

Thus, the optimal choice of algorithms of treatment and diagnostic measures in patients with surgical sepsis with different versions of the infection in the abdominal cavity and retroperitoneal space based on reliable prognostic assessment of operational risk (relative mortality risk) helped reduce the average number of deaths from 60% to 30%.

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Indicators of medical and demographic, socio -hygienic, physical and dental status of indigenous women of Taimyr Dolgan- Nenets Municipal District of the Krasnoyarsk Territory

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ABSTRACT

The paper presents the study of indicators of medical-demographic, social-hygienic, physical and dental status of 755 indigenous women of the Taimyr Dolgan-Nenets Municipal District of the Krasnoyarsk region.

Patients belong to socially vulnerable groups (low income and education level, remoteness of residence area, lack of adequate medical care), in connection with which there are big problems with health in general and in particular with the dental one. There is no permanent dental care in small settlements of North of Krasnoyarsk region, no dispensary registration and dental treatment of pregnant indigenous women of the North. Permanent dispensary dental care of indigenous women of the North of Krasnoyarsk region is a compulsory condition to improve the dental health of women and their progeny.

Keywords: dental status, indigenous women, mobile teams of dentists.

INTRODUCTION

Socio-economic situation in the Taimyr Dolgan - Nenets Municipal District of the Krasnoyarsk Territory, changed the lives of the indigenous women of the Far North. Social insecurity, unemployment, declining living standards, in connection with this stressful situation, insecurity could not but affect the health status of women, both somatic and dental. The largest share of indigenous nationalities Dolgan, then Nenets, Nganasan, Evenki constitute, which lead traditionally nomadic and sedentary. The position of women the many lifestyle factors determine: these are hygiene skills, attitude towards their health, culture and way of life [3].

In connection with the situation implementation of national projects in the Russian Federation, including health care, changed socio-economic conditions of the population and how a healthy lifestyle, allowed at the federal level through the budget to take a program to provide dental care of Indigenous Peoples of the North (1,3,4,6,9) . Government of Krasnoyarsk Krai adopted long-term target program to provide dental care in Taimyr Dolgan- Nenets Municipal District in 2012-2016. Oral health is an integral part of general health. Patients with much somatic pathology are also at risk of dental disease, which worsen their general condition. Poor

hygienic condition of the teeth, partial or complete absence of teeth affects the decrease of self-esteem as human beings, and to the stability of his body to different physical conditions. Conclusively proven that various somatic non-communicable diseases, various gynecological diseases, diseases of the oral cavity, poor nutrition, smoking, alcohol, are risk factors for the condition of general health. The presence of such factors largely depends on a person wants to fight for his health, and timely professional medical help (in this case dental) is one of the most important factors in recovery [5,7,8].

Therefore, the timely provision of dental care to remote communities is an important task for the state.

The purpose of the study. Improving the effectiveness of prevention and dental care to residents of remote settlements Taimyr Dolgan- Nenets Municipal District of Krasnoyarsk Krai.

MATERIALS AND METHODS

According to the long-term target program "Providing dental care of the Far North" (2012 2016), in 2013 dental care was provided to the population of the Taimyr Dolgan- Nenets Municipal District, Krasnoyarsk Territory, Taimyr eastern townships, etc. Syndassko, Popigaj, Katyryk. The total population in the three villages was 1300 people, of which the 60.0 % of the female population. Sources of funding: regional budget -15.0 %, the federal budget - 85.0%. Away team consists of dentists: dental surgeon, two dental therapist, dental orthopedic, dental technician and senior nurse (among medical interns). Work term average is 40 days. In the process used to assist the latest medical technology in the field of advanced materials science and dental equipment. Having a modern portable X-ray machine «REXTAR» (Korea), photo-polymerization device Demi Plus LED (manufacturer: KERR), mobile dental equipment «TASK FORSE» (USA) revealed dental disease at different stages of development, properly differentiate and apply the method of treatment. Figure 1 is a mobile dental office in Syndassko. Syndassko village - located 285 km from p. Hatangi, borders with the Republic of Sakha - Yakutia. It is one of the northernmost settlements in the world. The main occupation of the population is reindeer

herding, fishing and hunting wild reindeer on the north.

Fig. 1. Mobile dental office.

The study of small indigenous population of the three villages Taimyr Dolgan-Nenets Municipal District of Krasnoyarsk Krai. The total number of women surveyed was 755 persons in the age group from 15 to 65 years, including children under age 15 - 23. Division along ethnic lines as follows: 90.3 % of the population - Dolgan, 5.0 % - 2.2% Nenets - Nganasans, 1.2 % - Evenki, 1.0 % - the Yakuts .

Research methods included: questioning residents, which included part of the passport; issues of socio- economic well-being, the presence of somatic pathologies and oral examination, and analysis of primary medical records (outpatient somatic map). Thereafter, the replacement of dentition defects removable and fixed prostheses.

Statistical processing of the results was performed using the programs «Microsoft Excel» «Statistica 6», «SPSS 17.0 for Windows». The relationship between the independent variables, measured in nominal and ordinal scales were determined using Pearson ($\chi 2$), we used the method

of correlation and analysis of variance [2].

RESULTS AND DISCUSSION

In terms of socio - economic welfare of women three settlements 77.6 % reported as unsatisfactory, and only 22.4 % of respondents reported as satisfactory. Among indigenous women without primary occupation are the most of Nenets, they are mostly housewives. Indigenous women have marriage registration only 40.7% - Dolgan; Nenets - 26.7% . Among the nomadic and settled indigenous women had incomplete secondary education, secondary - 78.8 %, elementary education - 12.9 % higher education - 8.3%. Prevail somatic pathologies revealed by the survey and analysis of primary medical records in township clinics: respiratory diseases - 28.4% (various forms of bronchitis, tuberculosis) of the gastrointestinal tract - 24.5%; cardiovascular disease – 18. 2% cancer - 5.7%; gynecological diseases - 22.0 % other diseases associated with specific diseases (syphilis, hepatitis, HIV) - 1.2%.

Total visits to the dental examination was in Syndassko - 980, Popigaj - 769, Katyryk - 694. The index definition caries intensity (KPU) showed that 89.0% of women surveyed villages the average value of the Communist Party was 10,4 ± 0,43 (high intensity level of dental caries). Index of oral hygiene in the adult population was 2,2 ± 0,05, which is unsatisfactory.

Prevalence of dental hard tissue and periodontal centuries women aged 15 to 55 years old was found in 100 % of cases. In providing dental practitioner care were treated caries complicated caries, fissure sealing, conducting professional oral hygiene. The total number of seals was - 578, including the treatment of dental caries - 14.6%, on complications dental caries - 72.7 %, fissure sealing under the age of 15 years - 12.7 % of cases. Of these indicators, we can conclude that there is a high need for therapeutic treatment of teeth of indigenous peoples. Exhibited a high degree of correlation relationship in individuals with pathology of the gastrointestinal tract with complicated forms of caries posterior teeth in the age group 15 to 27 years r = 0,874 (p = 0.001). In women of childbearing age suffer from cardiovascular disease reveal an average correlation relationship with carious lesions of anterior teeth r = 0,657 (p =

0.001).

Within the scope of surgical dental care to the female population settlements conducted extractions. Totally 224 teeth were removed, including 39 temporary teeth, according to testimony in connection with the change of the bite. At the age of 19 to 60 years were conducted by removing the complicated forms of caries with destructive changes in the periodontium .Of the total number of removable dentures, making full removable plate dentures was 54.8%, indicating that the complete absence of teeth in the age group from 29 to 40 years. There are needs in prosthetics dentition in age from 19 to 30 years - 34.7 % of the total female population, from 31 to 45 years - 43.5 %, from 46 to 65 years - 90.0%.

It is clear that women need prosthetics in settlements Syndassko, Popigaj, Katyryk, with a large percentage of persons who need removable prosthetics.

CONCLUSIONS

1. Taking into account the disunity of small in number northern points of the Krasnoyarsk Territory, features of employment, it is necessary to improve not only the mobile forms of dental, but also outpatient gynecological care to the female population, especially pregnant women, which in turn should be focused on clinical examination and detection of pathologies at early stages.

2. It is necessary to eliminate the causes of socio-economic nature, negatively affecting the quality of life of indigenous women of the North, thus, which are preventable with the current level of access to health care.

3. Implementation of on-site projects requires the relationship of dental service with other institutions of general medical network, particularly of obstetric-gynecologic plan, as there was revealed correlation relationship of diseases of the oral cavity with gynecological pathologies ($p \leq 0{,}001$).

4. It is necessary to organize dental health social patronage of women in Syndassko, Popigaj, Katyryk with complete lack of teeth in the age group of 19 to 30 years.

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Ecological-Hygienic Evaluation of the Accumulation and Distribution of Lead Compounds in the Organs and Tissues of Yakutia Freshwater Fish

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ABSTRACT

We studied the content and distribution of lead compounds in the Republic freshwater fish in the Rivers Amga (Amginskiy District), Vilyui and lakes of Vilyuisk population, Chroma riv. lower reaches, the Indigirka riv. (Allaikhovsky District) and Kolyma (Srednekolymsky District) in 1996-2011. Studies indicated insignificant level of lead in the tissues and organs as herbivorous and carnivorous fish. Exceeding was detected in some of fish where industrial mining was taking place.

Keywords: environment, the human body, lead, food chain, toxicant.

The concentrations of heavy metals are rising continuously in the environment, they accumulate in different trophic levels of aquatic ecosystems through the food chain and body surface penetrate into the body of fish. To widespread and highly cumulative elements for fish lead and its compounds relate [5, 13, 15, 18, 21]. In recent years, as a result of human impact is a significant inflow into reservoirs of toxic substances, including lead. [11] Lead is a typical toxicant of aquatic ecosystems [16]. The lead content in the earth's crust is small (10 at.%), in the adult human body, it is 120 mg. Lead is a concomitant toxic element [6].

Total reserves of lead in the world, estimated at 100 million tonnes, mainly presented in the form of sulfates. In the environment annually from suburban sources comes from volcanic emissions, soil and silicate meteorite dust, sea salt aerosols, etc. up to 230 tons. Global allocation lead from natural sources is shown in Table. 1.

Currently, most of the territory of Russia is experiencing stress from loss of lead, exceeding critical for normal functioning of ecosystems [20]. The average level of lead pollution of natural water bodies is 138 million tons / year [10].

Lead is ingested with food. Among the foods most often exposed to lead contamination - fish (throughout life they are for your breath "filtered" a huge amount of water passing from capturing her various substances).

The main objects of our study were fish ponds of Yakutia, living under conditions of anthropogenic pollution. For all fish held full general biological analysis (morphometry, size-age composition, abundance estimates, etc.), in addition evaluated anomalies by post-mortem analysis, conducted biochemical analysis of fish (blood and determining the concentration of heavy metals (HM) in the organs and fish tissues).

Lead emissions to the atmosphere have increased dramatically in the past century, reaching 1970 4265h103 t [24]. Anthropogenic lead intake is much higher than natural. The combustion of oil and gasoline in the environment comes at least 50% of the total anthropogenic emissions of lead, which is a major component in the global cycle of this element [8, 23].

Moreover, automobile exhausts give about 50% of the total inorganic lead entering the human body, which is a consequence of its high proportion (75%) of these emissions. Another important source of anthropogenic lead is smelting nonferrous and ferrous metals, while the main natural source of his income is wind dust [1, 2, 3].

Significant source of lead in the environment is the mining industry. In some cases, the content of lead in solid wastes mines can be up to 20 thousand mg / kg. Despite the fact that this is one of the most important sources of lead on the earth's surface, marine and freshwater systems is of great importance atmospheric flow [22].

In river waters, lead concentrations ranged from a few tenths to a few micrograms per 1 dm3. [4] Getting into the aquatic environment, lead migrates predominantly composed of sediment, especially during the period of maximum turbidity. In the waters of all the facilities throughout the year it is almost 100% connected in complex compounds.

The predominance of suspended its forms over dissolved, due to the high affinity to the natural metal adsorbents. At the same time, high capacity lead-marked form strong complex compounds with organic substances. Inorganic salts of lead, except for its nitrates and acetates, are poorly soluble in water [12, 16]. NI Katalevsky et al [9] noted in his paper that the lead content in water increases from spring to autumn.

Manifestation of the toxic effect of lead compounds was observed in aquatic organisms at doses of 0.1 - 0.4 mg / kg. Lead chloride at a concentration of 0.01 mg / kg in water causes death

daphnia a day, while the lead nitrate has the same effect at a much higher concentration - 5 mg / l.

Are the most toxic organic compounds - tetraethyl lead and tetramethyl lead. Some fish species (rainbow trout, lamprey, three-spined stickleback) can serve as a convenient indicator of lead-contaminated aquatic environment as avoidance behavior manifested in these species even at minimal concentrations of this pollutant.

Eggs and tadpoles tested amphibian species are also highly sensitive to the toxic effects of lead compounds, and adults of the same species react biochemical changes (increase of ekskreatsii aminolevulinic acid) for lead content in the diet at doses above 10 mg / kg [12, 16].

Content and distribution of lead compounds in freshwater fish has been studied in pp republic. Mayya Amginskogo area vilui population, lower chrome, Indigirka (Allaykhovskiy) and Kolyma (Srednekolymskiy) in 1996 - 2011.

These studies, monitoring of water bodies of the Far North are absolutely necessary, as the lead on the food chain can be ingested.

The results obtained showed a slight level of lead content in the organs and tissues, such as herbivorous and carnivorous fish. Only in certain organs of certain species of fish lead levels exceeding MRLs.

As can be seen from the data (Table 2-6), lead found in all organs and tissues of freshwater fish Yakutia.

In the organs and tissues of fish caught from the river Vilyuy lead content greater than in the organs and tissues of fish caught from the river Indigirka Allaykhovskiy district and the Kolyma River Srednekolymsky district. Chrome on the river lead content in the organs and tissues of fish were more than Vilyuy river. On the river Mayya lead content in the organs and tissues of fish was less than all, due to the fact that there are not conducted industrial mining and natural water were unaffected by anthropogenic factors (Table 2).

Do carp caught from lakes Dengkyuda Nyurbinsky district and Ebe Vilyui area - small and large individuals - lead content does not exceed the maximum permissible levels for freshwater fish (MRL of 1.0 mg / kg). At the same time lead accumulates in the organs and tissues of the carp population in the following order: liver> bone> muscle> gill> intestine.

Published data on the accumulation and distribution of lead in the organs and tissues of freshwater fish are rather contradictory. For example, according K.H.Zhukusova et al [7], lead accumulates in amounts of 1.5 - 2 times higher than the MRLs in the gills, and research Wojciech J. (1989) (cited by [17].) more likely, it accumulates in the liver freshwater fish. By physiological and histological of the liver can be successfully and relatively accurately judge the state of the external conditions of the environment of a particular individual. [14] This is accompanied by various kinds of pathological changes. These include parenchymal degenerative changes - diffuse vacuolation, circulatory disorders and necrosis [19].

The examined fish Amginskogo district (b. Mayya) MAC exceedances of lead were found (Table 2).

The lead content in the liver of large individuals perch (Table 3) from 5 + to 7 + years, caught in the river Vilyuy, exceeded MRLs for fish products and was 1.305 mg / kg, and in the winter studies in the same population of perch content lead was 1.192 mg / kg.

Young specimens of pike river chromium (Table 4) lead content in the liver (in the summer) is approaching the maximum allowable level and is equal to 0.97 mg / kg, while in the adult muscle in the summer was 1.28 mg / kg, in the winter - 1.16 mg / kg, liver summer - 1.54 mg / kg, in the winter - 1.66 mg / kg, which was in excess of MRL pike muscles from 1.2 to 1.3, in liver - 1.5 - 1.7 times. Exceeding the MRL also manifested in the gills in adults in the summer up to 1 times and bone formations from 1.3 to 2.0 times, the young - to 1.1-fold (Table 4).

In the river Indigirka (Table 5) in adult perch in the liver exceeding MRLs of 1.29 mg / kg, which is more than 1.3 times the MRL values.

Perch of the Kolyma River, there was a slight excess of lead in the liver MRLs large individuals in the summer study, which was 1.21 mg / kg, from the river Indigirka it was 1.29 mg / kg (Table 5, 6).

In roach from the River Vilyuy large individuals aged 6 + to 8 + years in the liver of lead slightly exceed the maximum permitted levels of 1.11 mg / kg (Table 3).

Do chukuchana of Indigirka River (Table 5) in all organs and tissues of the lead content within the maximum permissible levels. Distribution of organs and tissues have been similar, as in other species.

It should be noted that the lead is one of the priority pollutants. At present time, a huge amount of information about the toxic effects of lead on the human body, the behavior of this element in natural environments.

Risk to human health, especially children, is compounded by the high toxicity of lead and its ability to accumulate in the human body.

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Table 1

Release of lead from natural sources (tons per year) [11]

natural source	range units	average value
Windblown soil particles	0,30 - 7,5	3,9
Sea salt spray	0,02 – 2,8	1,4
Volcanoes	0,54 – 6,0	3,3
Forest fires	0,06 – 3,8	1,9
Biogenic particles continental	0,02 – 2,5	1,3
Biogenic volatiles continental	0,01 – 0,38	0,2
Marine biogenic sources	0,02 – 0,45	0,24
Total emission	0,90 - 23	12,0

Table 2

Accumulation and distribution of lead in organs and tissues

of freshwater fish in Amga R. basin

research period	fish age	muscles	liver	intestines	gills	bones
Luce (*Esox lucius*)						
summer	до 2+	0,047±0,033	0,041±0,029	0,040±0,028	0,149±0,105	0,023±0,016
	от 4+ до 6+	0,130±0,092	0,109±0,077	0,062±0,044	0,250±0,177	0,047±0,133
winter	до 2+	0,032±0,023	0,035±0,025	0,027±0,019	0,118±0,083	0,018±0,013
	от 4+ до 6+	0,078±0,055	0,084±0,059	0,043±0,030	0,189±0,134	0,031±0,022
Roach (*Rutilus rutilus*)						
summer	до 2+	0,154±0,109	0,297±0,210	0,094±0,066	0,038±0,027	0,074±0,052
	от 4+ до 6+	0,280±0,198	0,376±0,266	0,197±0,139	0,075±0,053	0,200±0,141
Perch (*Perca fluvialitus*)						
summer	до 2+	0,057±0,040	0,069±0,049	0,042±0,030	0,146±0,103	0,318±0,225
	от 4+ до 6+	0,103±0,073	0,126±0,089	0,087±0,061	0,250±0,177	0,470±0,332
winter	до 2+	0,061±0,043	0,057±0,040	0,036±0,025	0,128±0,090	0,237±0,167
	от 4+ до 6+	0,099±0,070	0,102±0,072	0,074±0,052	0,265±0,181	0,401±0,283

Table 3

Accumulation and distribution of lead in organs and tissues

of freshwater fish in Vilyui R. basin

research period	fish age	muscles	liver	intestines	gills	bones
Luce (*Esox lucius*)						
summer	до 2+	0,510±0,360	0,589±0,416	0,098±0,069	0,285±0,201	0,311±0,220
	от 4+ до 6+	0,940±0,664	1,014±0,717	0,220±0,155	0,490±0,346	0,397±0,281
winter	до 2+	0,726±0,513	0,413±0,292	0,081±0,057	0,402±0,284	0,289±0,204
	от 4+ до 6+	1,127±0,796	0,978±0,691	0,512±0,362	0,970±0,685	0,421±0,297
Roach (*Rutilus rutilus*)						
summer	до 2+	0,703±0,497	0,583±0,412	0,164±0,116	0,288±0,203	0,161±0,114
	от 4+ до 6+	0,714±0,505	1,106±0,782	0,677±0,478	0,344±0,243	0,298±0,211
winter	до 2+	0,544±0,384	0,422±0,298	0,171±0,121	0,253±0,179	0,099±0,070
	от 4+ до 6+	0,876±0,619	0,711±0,502	0,277±0,196	0,411±0,290	0,160±0,113
Perch (*Persa fluviatilis*)						
summer	до 2+	0,785±0,555	0,577±0,408	0,358±0,253	0,531±0,375	0,470±0,332
	от 4+ до 6+	1,536±1,085	1,305±0,922	0,794±0,561	1,026±0,725	0,428±0,302
winter	до 2+	0,934±0,205	0,455±0,321	0,329±0,232	0,613±0,433	0,357±0,252
	от 4+ до 6+	1,859±1,314	1,192±0,842	0,613±0,433	0,815±0,576	0,401±0,283

Table 4

Accumulation and distribution of lead in tissues and organs of pike

and broad whitefish Chroma R. basin

research period	fish age	muscles	liver	intestines	gills	bones
Luce (*Esox lucius*)						
summer	до 2+	0,72±0,51	0,97±0,68	0,55±0,39	0,59±0,42	1,16±0,82
	от 4+ до 6+	1,28±0,90	1,54±1,09	0,97±0,68	1,03±0,73	1,97±1,39
winter	до 2+	0,57±0,40	0,88±0,62	0,43±0,30	0,87±0,61	0,98±0,69
	от 4+ до 6+	1,16±0,82	1,66±1,17	0,82±0,58	0,94±0,66	1,32±0,93
Chir (*Coregonus nasus*)						
summer	до 2+	0,54±0,38	0,82±0,58	0,46±0,32	0,59±0,42	0,93±0,66
	от 6+ до 8+	0,91±0,64	1,58±1,12	0,51±0,36	0,71±0,50	1,36±0,96
winter	до 2+	0,44±0,31	0,63±0,44	0,28±0,20	0,51±0,36	0,68±0,48
	от 6+ до 8+	0,78±0,55	1,37±0,97	0,46±0,32	0,70±0,49	1,27±0,90

Table 5

Accumulation and distribution of lead in organs and tissues of freshwater fish in Indigirka R. basin

research period	fish age	muscles	liver	intestines	gills	bones
Luce (*Esox lucius*)						
summer	до 2+	0,27±0,19	0,41±0,29	0,12±0,08	0,28±0,20	0,31±0,22
	от 4+ до 6+	0,74±0,52	0,91±0,64	0,62±0,44	0,52±0,37	0,69±0,49
winter	до 2+	0,29±0,20	0,36±0,25	0,15±0,11	0,34±0,24	0,49±0,35
	от 4+ до 6+	0,41±0,29	0,60±0,42	0,32±0,23	0,28±0,20	0,52±0,37
Dace (*Leuciscus leuciscus*)						
summer	до 2+	0,38±0,27	0,57±0,40	0,44±0,31	0,51±0,36	0,38±0,27
	от 4+ до 6+	0,67±0,47	0,81±0,57	0,63±0,44	0,59±0,42	0,67±0,47
winter	до 2+	0,45±0,32	0,48±0,34	0,47±0,33	0,55±0,39	0,49±0,35
	от 4+ до 6+	0,41±0,29	0,62±0,44	0,45±0,32	0,69±0,49	0,52±0,37
Perch (*Persa fliviatilis*)						
summer	до 2+	0,51±0,36	0,81±0,57	0,42±0,30	0,49±0,35	0,72±0,51
	от 4+ до 6+	0,77±0,54	1,29±0,91	0,59±0,42	0,63±0,44	0,81±0,57
winter	до 2+	0,46±0,32	0,76±0,54	0,38±0,27	0,50±0,35	0,52±0,37
	от 4+ до 6+	0,74±0,52	0,87±0,61	0,51±0,36	0,67±0,47	0,77±0,54

Table 6

Accumulation and distribution of lead in organs and tissues of freshwater fish in Kolyma R. basin

research period	fish age	muscles	liver	intestines	gills	bones
Dace (*Leuciscus leuciscus*)						
summer	до 2+	0,31±0,22	0,41±0,29	0,14±0,10	0,29±0,20	0,31±0,22
	от 4+ до 6+	0,79±0,56	0,92±0,65	0,57±0,40	0,51±0,36	0,84±0,59
winter	до 2+	0,35±0,25	0,37±0,25	0,17±0,12	0,38±0,27	0,45±0,32
	от 4+ до 6+	0,38±0,29	0,58±0,41	0,29±0,20	0,31±0,22	0,51±0,36
Chukuchan (*Catostomus catostomus*)						
summer	до 3+	0,45±0,32	0,73±0,52	0,29±0,20	0,39±0,28	0,65±0,46
	от 6+ до 8+	0,61±0,43	0,84±0,59	0,41±0,29	0,45±0,32	0,91±0,64
winter	до 3+	0,41±0,29	0,57±0,40	0,25±0,18	0,41±0,29	0,67±0,47
	от 6+ до 8+	0,58±0,41	0,73±0,52	0,59±0,42	0,64±0,45	0,98±0,69
Perch (*Perca fluviatilis*)						
summer	до 2+	0,51±0,36	0,83±0,59	0,41±0,29	0,48±0,34	0,71±0,50
	от 4+ до 6+	0,69±0,49	1,21±0,85	0,58±0,41	0,58±0,41	0,88±0,62
winter	до 2+	0,42±0,30	0,72±0,40	0,38±0,27	0,51±0,36	0,48±0,34
	от 4+ до 6+	0,66±0,47	0,98±0,69	0,43±0,30	0,66±0,47	0,81±0,57

Arctic Medicine. Paradoxes and Problems

D.G. Tikhonov, F.A. Platonov, V.P. Nikolaev

ABSTRACT

On the basis of analyzing the views of scientists and experts, and on the basis of their data, the authors express their point of view on the desirability of providing the Arctic (North) medicine as an independent field of theoretical knowledge and practical activity like, for example, tropical medicine.

Keywords: geographical distribution of the population, the arctic, the arctic (north) medicine.

At different times Avtsyn A.P., Orekhov K.V. from the USSR RAMS, North researchers Bezrodnykh A.A., Tikhonov D.G., Khasnulin V.I. [et al.] put forward the Arctic medicine as a new section of medical science [1, 6, 7, 9, 10, 11]. The existence of considerable controversy in the scientific medical community about the desirability of distinguishing the Arctic medicine, for the first time in 1998, Professor Khasnulin V.I. publicly expressed in his book "Introduction to polar medicine" [11].

In 2009 and 2010 two editions of MD, Professor Tikhonov D.G. "The Arctic medicine" monograph in Moscow and Yakutsk were published [8]. In the book for the first time the definition of term, goals and objectives of the Arctic medicine were founded and given: "The Arctic medicine is an area of medical science that studies the features of the functioning of the human body and its diseases in the Arctic in order to develop the most effective and practically acceptable means and methods of prevention, diagnosis and treatment".

Monograph received a positive assessment of the scientific community. In his review of the monograph RAMS Academician V.P. Kaznacheev noted, "... it is the first in 30 years and a very deep attempt to allocate as a subject of study health of indigenous and non-indigenous population, whom destiny links with a common homeland - Arctic Russia" [5]. Doctor of medical sciences, professor, honored worker of science, M.A. Tyrylgin in his review of the monograph stressed: “In the result of his study Tikhonov D.G. came to the important original, but seriously substantiated conclusions: in the arctic regions human diseases have their own characteristics, not only in its prevalence but also in clinical manifestations, risk factors, etiopathogenesis and require inclusion in the process of learning and practice”.

In 2009, development Programmes of North (Arctic) and North-eastern federal universities were approved by the RF government, where Arctic medicine was declared as one of the main directions of research. In Arkhangelsk in 2003 the Research institute of Arctic medicine was founded, there is Arctic medicine center in Oulu (Finland). Every four years the International Congress on circumpolar medicine takes place; there were already 14 Congresses. But the paradox! Until now, the Arctic medicine as an independent branch of medicine is not recognized. In this regard it should be noted that the famous explorer of biomedical problems of the North, Academician of the USSR RAMS A.P. Avtsyn in 1985 wrote: "There is other attitude to the proposed term “northern medicine”, which is well known to the soviet doctors”.

Some foreign researchers relate to the recognition of the independence of the northern medicine with doubt, arguing that it did not have its own specific nosography, like, for example, tropical medicine [8]. From our point of view, there is no reason to doubt the appropriateness of allocating northern medicine as an independent field of theoretical knowledge and practical activity. It should be noted that the infectious nosography of northern circumpolar territories is very original [4], and contrary to popular belief reminds resemblance to tropical medicine. Next, in 1998, in his book “Introduction to polar medicine” V.I. Khasnulin writes: "Even today, at the turn of the third millennium, many scientists, doctors living in the middle latitudes and not test the effect of the North to themselves, argue that any particular problems for human health in the high latitudes cannot exist. In their view, the functioning of homeostatic systems in the human body in the North has no peculiarities, and the extreme climate and geophysical factors absolutely do not mean anything to the development of a particular disease. Moreover, the conclusions of scientists such as A.P. Avtsyn, V.P. Kaznacheev, N.R. Deryapa, N.V. Vasiliev, L.E. Panin, G.M. Danishevskii et al., considered either eccentricity or artifacts. How one can explain such claims if it is ignorance or a tribute to some policy- the question is not a simple one"[11]. Our article in the journal «International journal of circumpolar health» (2013) on Arctic medicine they decided to publish with a mark as a point of view from Russia [12]. It seems that thousands of researchers around the world are engaged in Arctic medicine, not knowing what they do, as there is no definition of Arctic medicine in general. However, the definition of Arctic medicine, offered by us, has not been commented.

Nevertheless, according to some forecasts, sounded at the XIII international congress on circumpolar health (Novosibirsk, June 12-16, 2006) to the northern regions in the future can move about 1.5 billion population, not adapted to the cold climate from the more southern areas of the Earth.

On the territory of the Russian Far North currently about 11 million people live, and in the coastal zone not more than one million people. Thus, in total, on the territory of the Far North in the future its population may increase to the current population of the whole of Russia. On the preservation of the dominant share of Russians in the future population of the Far North must take care now, not for nothing Russia is a country that won the cold [3]. Current state of health of the population of the Far North is far behind the nationwide figures. Solving these problems is an urgent problem of our time. Arctic medicine will help to solve these problems.

Based on the foregoing, the logical **conclusion** is that the health care system requires reform of the arctic regions, taking into account features of human pathology in the North. The need to modernize the health care system in the Far North has arisen due to a lack of high efficiency of the existing health care system, which is partly the result of medical care without regard to the specifics of the north. Arctic medicine - is a modern new area of medical science that can actually lengthen life expectancy and reduce the mortality rate of the population of the Far North.

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Arctic Territories: Demographic and Socio-Economic Problems (on the example of the Republic Sakha (Yakutia))

A.A. Pakhomov, T. S. Mostakhova

ABSTRACT

The paper analyzes the demographic situation in the Arctic, a region with indigenous northern peoples on the example of the Sakha Republic (Yakutia). The problems of the modern social and economic situation of the indigenous peoples of the North connected with the development of the traditional Northern branches are considered. Measures on improvements of the state policy towards the indigenous numerically small people of the North are proposed.

Keywords: scientific researches, Artic zone, demographic safety, indigenous peoples of the North, economic activity, traditional branches of the North.

The Arctic is that macroregion where the vector of Russian history is actively directed today. Sources of such orientation are obvious. This is the most powerful natural resource potential, which is possessed by the Arctic zone. And this is geopolitical significance of region, which acts as an outpost of preservation of territorial integrity of country.

Occupying only 18% of territory of the Russian Federation, the Arctic accumulates more than 90% of nickel and cobalt, 60% copper, more than 96% of platinum metals, about 80% of gas and 60% of oil of Russia are extracted [1].

It is not accidental the Arctic zone is a special object of state policy of Russia. There were adopted Principles of state policy of the Russian Federation in the Arctic for the period till 2020 and a further perspective approved by the President of the Russian Federation D.A. Medvedev on 18 September 2008 № Pr-1969, the Strategy of Development of the Arctic zone of the Russian Federation and safeguarding of national security till 2020 approved by the President of the Russian Federation on 8 February 2013 № Pr-232. There is the Decree of the Russian President of 02 May 2014 № 296 "On the land territories of the Arctic zone of the Russian Federation."

The Arctic zone of Russia includes territories administratively attributed to different subjects of the Russian Federation, including to the Republic of Sakha (Yakutia). At the same

time, in the structure of the latter in the republic only the territories of 5 districts are included - Allaikhovsky, Anabarsky, Bulunsky, Nizhnekolymsky and Ust-Yansky districts.

Recent years have been noted by strengthening of attention to the problems of socio-economic development of the Arctic territories. The necessity of improvement of normative basis for the state Arctic policy is due to the fact that the situation in the Arctic region remains extremely tense. A transition to market relations was painfully reflected on the social situation in the Arctic regions of Russia. The quality of life of majority of population has sharply deteriorated, which have had an impact on the state of health and life expectancy. Migration processes have become unmanageable.

The level of real incomes of the main social groups went down. And demographic indicators significantly deteriorated. A migration outflow of population from the Arctic Circle continues, since the work in the Arctic is unfortunately no longer as economically attractive as in former years.

Demographic aspects of sustainable development of macroregion are some of key aspects. Demographic safety is one of components of national security. This aspect is particularly topical for the Arctic, which is significant in terms of geopolitics. Many Arctic territories already now represent spaces depopulated enough. Demographic potential is only supported by the local population, in the first place by indigenous small-numbered peoples of the North where quite clearly designated problems of preservation of demographic security are present. Practice shows that the demographic problems for the northern territories not only retain their significance, but are aggravated too.

This is clearly demonstrated by the example of the Republic of Sakha (Yakutia), the biggest in terms of territory entity of the Russian Federation.

In the Republic of Sakha (Yakutia) a tendency of demographic development is a reduction of population size, which began since 1991.

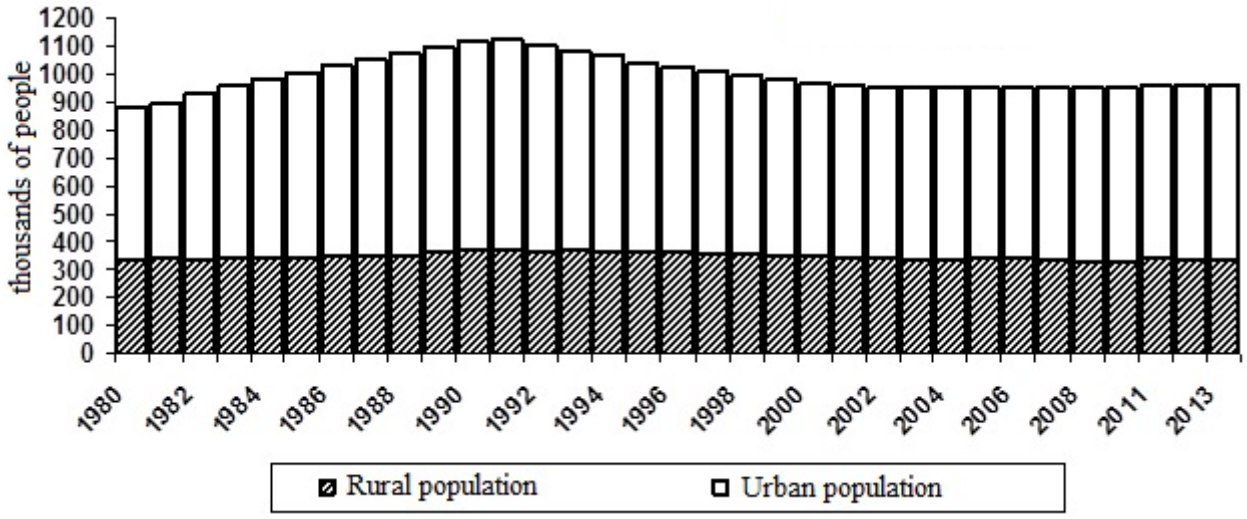

Fig. 1. Dynamics of population size of Yakutia for 1980-2013

A curtailment of town-forming mining production led to the migration from unpromising settlements and respectively to the intensive migratory outflow. In formation of population of region a change of components of its growth happened – the migratory factor ceased to play the dominant role, which had been characteristic for the previous period (fig. 2).

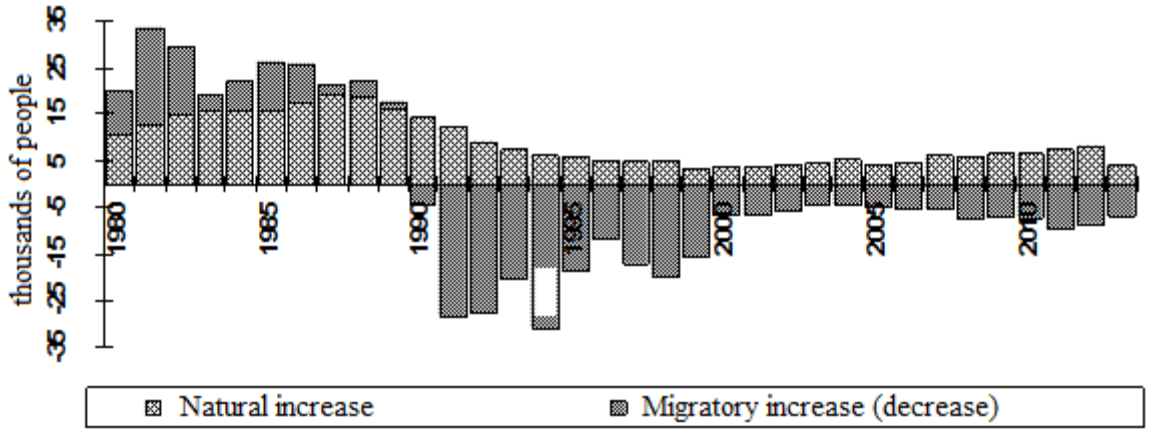

Fig. 2. Relation of natural and migratory increase in population of Yakutia, 1980-2013

The outflow of population outside of the republic is not compensated by the natural increase, which still has a positive quantity. In 2000 it was 3.9‰, in 2006 - 4,7‰, in 2011 - 7,8‰ (tab. 1).

Table 1

Dynamics of coefficients of natural increase of population of the Republic of Sakha (Yakutia) for 2000-2013

Years	the Russian Federation	the Far Eastern Federal District	the Republic of Sakha (Yakutia)
2000	-6,6	-3,5	4,0
2001	-6,6	-3,5	3,7
2002	-6,5	-3,3	4,4
2003	-6,2	-3,3	4,9
2004	-5,6	-3,1	5,3
2005	-5,9	-3,8	4,1
2006	-4,8	-2,5	4,7
2007	-3,3	-1,2	6,4
2008	-2,5	-1,0	6,1
2010	-1,7	-0,6	7,0
2011	-0,9	-0,3	7,8
2012	0,0	0,9	8,5
2013	0,2	1,3	8,8

In the demographic development a transition to a modern, so-called rational type of population reproduction happens. A decline in fertility and growth of mortality of population became the main tendencies of this period of demographic development. The result of this interaction becomes a decline in the natural population increase.

With respect to the fertility as the first component of natural reproduction the dynamics of recent years was marked by positive developments: this is the increase in the absolute number of births and the overall fertility coefficient (tab. 2).

Table 2

Dynamics of total fertility coefficients for 2000 -2013 (‰)

Years	the Russian Federation	the Far Eastern Federal District	the Republic Sakha (Yakutia)	Difference of coefficients	
				RS (Y) / RF	RS (Y) / FEFD
2000	8,7	9,7	13,7	1,57	1,41
2001	9,0	10,3	13,9	1,54	1,35
2002	9,7	11,0	14,6	1,51	1,33
2003	10,2	11,6	15,0	1,47	1,29
2004	10,4	11,9	15,5	1,49	1,30
2005	10,2	11,5	14,3	1,40	1,24
2006	10,4	11,5	14,4	1,38	1,25
2007	11,3	12,3	16,1	1,42	1,31
2008	12,1	12,6	16,2	1,34	1,29
2009	12,4	13,0	16,8	1,35	1,29
2010	12,5	13,2	16,8	1,34	1,27
2011	12,6	13,2	17,1	1,36	1,30
2012	13,3	14,0	17,8	1,330	1,27
2013	13,2	13,9	17,5	1,32	1,26
2013/2000	151,72	143,29	127,73	x	x
2013/2006	126,92	120,86	121,52	x	x

In 2011 according to the total fertility coefficient Yakutia took the 1st place in the Far Eastern Federal District and the 6th place in the Russian Federation (17,1‰). According to the results of 10 months of 2012 Yakutia having the total fertility coefficient 17,5‰ is located on the 7th place after the Republic of Tuva (26,7‰), the Chechen Republic (26,3‰), the Altai Republic (22,8‰), the Republic of Ingushetia (22,5‰), the Republic of Dagestan (18,7‰), and the Khanty-Mansi Autonomous Okrug – Yugra (17,7‰). Nevertheless, the total fertility coefficient indicates the long-term tendency of decline in fertility.

Compared with the Russian Federation as a whole and the Far Eastern Federal District Yakutia nevertheless stands out by higher values of total fertility coefficient being almost at the level of simple reproduction of population (tab. 3).

Table 3

Dynamics of total fertility coefficient of population of the Russian Federation and Far Eastern Federal District

(the average number of children per 1 woman)

Years	the Russian Federation	the Far Eastern Federal District	the Republic Sakha (Yakutia)
2000	1,195	1,256	1,77
2001	1,223	1,322	1,78
2002	1,286	1,392	1,85
2003	1,319	1,443	1,87
2004	1,340	1,466	1,91
2005	1,287	1,404	1,74
2006	1,296	1,392	1,73
2007	1,406	1,487	1,92
2008	1,366	1,524	1,94
2009	1,537	1,575	2,01
2010	1,567	1,625	1,998
2011	1,582	1,657	2,057
2012	1,691	1,780	2,166
2013	1,707	…	…

A different demographic sphere is characterized by a considerably larger range of problems – the mortality of population.

An overall indicator in the sphere of mortality is the life expectancy at birth. In the early 60s the life expectancy at birth in the Russian Federation was significantly higher than in the countries of the so-called third world. Russian women lived 17 years longer than women of

Turkey, almost 20 years longer than Chinese women. In men indices of life expectancy were higher by 13 and 16 years, respectively [2]. Russian men lagged behind by only 3.4 years from the men who lived in the US or Japan. The Russian women had a probability to live almost till the same age as Japanese women, and only 2.5 years less than American women. In other words, Russia had the life expectancy, which was not much different from the developed countries of the West.

Currently the situation in the sphere of mortality cardinally changed. Low indices of life expectancy - this is the proof of not only poor health state, but also social problems in the country as a whole. In recent years the duration of life exceeds the level of 70 years, which was recommended by WHO, only for the female population [3]. In the structure of causes of death the considerable specific weight of deaths from accidents, poisonings and injuries is retained for a long time, the mortality as a result of alcohol intoxication is especially considerable. Supermortality of men is the essential characteristic of modern processes of mortality. It continues to retain the excess of coefficients of mortality in men as compared with the analogous indices in women, particularly in a working age group [4].

A considerable role in the formation of population of the Arctic and northern territories is played by the migration. The Far East region as opposed to the federation as a whole has been losing its population through the past 2 decades, although a negative coefficient of migration balance slightly decreased. An even more difficult situation is observed in the Republic of Sakha (Yakutia). Although in the recent years the coefficient of migration outflow is reduced but nevertheless it remains twice as much than according to the Far Eastern Federal District as a whole [5].

The presented results allow to judge that in the Republic of Sakha (Yakutia) substantial transformational processes happen in the reproduction of population that makes actual the elaboration of new approaches to the content and mechanisms of implementation of demographic policy [6].

One of distinctive features of the Arctic zone is not only the wealth of its natural resource potential. The Arctic is the territory of settlement of indigenous small-numbered peoples of the North (hereinafter - ISPN).

It seems that in the sustainable development of the Arctic this should also be given a worthy place too. The peoples of the North have a small size. Hence, measures of state support should separately be described in detail.

There are many enough problems in the sphere of ISPN. This is a low level of life, and problems in relationships with a business community, and a drop of national identity, and many other things.

The total number of indigenous small-numbered peoples of the North of the Republic of Sakha (Yakutia), according to preliminary data of All-Russian census of 2010 amounted to 40.2 thousand people, including the Evenki - 26.1 thousand people, the Evens - 9.8 thousand people, the Dolgans - 1.9 thousand people, the Yukagirs - 1.3 thousand people, and the Chukchi - 0.6 thousand people. As compared with 2002 the number of small-numbered peoples of the North increased by 21% (tab. 4).

Table 4

Population dynamics of indigenous small-numbered peoples of the North of the Sakha Republic (Yakutia) for 1989-2010

	According to data of census of 1989 (thousands of people)	According to data of census of 2002 (thousands of people)	According to data of census of 2010 (thousands of people)	Change of quantity by 2010 as compared with 1989, %
the Evenki	15,9	18,2	26,1	164,2
the Evens	10,6	11,7	9,8	92,4
the Yukagirs	0,8	1,1	1,3	162,5
the Chukchi	0,5	0,6	0,6	120,0
the Dolgans	0,5	1,3	1,9	380,0
Total	**28,2**	**32,9**	**40,2**	**142,6**

The indigenous small-numbered peoples of the North live on the territory of 21 municipal districts of the Republic. The small-numbered peoples of the North are less than 6% in these districts. 70 villages of 21 uluses (districts) of the Republic of Sakha (Yakutia) enter into the List of places of traditional residence and traditional economic activity of indigenous small-numbered peoples of the Russian Federation.

A presence and worsening of demographic problems was mentioned as far back as at the end of the last century. Thus, F. S. Donskoy asserted about the reduction of natural increase of population for 1990-2003 by a factor of 3.6, including the Evenki - 9.4 times, the Dolgans - 10.4 times, the Selkups - 39 times, the Eskimos, the Khanty, the Mansi, the Evens - 3-4 times [7].

The economic situation of peoples of the North is related with the development of economic sectors in places of their traditional residence. The main kinds of economic activity of indigenous small-numbered peoples of the North remain such traditional sectors of economy as reindeer breeding, hunting and fishing. Currently one has to state that the material basis of

existence of indigenous population of the North, the Arctic is undermined - the traditional industries. A reindeer population decreased by 2.5 times, production volumes of fish and trade furs sharply decreased as well as wild hoofed animals, game birds, harvesting of wild berries, mushrooms, medicinal plants, and technical raw materials. It is intensively reduced and deepens degradation of reindeer pastures, pollution of water bodies and air space, disturbance of soil cover, a habitat of animals changes, species composition is depleted, their numbers are reduced.

Currently, nomadic tribal communities must support an ethnoforming role of reindeer breeding as a form of self-organization and self-employment of indigenous small-numbered peoples of the North designed to preserve the traditional economic activity and a lifestyle of indigenous small-numbered peoples of the North.

The health status of indigenous population of the North acts as one of essential elements of social position of these peoples. Lower indicators of health are typical for the small-numbered peoples of the North of the Republic of Sakha (Yakutia). Indicators of development of health infrastructure are also low in the regions of compact residence of peoples of the North.

A reduction of health care resources is to a large extent related to standards in the sphere of health care, which completely ignore the specific of the North (settlement dispersion, absence of constant transport connection, and so on).

A shutdown of preschool institutions and part of schools because of ungradeness became one of results of the transition to a market economy.

Thus, there are well-defined problem points in the modern socio-economic state of indigenous small-numbered peoples of the North. These can include threats to the demographic potential of these peoples, rather high unemployment figures, low per capita income, which in turn is related to predominant employment in traditional sectors of the North (reindeer breeding and trades), where ones of the lowest figures of wages are observed.

The conclusions, which can be drawn from the above-stated, are obvious. The Arctic increasingly becomes an actual center of economic gravity. The indigenous peoples of the North should find their place in modern life; they should not remain an isolated civilizational enclave.

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Rybak O.G., Luchsheva L.F.

Situational Analysis of Aberrant Deviant Eating Behavior in Older Age Groups in Khabarovsk (on the Example of Socially-Organized Collective)

ABSTRACT

The paper presents the analysis of application of the indicator of the dental pathology development risk, according to the recommendations of the European Commission and the program of joint actions on monitoring of dental health “Daily intake of food and drinks" in pension age persons, living in the "Social house №1 of Khabarovsk veterans ", Khabarovsk. As the study showed the indicator interpretation was not resultative, which was expressed in the assessing index of the CFE (caries, filling, extracted teeth) and the number of surviving functioning teeth not more 8. 86±1. 59 on each subject.

Keywords: gerontology, geriatrics, nutrition behavior, dental health indicator.

INTRODUCTION

Dental diseases affect overall health, causing considerable pain and suffering, are changing the human diet, his speech, welfare, i.e. on the quality of life [2].

Dental health and nutritional behavior is determined by the way of life and its components [5,7], which includes: nutrition, bad habits, polymorbidity. The determining factor of oral health in all segments of the population according to the European Commission of indicators dental health (ECIDH) are the nature and mode of supply. Daily consumption of food and drinks" - the indicator of the risk of dental diseases. This indicator is recommended for people aged from 5 to 60 years and older. European Commission, Directorate-General health and consumer protection conducted the action on health monitoring and recommend the use of indicators to determine the directions of work of interested health authorities in the prevention of diseases, including dental.

Definition of the indicator "the Daily consumption of food and drinks" is calculated, from the calculation of the frequency of daily meals and drinks population of this age group. The numerator is indicated the number of people who reported the frequency of meals and drinks; the denominator is the total number of investigated. Interpretation of the indicator is as follows: less than 3 times - low risk, from 3 to 5 times the normal risk from 5 to 10 times higher risk, more than 10 times - very high risk [1].

Numerous observations suggest that a large number of older people eat correctly, in their diet dominated by food containing animal fats with excessive amount of flour products and

sweets. Rational nutrition age affects the evolution of man, it slows down and improves hormonal regulation, translating metabolism at a less intense and more long-term operation. Ageing leads to a natural reduction in the need for nutrients and energy. The intensity of metabolism in the elderly is reduced in direct correspondence with increasing age [3,6,7,8].

Rational nutrition in old age (geodietica) is an important factor in the prevention of pathological layers on the natural aging. The energy needs of the body in old age decreases due to a reduction in activity and, accordingly, reduce the intensity of metabolism and digestion, which is consistent with the overall activity of this category of people [4].

Research objective: to reduce the burden of chronic systemic diseases, including dental through the correction of eating behavior and habits based on the definition of the indicator "the Daily consumption of food and drinks" among people of older age groups.

MATERIALS AND METHODS

The study was conducted on the basis RSI "Khabarovsk social house veterans №1", Khabarovsk. For analysis, we used a uniform card, interviewing and questionnaire with subsequent statistical processing.

We conducted exhaustive research, analyzed 122 patient cards, including somatic pathology, test results, discharge epicrisis, physiological condition of an organism of the subject. We counted verified nosological forms of each patient (the indicator "number of diseases/one patient") in different age cohorts. The total number of surveyed was subjected to distribution by the WHO age gradation of persons over the working age in 3 groups:

1. 60-74 years - old age. The average calendar age 70,24±0,71 years (25 persons)
2. 75-89 years - old age. The average calendar age 83,33±0,41 years (89 persons)
3. 90 years and older - long-livers. The average calendar age 92,38±0,53 years (8 people)

RESULTS AND DISCUSSION

It is established that the index of multifactorial diseases in recognition is in a group of elderly - 4,08±0,37, patients senile age - 5,27±0,16 and 5,63±0,59 - long-livers. The share of the gastro-intestinal tract (GIT), including the abnormal nature, have 8.06% of polymorbidity. In the mouth the clinical picture of pathology of the digestive tract presents pyostomatitis, smoothness filiform papillae language, erosive lesions, etc. which are accompanied by a burning sensation, ageusia, the pain of the oral cavity. According to the WHO target indicator, the number of surviving functioning teeth to 60 years of age in each should be at least 20 teeth. In turn, the index of the CFE (caries, filled teeth, extracted teeth) in groups naturally increases with age: older - 22,64±1,03, elderly - 24,02±0,57, centenarians - 26,75±0,48.

Analysis of the questionnaires showed that during the day the elderly eat more 3,76±of 0.27 times, representatives of elderly 3,37±0,17 times and centenarians - 2,37±0,37 times. Preference in the diet is given first of all flour products, vegetables and less meat, dairy and sour-milk production. Between-meal snacks include sweetened tea, fruit drinks, coffee and confectionery, canned food. And some of the surveyed noted the use of certain vegetables and fruits soft consistency.

The survey showed a direct correlation to the quality of power from the state of oral health. 100% of respondents declared impossibility of the use of certain classes of products due to complete/partial edentulous, inflammatory diseases of a mucous mouth, taste perversion, disadaptation to new orthopedic constructions.

CONCLUSIONS

1. The gastrointestinal pathology in the examined is 8.06% of pluripotency that may be formed with age under the influence of interference dental morbidity.
2. We identified low risk of long-livers and normal risk of representatives of old age and elderly development of diseases of the oral cavity, according to the recommendations of the program of development of the European global indicators dental health.
3. In the study, the use of the indicator "the Daily consumption of food and drinks" does not characterize the risk of dental diseases. Quality of gerodietica can't be proven and is not effective, since at the time of the study in persons over the retirement age, the number of preserved functioning teeth is 8.86±1. 59.
4. Deviant feeding behavior among people of older age groups is characterized by low awareness of rational nutrition, poor adherence on the part of medical workers, the economic cost of the unit's food preferences.
5. The health of the oral cavity effects on the frequency of consumption and characteristics of food and drinks, as expressed in the index the index of the Communist party in groups.
6. It is necessary to implement socio-educational programs, "Health schools", individual and/or group seminars, publications in the mass media for correcting formed deviant eating behavior among people of older age groups.

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Products of Plant and Animal origin as Modifiers of Active Systems Drug Metabolism: Pharmacogenetic Aspect

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ABSTRACT

The paper deals with the topical issue of the drug's interactions with components of commonly used food and remedies of traditional medicine (folk medicine). Similar studies are needed for a personalized approach to the treatment. In particular, the effect of traditional and new food, plants, which are used in traditional medicine, the characteristics of the person's lifestyle on the activity of enzymes of the family of cytochrome P-450 involved in the metabolism of drugs and actively studied in pharmacogenetic studies has been shown. Presented problematics is the basis for a thorough gathering of the medical history referring to the ways of life (food, bad habits) of the patient in the appointment of appropriate therapy.

Keywords: drugs, pharmacogenetics, cytochromes P-450, food, remedies of the traditional medicine.

Modern official medicine is faced with a growing number of interactions of drugs with components of food, which is commonly used and remedies of the traditional medicine. Particular attention is paid to their influence on the activity of extensive system enzymes of family cytochrome P-450, which are involved in the metabolism of many drugs and which are actively studied in pharmacogenetic research. The **aim** of the present study was to analyze the available information about potential interactions of the drugs and products of plant and animal origin, which are used in human nutrition and as remedies of the traditional medicine. Similar studies are needed for a personalized approach to the treatment.

MATERIALS AND METHODS

The information search, analysis and generalization, system analysis were used in the paper.

RESULTS AND DISCUSSION

In addition to individual pharmacogenetic differences in reactions to drugs and food products, the situation is complicated by the possible interactions of these components regardless of the genotypic characteristics of the patient, which are illustrated below.

Positive and negative results of such interaction in preclinical and clinical practice in a number of cases are predictable, but sometimes have unpredictable nature. The reduction of

neurotoxicity of cytotoxic drugs while the simultaneous application of plant and animal origin is the example of conditionally positive drug interactions. Thus, neuropathic effects of oxaliplatin are reduced when administered to mice injections of diluted bee venom [15], rats – eel calcitonin [1], salmon calcitonin [2], turmeric [3], and green tea extract [10]. The use of grapefruit juice (a potent inhibitor of CYP3A4) during therapy with drugs that are substrates of cytochrome CYP3A4 refers to the examples of the negative nature of the interaction. It was first time such an unexpected interaction has been described for the simultaneous use of felodipine and alcoholic drink, in which the grapefruit juice was added to mask the taste. Subsequent studies have shown that grapefruit juice reduced first-pass metabolism of felodipine by selective post-translational reduction of the expression of CYP3A4 in the intestinal wall. In particular, the 24-hour duration of action on the organism of a grapefruit and grapefruit-based products results in the fact that their repeated consumption contributes to a significant increase of the oral bioavailability and a cumulative increase of AUC and C_{max} in the several simultaneous use of drugs, in particular, most of dihydropyridine calcium channel antagonists, terfenadine, saquinavir, cyclosporine, midazolam, triazolam, verapamil, lovastatin, cisapride, astemizole et al. [5]. It is known that such action of a grapefruit is associated with the presence furanocoumarin bergamotin in it. This active component is in other products used by man, in particular, limes, on the activity of CYP3A4 and on the pharmacokinetics of several drugs is affecting in the same way [6]. Potential drug interactions are typical for the more modern drugs, which include targeted drugs and biologics, many of which continue to be at different stages of clinical trials. Thus, during the treatment by tyrosinekinase inhibitor bosutinibom urged to avoid the use of grapefruit in the form of fruit and juice, as well as related citrus fruits (eg, bitter oranges) [4].

In addition to grapefruit in Ukraine became available other exotic fruits and vegetables, which are consumed by the population in large numbers in the recent years. At the same time, reception of drugs whose metabolism is associated with the cytochrome system and the simultaneous use of these products may not be innocuous. For example, the effect on the activity of several cytochrome P450 (CYP1A1, CYP1A2, CYP2E1 and CYP3A11) of six tropical fruits, namely, banana, mangosteen, guava, pineapple, mango and papaya was investigated in a recent study in mice. The pineapple juice appeared the most potential inhibitor against these enzymes, so the consumption of it in large quantities over a long period of time can lead to side effects in the case of the use of drugs - substrates of these options cytochromes [7].

It was shown a possible effect on drugs metabolism of traditional plant products of local population, such as cranberries. In particular, the use of cranberries and cranberry juice in the treatment of warfarin can lead to increase international normalized ratio (INR), which is a key measure of blood clotting [8].

Another important problem is the uncontrolled use of a population of herbal tinctures and teas as a means of national folk medicine during concomitant therapy. The classic and most-studied example is the induction of the activity CYP3A4 by the components of St. John's wort, often used to treat depression. [12]. Thus, the Office of the Food and Drug USA (FDA) does not recommend the combined use of St. John's wort extract with oral contraceptive drugs, selective serotonin reuptake inhibitors and inhibitors of HIV protease.

Familiar foods of animal origin, in particular, honey, can also have an effect on the concomitant medication, and these effects may have an individual ethno-geographical nature. Thus, in vitro study, it was shown that the wild honey Tualang, found in Malaysia inhibited CYP2C8 activity [13], at the level of macroorganism could potentially lead to a change in the metabolism of drugs, which are metabolized by this enzyme, in particular, a potent opioid buprenorphine. In another study, the effect of honey produced in the highlands of the Western Ghats (South India) on the enzyme activity of CYP3A4, CYP2D6 and CYP2C19 was studied on the volunteers within 7 days. It has been found that the use of honey led to the induction of only variant CYP3A4 [14].

At the same time, there are screening tests, indicating the absence of potential interactions between foods commonly used in the population, which is at the same time the remedies of traditional medicine, with drugs. In particular, the study on human volunteers did not reveal the effect of garlic extract on the activity of the enzymes CYP2D6 and CYP3A4 [11].

We should not underestimate the fact that in addition to food and remedies of traditional medicine, bad habits rights, in particular, the use of alcohol and nicotine may influence on the drug metabolism. In particular, it was shown the effect of nicotine on neuroleptic metabolism of clozapine and olanzapine in connection with the induction of the enzyme CYP1A2 in schizophrenic patients [9].

Thus, the simultaneous use of several drugs, except of which are not narcotic drugs and antidepressants, and use certain foods and remedies of traditional medicine may contribute to the temporary change in metabolizer's phenotype and, accordingly, the risk of side effects, even when using the information about the respective genotyping. A presented problem is the basis for a thorough medical history analysis in the order of the ways of life (food, bad habits) of the patient in the appointment of appropriate therapy.

CONCLUSIONS

1. The analysis of interactions of drugs with components commonly used food and traditional medicine was conducted.

2. The influence of food, plants used in traditional medicine, features the image of a person's life on the activity of enzymes of the family of cytochrome P-450, which are involved in the metabolism of drugs.

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Manufacture of Specialized Children's Foods from Local Supplies in Sakha Republic

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ABSTRACT

This article reviews data on manufacturing children's foods derived from animal raw materials supplied by local farms of Sakha Republic.

Study of reindeer milk from different farms revealed that it might serve as a substitute for human milk after certain processing. This is mainly due to its high nutritional value and technological features.

This is also true for horse milk. It contents is significantly different from cow milk but close to human milk.

Considering close similarity of fat from young species of Yakut horse to milk fat in contents of middle-chain fatty acids, it may be viewed as an additive for adjustment of fat contents.

Keywords: breast-feeding, horse milk, fat of young species of Yakut horse, children's foods.

During the past 5 years in the Sakha Republic (Yakutia) the number of breastfed children up to 6 months remains almost at the same level and ranged from 48.1% in 2007 to 49.7 % in 2012, but the number of children up to 12 months is almost 2 times lower (26.7% in 2007 and 29.5% in 2012). For comparison, in the Russian Federation in 2010 number of breastfed up to 6 months was 40% of children, up to 12 months - 39.9%.

The main reason to stop breastfeeding at any stage is the reduced lactation – 70% of all causes. The reason for stopping breastfeeding was also hypogalactia in 60,7% of the cases, in the second place is the refusal of the child (17,3%), in the third place is lack of time (5,1%).

Increasing of breastfeeding duration in the Sakha Republic (Yakutia) remains a serious problem. In this regard the establishment of breastfeeding centers, increasing the number of schools for the pregnant that are aimed to improve the hygienic education to support and promote breastfeeding in the Arctic North deserve careful consideration.

Scientific and Practical Centre for the Protection and Support of Breastfeeding under the Health Ministry of the Sakha Republic (Yakutia) has been working to support breastfeeding on the basis of Yakutsk city clinical hospital. That work helped to increase the rates of breastfeeding

in the obstetrics of Yakutsk city clinical hospital: it has increased from 63% in 2006 to 99% in 2013 at discharge.

Currently, the problem of child nutrition, especially infants, is of great importance in terms of health strengthening of the younger generation. There is no secret that in maternity hospitals more mothers refuse from newborns, that's why maternity homes, orphanages have a great need for artificial feeding for babies. Moreover, about one-third of the babies from the first days of life require additional food. [5]

The most balanced food for infants is breast milk, which is considered as the "gold standard" of optimal nutrition, experienced by thousands years evolution of mammals and man. According to the research of YSC of SB RAMS (Yakut Scientific Center of the Siberian branch of the Russian Academy of Medical Sciences) the rate of breastfeeding widely varies from 13% to 95% in the settlements along the Arctic coast of Yakutia.

Still on the territory of Russia there are cases when infants are fed by wjole cow's and goat's milk and non-adapted milk mixtures. [6]

Research shows that the breast milk of indigenous women of the North (Khanty and Chukchi), who are historically leading the traditional nomadic way of life, is more nutritious in biochemical parameters. [1]

Nutritionists, specialist of infant feeding institutions have developed recipes and cooking techniques of various breast milk substitutes based on cows' milk enriched by a dozen of components. But even the best components do not contain biologically active substances, that's why children have eating disorders, allergies, diathesis. [3, 6]

Comparative analysis of chemical composition of breast milk and the milk of farm animals bred in the Sakha Republic (Yakutia) showed that mare's milk in its composition is close to breast milk, and contains on average per lactation: 2,20% of protein, 1,40% of fat, 6,3% of milk sugar; meanwhile breast milk contains 1,25% of protein, 3,5% of fat, 6,5% of milk sugar; reindeer milk contains 11,5% of protein, 24,8% of fat, 3,4% of milk sugar; cow's milk contains 3,4% of protein, 3,8% of fat, 4,7% of milk sugar. Mare's and women's milk have an acidity in the range of 5.5 °T, cow's and deer's – 3 times higher and reaches up to about 17-19 °T, however, the high nutritional and technological properties of reindeer milk after processing might probably be a worthy contender to replace breast milk when feeding children.

At the same time mare's milk can serve as full nutrition for children. Its composition is significantly different from cow's milk and is close to breast milk. Under the action of gastric juice mares' milk is not folded into cheesy clots in the digestive tract of the child, as cow's, unacceptable for the infant [2].

Medical requirements are very strict to the quality of mares' milk. In the Republic of Sakha (Yakutia), especially in recent years, ecological purity of mares' milk is provided when the soil has almost no fertilizers and pesticides.

In the diet of children who are bottle-feeding, the mares' milk can be 50% of the total needs of breast-milk substitutes.

In accordance with the modern concept of a balanced diet biologically high-grade dairy products should be in the diet of children, appropriate to age-related physiological features of child's organism.

The organization of industrial production of baby food is a new trend in the industry. It provides the expansion of the product range, improving the quality of children's dairy products and transferring their production to the modern scientific-industrial base. [3, 6]

The production of dried product on the basis of mare's milk will expand the range of baby products, manufactured in our country, and will facilitate the task of the artificial feeding of children from birth to one year, who are sensitive to cow's milk.

Choice of mare's milk component is not accidental, because it has high content of albumin like the milk of the woman. Albumin is precipitated in the form of small flakes, because of this mare's milk proteins are well absorbed by the stomach of the child and have high biological activity [7, 2].

Albumins contain a lot of sulfur. Mare's milk casein consists of fractions of α-, α -, β-, γ-casein. While α - and β-casein makes up 86.7% of the total casein and B-lactoglobulin and α-lactoglobulin - 77% of whey proteins. Mare's milk, like human milk contains large amounts of immunoglobulins up to 9.5%. Essential amino acids of mare's milk proteins are the most favorable ratio for the infant.

The fat of mare's milk is finely dispersed; fat balls are smaller and better absorbed than the fat globules of cow's milk. The content of linoleic acid in mare's milk and in female milk is much higher than in the fat of cow's milk. This acid belongs to the group of essential acids, as it is not synthesized in the body and activates the immune function of the child's organism.

Compared to cow's milk the average diameter of the fat globules of mare's milk as well as in human milk is smaller. The fat of mare's milk is of white color. It consists of small grains that are in the gel state.

Compared with cow's milk mare's milk like woman's is much richer in C, b vitamins, but poorer in vitamin PP. Adaptation of vitamin composition is carried out by adding vitamins A, D2, E, PP, SC, B1, B2,B3 and B12. The acidity of mare's milk, as the acidity of woman's milk is low - 6° [2].

The use of infrared or spray drying to obtain a solid powder product is required in order to preserve all biological qualities of milk. The following usage of dried reindeer and mare's milk, including milk products are available: development of therapeutic feeding mixtures for gastrointestinal, post-surgical and other patients; additive to infant formula or as the basis for new environmentally healthy baby food. Reindeer milk can serve as the basis for creating not only medicines, but also for the production of prophylactics. We should assume that the biological qualities of reindeer and mare's milk will provide the demand of these products on the world market [4].

One way of approaching composition of substitutes to breast milk is the refusal of using fat cow's milk as the base and replacing it by a composition of beef and pork fat, and also coconut and other vegetable oils. In the preparation of such compositions it is needed to consider the fatty acid structure of the components and also to achieve identity of the melting temperature and other physico-chemical parameters to woman's milk fat.

It is remarkable that composition of garbarini fat and milk fat is close by content of medium chain of fatty acids. Our studies revealed that by the content of medium chain of fatty acids (MCFA) foals' lipids aged of 6 months approach the lipids of milk fat. Their number is significantly higher (7-9 times) than in the foals' fat aged of 30 months. At the same time, the number of MCFA in horse meat fat obtained from 6 months foals, 7-8 times higher than in beef fat (content of capric acid, respectively 0,82 and 0.10%, lauric - 3,03 and 46%). Triglycerides containing, MCFA unlike triglycerides with long chain are quickly hydrolyzed by pancreatic lipase, do not require the presence of bile acids for hydrolysis, are more easily absorbed into the cells of the intestinal mucosa without prior complete hydrolysis, and after suction enter directly into the system of the portal vein, but not in the lymphatic system. All these digestion and absorption features of triglycerides with an average carbon chain length of fat acid make possible their utilization for various disorders of fat intake [5].

Therefore, one way of approaching composition of substitutes to breast milk may be the usage of the garbarini fat as the basis and it will help to reduce the number of children with stunted growth and malnutrition.

Taking into account the significant prevalence of nutritional imbalances among children and teens including insufficiency of essential micronutrients (vitamins and minerals) in the feeding, which is observed in 60-90 % of children and teens, the most important task is to increase the nutritional value of food used in preschool and school nutrition. With regard to milk and dairy products, the main way to increase their nutritional value is the enrichment of essential nutrients (from 20 to 50 % of the daily requirement for the amount of product provided daily set of products): vitamins (C, b vitamins, β-carotene, complex AES), minerals (Fe, Ca, I, F, Se and others), dietary fiber, probiotic and prebiotic components.

The most common and economically justified here is the enrichment of the product with vitamin-mineral premix, containing a complex of vitamins and minerals, usually 8-12 nutrients, deficiency of which is a priority for this region. Another way of increasing the nutritional and biological value of products is a special selection of raw materials and development of science-based formulations of products for preschool and school feeding (food purpose).

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Problems of Alienation and Stigmatization in Psychiatry

M.P. Dutkin

ABSTRACT

The article considers the problem of increasing the number of depressed patients worldwide. The main reason for this phenomenon is the phenomenon of “alienation”. The author lists three main types of alienation. The main problem in Russian psychiatry is the stigma - hanging shameful labels on people seeking help from a psychiatrist or psychotherapist. Social measures to combat depression and anhedonia are considered.

Keywords: suicide, depression, alienation, mass media, stigma in psychiatriy, struggle with depression and anhedonia.

Worldwide there is a growing number of peoples suffering from mental illness. The main reason for this negative process, we consider the phenomenon of "alienation''. Alienation when this takes place in three different planes: 1) the alienation of modern man from his own nature; 2) alienation from people and society; 3) alienation from oneself.

"Alienation from nature" leads to the fact that people begin to depend on technology. "The technologization of the spirit", "technologization of mind" can result in a loss of spirit and mind. The technique separates the person from the ground and stabs his religious and spiritual values and is changing the biological organization of people's life. "Alienation from nature" leads, for example, to that in the world there is a growing number of homosexual couples.

"Alienation from the peoples" leads to loneliness, even sociophobia, the reason of which is the passion of young people playing computer games, Internet communication, at which live communication between people disappears.

"Alienation from oneself" or "self-alienation" is manifested in the loss of meaning of life. The loss of meaning of life in modern humans is confirmed by the data of world statistic on suicides die men are 3-4 times more often than women. Most women have the meaning of life in the presence of their own children. Therefore, the peak of suicides in women occurs at the age of 65, when grown-up children and grandchildren leave her house, and she feels abandoned and useless.

Negative phenomenon "alienation" leads modern people to anhedonia and depression, neurotic disorders.

According to the World health organization, up to 20% of the population in need of specialized mental health care, and in the Russian Federation, this figures reaches 25% [1]. Among mental disorders in the world leads depression – it affects more than 350 million people. According to expert estimates, the number of people who have one or the other light neurotic disorders in our country reaches 9 million. According to various sources, from 18 to 39% of cancer patients and up to 20% with ischemic heart disease suffer depression.

According to the head of the Department of mental and behavioral disorders, Moscow Institute of psychiatry, doctor of medical Sciences A. Avedisova, in Russia up to 50% of somatic and neurological patients suffer depressive disorder [ibid].

Directly with depression related to the problem of suicide, the frequency of which exceeds in Russia some who critical level of 20 suicides per 100 thousand population. In the world the average frequency of suicide is 14 cases on 100 thousand population.

According to the gradation of the World health organization, in Yakutia, the suicide rate is estimated as critical. In our country the number of suicides was (in recalculation per 100 thousand population): 2010 – 40.8 (in Russian Federation – 23.5). 2011 – 39.7 (RF – 21.7), 2012 – 40.1 (RF – 20.2). In1995, Russia was recorded 42 cases of suicides per 100 thousand populations. Dynamics of suicides in the Republic of Sakha (Yakutia) has no tendency to decrease and three times the global figures, two times higher than likely to be national figures.

In the Russian Federation a major problem in the treatment of depression is the stigma of psychiatry in society and the associated social consequences.

The word “stigma” in translation from Latin means “open wound” and comes from the Greek word “stigma”. From the second half of the XIX century, the word began to be used figuratively as “a label”.

In the modern world the concept of “stigma” is used in sociology as a specific feature, when a person is ascribed to some negative traits, the person seeking help from a psychologist or psychiatrist, afraid that society will consider it for “crazy”.

First, the most common stigma associated with conviction of the majority of Russian people that mentally ill people are dangerous. When “the dangerous” no matter what disease they have and how this disease in a particular patient manifests. Therefore they should be avoided, even to isolate from society.

The second common stigma associated with conviction of the people is that mental illness is a chronic disease, and therefore it is impossible to get rid of it.

The third stigma is to persuade people that all mentally ill people are mentally retarded people, fools. Hence all these are common in our society taunts like “idiot”,”imbecile”.

Ultimately, the above stigma prevalent in society stamp, labels prevent people suffering from depression and other neurotic disorders to seek help from a psychiatrist, the psychotherapist, the psychologist. These patients are forced to seek the help of sorcerers and witch doctors that in our society is not objectionable. This "aid" does not help, but only confuses judgments and inferences in the psyche of the patient, leading to irrational thinking.

Psychiatrists must take responsibility for the stigmatization of mental disorders, because nobody else is going to solve a social problem. We must become active advocates for people with mental disorders, to try to improve the quality of life of patients, to monitor cases of discrimination against them in society.

The mass media can be an important source of knowledge in the coverage of mental health issues and become a source for the formation of new social relation and attitudes. TV programs should be alive, vibrant, and dynamic, in order to stay for long in the memory, like they give information in channels “Discovery” and “National Geographic”.

Recently available source of knowledge is the Internet, therefore, psychiatrists should provide easy to understand information about mental disorders, to be weighed the facts and to refute incorrect information.

The most important task of the medical community and the state is the organization of effective and humane care to patients with mental disorders, including depression. Patients need psychological support and social protection, therefore, knowledge about mental health should be disseminated in society.

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Capabilities of Graphene Oxide Application as a Nanostructured Quencher at the Development of New Fluorescent Test Systems for DNA-Diagnostics

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ABSTRACT

Review is devoted to the description of approaches to using the graphene oxide as a nanostructured quencher for DNA diagnostics of SNPs. High importance of the field of DNA diagnostics for modern medicine, and also the need for its further development in the direction of the mass introduction of modern DNA diagnostics methods in clinical practice are substantiated in the introduction.

The review discusses the most widely used modern methods of DNA diagnosis of hereditary diseases at the present time. Advantages and disadvantages of modern fluorescent DNA diagnostic techniques (techniques based on real time PCR and PCR with end-point signal detection) as the most widely used in modern medical practice are discussed more precisely. There are unique physicochemical properties of graphene oxide with respect to DNA, allowing to create a new type of test systems based on graphene oxide and intended for DNA diagnostics of hereditary diseases observed. The details of several approaches to the establishment of such test systems based on the use of graphene oxide as a substitute of molecular quenchers were described. The scheme and operation of test systems, its component composition and key performance indicators was examined. Economic benefit of replacement of molecular quenchers by graphene oxide is substantiated.

This review outlines the shortcomings and limitations of existing approaches to the creation of test systems based on graphene oxide, examined the potential of their adaptation for use in laboratory DNA diagnostics.

Conclusion gives the withdrawal of the prospects and the need for fluorescent test systems based on graphene oxide intended for laboratory DNA diagnostics of hereditary diseases.

INTRODUCTION

Innovative methods of medical diagnosis based on cutting-edge developments and principles are important in the modern world. At the end of XX - beginning of XXI century one of these methods became the DNA diagnostics, which opening previously unachievable horizons in the field of predictive and preventive medicine [10]. DNA diagnostics is widely used for the detection of hereditary and multifactorial diseases, diagnostic of infections, determination of consanguinity, forensic practice and veterinary medicine. The volume of production of test systems for DNA diagnostics in Russia was estimated at 15.7 million units in 2010 [2]. Significant part of the ongoing medical genetic researches is currently focused on the diagnostics of monogenic diseases (which total number currently stands at more than 5,000 nosology [13]).

An important aspect of this developing field of medicine should be its mass character - the widespread introduction of DNA diagnostics to medical practice will significantly reduce the genetic load of the population, improve the gene pool, health and quality of life. To speed up this process, people must have modern and affordable test systems for DNA diagnostics which will provide fast, high quality and inexpensive tests.

Problems of modern DNA diagnostics methods

At the present time there are some basic principles for the molecular diagnosis of mutations [1]. There are classical methods based on PCR - RFLP with registration of results by electrophoresis; method of DNA sequencing according to Sanger; fluorescent techniques: Real-Time PCR and End-Point PCR; and methods based on biochips technology. But almost all of the standard methods of analysis used in the present time have both advantages and disadvantages that limit their potential of applications in the field of laboratory DNA diagnostics.

Currently, methods of fluorescent DNA diagnostic of polymorphisms have emerged as a popular tool in the practical medicine: PCR with the endpoint detection and the Real-time PCR [6] allowing a determination of amplicons quantity during PCR process. In the past five years fluorescent methods are successfully have been used in major diagnostic and research centers of developed countries due to the simplicity and rapidity of analysis performance, high reliability of the results, economizing of production space, reducing the number of staff and demand quantification of DNA / RNA. In the practice due to these advantages there is a gradual ousting of the classical PCR – RFLP. However, the best existing fluorescent test systems for DNA diagnostics of polymorphisms are based on the usage of complex circuits with different DNA probes (TaqMan, LightCycler, Scorpion, Molecular Beacons). The structure of these probes usually includes a fragment of the fluorophore and a fragment of fluorescence quencher molecule.

Fluorescence quencher provides the absence of fluorescent signal in the case if the probe is not embedded in the structure of the amplicons (the amplification have not occur), and if amplification is successful and the probes are embedded into amplicons during PCR, the accumulation of the fluorescent signal can be observed. Using of such structure provides a high reliability of the results and allows even quantitative DNA diagnostics with an assessment of the kinetics of the fluorescent signal accumulation in the case of real-time PCR.

However, such fluorescent test systems have one major drawback - the complex structure of DNA probes which leads to stability problems and increases the cost of the test system due to the complicated process of synthesis and purification of probes. It leads to high price/quality ratio for these test systems and hinders their wide introduction into practice of public health [16]. But at the moment, namely fluorescent methods are the most promising (in qualitative and

economic aspect) for introduction to clinical medicine. Therefore topical problem is a development of its potential - creation of such test systems based on improved or new principles of work that will simultaneously allow improvement of qualitative results and economic viability of DNA diagnostics.

The unique properties of graphene oxide for use in fluorescent test systems

At recent years scientists came to the discovery of new materials with unique properties, including properties of fluorescence quenchers [7]. In particular, researchers have found that grapheme oxide and its derivatives can be very effective quenchers for different organic fluorophores [11] and quantum dots [8]. Comparing to other quenchers, grapheme oxide showed the highest quenching effect of different fluorophores with low background and high signal-to-noise ratio [9,12]. This effect is caused by adsorption of fluorophores on the surface of graphene oxide and realization of FRET-effect in the form of excitation energy transfer from the fluorophore molecules to the surface of graphene oxide with its subsequent scattering.

A key feature of some derivatives of graphene (in particular - its oxide) is also its high affinity to the single-stranded DNA molecules, in contrast to double-stranded [15] (figure 1).

Due to these properties of graphene oxide, it is possible to develop various biosensor test systems on the basis of graphene oxide - better (in quality and economically) analogs of fluorescent systems for DNA diagnostics of mutations based on methods of real-time PCR and PCR with endpoint detection.

Approaches of development of fluorescent test systems based on graphene oxide for DNA diagnostic of SNPs

Last 2-3 years active study on the development principles of working of such test systems in the world has been made. To date, there were published different approaches for the diagnosis of point mutations in DNA, which may cause hereditary diseases and cancer; were formulated the general ideas and principles on prototyping biosensor test systems based on graphene oxide. Such several approaches developed over the last few years will be examined next:

One of the easiest approaches of development of such test was described in the study of S. He et al. [3]. Researchers applied the scheme, which uses a hybridization reaction of fluorescently labeled oligonucleotide probes (**P5-P7**) with the target molecule (**T7**) in a solution followed by addition of graphene oxide suspension into the solution (Fig. 2)

Hybridization of fully complementary single-stranded oligonucleotides forms a DNA duplex, which does not adsorb on the graphene oxide surface. It leads to presence of fluorescent signal as the characteristic of presence of hybridized probe in the final solution.

It was found that the difference in one nucleotide in the target molecules (**M1-M3)** does not lead to their complete hybridization with the probe **P1** (Fig. 3). It allows detecting any point mutations in DNA structure using fluorescent signal with the scheme described above.

This approach is the result of development of the earlier ideas laid down in 2009 [4]. However, unlike the old idea new approach allows the realization of multiplex analysis: different target oligonucleotides can be determined with a high signal/noise ratio using different probes labeled with fluorophores with different wavelengths of emission (**P5-P7**). In this case, each target oligonucleotide being added to a solution will only match the fluorophore that is associated with the fully complementary oligonucleotide probe.

Authors also found that the order of addition of graphene oxide and oligonucleotides can be any for this test system (Fig. 4 a, b). Even by adding a solution of the target molecule **T1** to a solution of graphene oxide with adsorbed probe molecules **P1** on its surface, the final solution later becomes to have fluorescent properties due to probe and target hybridization. It leads to form a poorly adsorbable DNA duplex and its subsequent desorption from the surface of graphene oxide.

The approach described above has been also improved in other work [14]. There was created new test system using covalent linking of fluorescently labeled oligonucleotide probes with the graphene oxide surface (Fig. 5 b). This approach, unlike the others (Fig. 5 a) allows to enhance the quality of DNA analysis results because of small probability of nonspecific offsetting substitution of probes which are adsorb on the surface of the graphene oxide in the process of analysis.

Researchers used the carbodiimide method of linking probes with graphene oxide surface. It affords to make the reusable test system for DNA diagnostics due to the possibility of "cleaning" of modificated grapheme oxide. It is important to note that in terms of reusable graphene oxide for DNA diagnostics, this work is so far unique.

Investigating the kinetics of fluorescence signal appearance in a solution of the modified graphene oxide after the addition of an oligonucleotide target (with and without the mutation), the authors were able to obtain the intensity ratio ~ 1.5 for the fully complementary and mutant target (Fig. 6). Limit of detection of complementary target for this test system was 1.5×10^{-10}M, which is a good indicator in the comparison of this approach with test systems with a "non-covalent" ways of oligonucleotides linking.

Other authors [5] developed the idea of using a fluorescent intercalation agent as SYBR Green (instead of fluorescent probes) and the suspension of graphene oxide for the detection of mutations in DNA. Scientists have found that by adding a mixture of oligonucleotides fully complementary to each other (probes and targets) with SYBR Green to a suspension of graphene

oxide is retain the fluorescence in the final solution, indicating the intercalation of a SYBR Green into a double helix structure of formed DNA duplex. But complete hybridization does not occur in the case of the presence of a mutation in the probe molecules. In that case fluorophore is adsorbed on the surface of the graphene oxide, which results to absence of fluorescence in the final solution (Fig. 7).

Experiments have shown that the registration of single nucleotide mutations using graphene oxide suspension attained significant signal / noise ratio (25-90) at the 10 nM concentration of the oligonucleotides. That provides high sensitivity for this method of analysis (Fig. 8).

Using the data obtained in the course of research experience, the authors have created a prototype of fluorescent microchip with the ability to distinguish the quantitative composition of the test mixture of oligonucleotides (Fig. 9).

Prospects and possibilities of adaptation of existing approaches for laboratory DNA diagnosis of hereditary diseases.

In general, over the last 3-4 years in the foreign literature there were described more than ten entirely different approaches to the development of fluorescent test systems based on graphene oxide for DNA diagnostics of mutations. In all works graphene oxide is used for two main purposes:

1) For logic recognition of single and double-stranded DNA molecules due to their different affinity with respect to graphene oxide

2) As a nanostructured quencher of fluorescent agents instead of molecular quenchers, which are prevalent in DNA probes in modern fluorescent test systems.

It should be noted that so far all of the above studies are generally aimed at demonstrating the potential use of graphene oxide in the field of creating DNA test systems. But graphene oxide have not yet found application in the field of laboratory DNA diagnostics of diseases. Published approaches need serious adaptation for use in DNA diagnostics laboratory because of two main reasons:

1) In all developed approaches presently used single-stranded oligonucleotides, while in the standard PCR - a key step in any procedure of DNA diagnostics - formed double-stranded DNA molecules (amplicons).

2) All developed test systems designed to operate with a sufficiently short oligonucleotides (15-25 b.), while the amplicons formed during the classic PCR cannot have length less than 50 bp.

The distinguishing characteristic of graphene oxide is the simplicity and low cost of its synthesis, as well as high stability colloidal suspensions. For comparison, on the basis of the data

about using graphene oxide in DNA diagnostics [3, 4, 5, 14], the mass of graphene oxide required for quenching 1 nM fluorophore is from 0.1 to 1 mg. In test systems with molecular quenchers (TaqMan, LightCycler) used are equivalent amounts of the fluorophore and quencher: for 1 nM fluorophore - 1 nM of quencher. The ratio of the average commercial prices of 1 mg of graphene oxide (eg from European brand «Graphenea») and 1 nM of quencher (eg Black Hole type from «Synthol", Russia) is about 1: 3. The share of the quenchers cost are usually 10-15% of the total cost of test system. Therefore, the use of graphene oxide as nanostructured quencher fluorescence can lead to creating a new class of fluorescent test systems with reduced cost and improved quality of DNA diagnosis in comparison with existing fluorescent test systems which are used expensive and low stable molecular quenchers.

CONCLUSIONS

Thus, despite of extensive research opportunities for application of graphene oxide in the field of creating test systems for DNA diagnostics, it have not been currently created such test systems intended for laboratory use. Ongoing researches of finding new approaches and adaptation of already existing approaches for the development of test systems based on graphene oxide and their implementation in clinical laboratory practice is an interesting challenge for researchers.

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Outpatient Psychiatric Care (Historical and Modern Aspects)

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ABSTRACT

Here a review of modern approaches to outpatient psychiatry care is represented and dynamics of problems and achievements in remodeling the "psychiatric hospital - branch of psychiatric hospital (psychoneurologic dispensary)" are analyzed. In particular, the dynamics of shifting psychiatry care from hospitals to their branches (psychoneurologic dispensaries), combined with the decrease in bedspace during the last 7-8 years is shown.

The positive sides and perspectives of therapy and rehabilitation of mental patients in day patient facilities and by using patronage in modern conditions are described. The arguments supporting feasibility and advisability of giving priority to the outpatient psychiatry services during the last decades (pathomorphism of psychic disorders, implementing new generations of medicines, developing the methods of social-activating rehabilitation) are analyzed. Also the concept, according to which in case of spending as little time in psychiatric hospital as possible the self-conscience of mental patient changes less, which provides higher chances for one to see oneself as a full-fledged member of society, is reflected. Consequently, therapy and rehabilitation in case of outpatient care get a social motivation, which increases their efficiency.

Several modern approaches to psychiatry care are represented in historical aspect of succession of Old Russian territorial (local) psychiatry.

Keywords: outpatient psychiatry care, rehabilitation, psychiatric care organization.

Worldwide trends in the development of psychiatric services in recent decades have largely changed. Many psychiatrists stress that the increase in the number of patients with non-acute conditions must be taken into account [9, 15, 27, 29, 37].

Frequency of dissimulation of psychotic disorders also increases being one of the reflections of the complexity of finding one's micro-social "niche" in modern society. In general, the multiple-factor pathomorphosis of psychiatric disorders, including therapeutic one, socially caused [4, 28, 33], in turn, emphasizes the significance of the available multidimensional psychiatric care, which does not exclude a feasible employment. Fears of economic instability, complicated interethnic relations are factors causing both abovementioned psychopathologies at neurotic level, acute and chronic responses to stress and sudden exacerbation of chronic mental disorders, changes of latent form of disease into clinically apparent form, including forms with auto- and heteroaggression. According to Russian Statistics Bureau data, an increase in proportion of elder age groups from 22.9% in 2013 to 29% in 2031 is expected in Russia [20], which naturally involves the increase in proportion of psychiatric patients older than 50 years old. Given the age dynamics of mental disorders (fading severity of symptoms, the actualization

of vascular disorders), outpatient psychiatric care may become more and more important for this group of patients as well [10, 11, 15, 18]. Patients living alone make 1/3 of all elderly patients with mental disorders. They are in a group of high risk of social exclusion/disadaptation; in particular, committing socially dangerous acts, suicide attempts [11, 15, 18].

For over 10 years the prospects of Russian psychiatry provoke debate among physicians of all specialties and, of course, in society. For example, at the meetings of the Public Council on Mental Health it was repeatedly pointed out [10, 27] that the development of psychiatry should go in the direction of "moving it to outpatient care departments and ambulatories". Specific aspects of outpatient psychiatric care are considered in the order of the Ministry of Health Care of Russian Federation № 566, dated May 17, 2012. Many specialists see the reserves, which can be used to improve the structural efficiency of psychiatric service, in a more dynamic development of outpatient forms of assistance. It is obvious that not only quantitative but also qualitative indicators of the activities of psychiatric institutions are important. The entrenched vision of a psychiatric diagnosis as a discrediting fact also makes outpatient forms of therapy of the mental patients in Russia (in accordance with international practice) particularly significant [17, 31, 33]. However, it is evident that many aspects of outpatient psychiatric divisions' activities remain insufficiently thorough, non-integrated into a united medical-social network. As of 2006 [7], the restructuring of the network of psychiatric institutions in Russian Federation was going forward extremely slow and even by 2006 the intended parameters were not met. In the total volume of financing for mental care in 2003, hospital care accounted for 90.2%, and outpatient - for 9.7%. After three years, the number of places in day care facilities increased by 14.5% and the number of days patients spend in such facilities - by 22.6%. Visits to psychiatrists and psychotherapists decreased by 6.6%. According to G. Gurovich et al. [9] by 2012 - 2014 a significant reduction in hospital accommodation took place, mainly by reducing the duration of treatment of patients with psychotic disorders (and thanks to the reduction of percentage of such patients in hospitals), reducing hospital admissions [9]. It should be emphasized that, historically, already in the times of Zemsky (territorial) medicine is Russia, long stay of a patient in a psychiatric hospital was considered wrong, because lack of proper activities and incentives contribute to progressive personality decline due to the detachment from familiar life. Though here we should highlight that "long stay" at those times usually meant years! According to data of early 2014 [19], for 15 years the number of patients, staying in a psychiatric hospital for over a year, does not decrease, remaining quite high - about 23% per 100 000 people, and in some regions – up to 50% . Thus, there is an obvious need to further improve the efficiency and quality of psychiatric care, in accordance with the concepts of modern medicine and society, as well as the development of alternative models of psychiatric services [17, 28, 30]. Many authors

– I. Gurovich [7, 9, 15], V. Yastrebov, V. Mitikhin [31], A. Churkin [28] - highlight the socio-economic importance of expanding different types of outpatient psychiatric care.

In our view enlarged outpatient psychiatric institution is important, but not everywhere (especially not in the areas with low population density where hospitals and outpatient departments are territorially far away from the patients – in Central Asia, regions of Russian Far North, and etc.), but in great towns (Moscow, St.–Peterburg, Novosibirsk, Ekaterinburg and etc.). A significant portion of patients, according to domestic and foreign experience, never gets into psychiatric hospitals. Freedom of movement without departing from the usual environment, and a deep familiarity and cooperation of doctors with the representatives of patient's environment - all of it plays in favor of the success of treatment [2, 3, 5, 24].

As practice shows, the most optimal option is the availability of an outpatient department as **a** part of enlarged **psychiatric institution (complex) created** through the functional association with the ordinary hospital, day care unit and night hospital, rehabilitation center, self-help groups and groups for mutual support. In the guidelines of "The Order of the Provision of Psychiatric Care» (a document approved by the Ministry of Health of Russian Federation), night hospital is not mentioned as something which is not widespread in Russia. However, in some places of Moscow region, such institutions seem to be necessary and even function already. Due to a totally different pace of life in this region in general, relatives often do not have enough time and patience to care for patients after intensive work and spending many hours in transport, surrounded by many stresses of metropolis. Therefore, at nights patient may feel more comfortable not in a family, but with medical stuff of hospital. Often such discomfort at nights at home concerns lonely elderly patients as well. Thus, outpatient complex has multiple functions.

O. Nesiforova, I. Bekker [22] describe the experience of functioning of the newly established round-the-clock "first psychotic episode" unit, affiliated to outpatient branch of psychiatric hospital in the city of Naberezhnye Chelny. After hospitalization this form of follow-up patient care (with a flexible schedule during the day) is used, so that it does not interfere with patients' studies and work. The rest of "night places" in hospital are used for the differential diagnosis of recruits. In some cases relatives of patients may also stay there.

Day care units first emerged in the USSR in 1930s [30] and were the first kind of institutions, which combined all the advantages of outpatient and inpatient care. Since 1999 till 2006 number of places in such units, affiliated with psychoneurological dispensaries has increased in Russia by 18% [9, 30].

Further development of the best possible conditions of admitting patients into day care units seems to be important. Despite numerous studies, including methodological ones, many physicians, according to out data, have different approaches regarding the appropriateness and

expected effectiveness of sending their patients into this unit. Therefore we find it necessary to emphasize that only patients with normalized behaviour and positive attitude to treatment; potentially in need of correction of their maintenance therapy when daily medical supervision is required; patients with acute exacerbation of old psychopathological disorders or decompensation within the borderline states; patients in the early stages of mental illness or its aggravation - for diagnosis, treatment, as well as prevention of relapse; patients with an unclear diagnosis, if it can be clarified in the conditions of a day care unit, are to be admitted into such units. It seems appropriate to use "test" admittance into day care units for those patients whose mental state and behavior makes it potentially difficult for them to follow the regime of such units; persons with a tendency to substance abuse, with significant psychosomatic disorders.

According to Y. Fedorov [26], a modern outpatient care unit team is more than just a sufficient number of well-prepared specialists. For example, in day care unit created on an outpatient basis (psychoneurological dispenser) one should use highly professional team of psychiatrists, psychologists and psychotherapists. Historically, psychotherapeutic treatment appeared in day care units in the early 1990s; the interest to it was actively supported by physicians and psychologists. A club of former patients "Steps"(Stupeni) is described, where patients were engaged in psychotherapeutic artwork in a group and individually, which, according to the author, had a positive effect on their condition.

In our view, a large and not entirely solved issue is the rehabilitation of mental patients. I. Gurovich [9] emphasizes the importance of organization and development of departments of outpatient rehabilitation - without losing already existing and operating methodical approaches. The author draws attention to the "signs of our times" - the disappearance of the economically disadvantageous “labor treatment” workshops that constituted a significant aspect of life for many mental patients only 15-20 years ago. At the same time, he notes the importance of a new understanding of rehabilitation - as the optimization of social adaptation by restoring mental abilities and capabilities lost due to illness. The so-called cognitive rehabilitation is considered to be a promising solution [9, 35]. Certainly, the restoration of social functioning in modern conditions requires a systematic approach involving a variety of new methods of activating of intact psychic functions while maintaining the role of the family and feasible employment.

Naturally, the stay at the day care unit of a branch of a psychiatric hospital, just like a stay in a conventional hospital, should gradually bring patient into the rehabilitation department. But it is not always possible to ascertain really "smooth" transition – it takes time to clarify the appropriateness of such move to patient and patient’s relatives. E. Chukanova [27], comparing two groups of patients with schizophrenia and schizophrenia spectrum disorders in the outpatient branch – those who received and those who did not receive comprehensive psychosocial support

- concluded that the quality of life, social, family and labor performance were significantly improved in the first group. In our view, both in day care units and in rehabilitation departments of outpatient institutions pharmacotherapy should be combined with psychotherapy and recurrent work with a psychologist. Exercise machines and gymnastics are highly recommended in such institutions because physical condition is inseparable from mental health. In addition to traditional pharmacotherapy, already in day care unit patients may receive psychosocial treatment (art therapy, music therapy, dramatherapy and etc.), i.e. rehabilitation acts as a prevention of mental condition deterioration. One can attract sponsors for the employment of the patients in workshops (this helps reduce sponsor's taxes): so that some products, created by patients, would go on sale or sponsor would supply them with materials and orders. In an ideal case it is possible to consider one's interests or develop new ones during the work in the occupational workshop - that will help patient in the future. Art therapy may also have economic aspect – art objects can be sold. It is possible to involve relatives into music therapy. Many aspects of the work of outpatient branch of psychiatric hospital have their prototype described in the works of the 19th century psychiatrists [2, 3, 5, 16, 21]. For instance, it was emphasized that a psychiatric facility should be cozy, the food should be nutritious, patients need to go for a walk, they should have feasible employment, which "**protects them from** dullness and gives them a feeling of satisfaction when seeing the results of their work"[24].

According to V. Serbsky [24], perfectly in tune with the modern approach, patients should have the opportunity to perform their religious rituals, which is already put in practice everywhere. Outside the psychiatric institution, in case of an accidental meeting, the best way to communicate with patients is in the same way one communicates with healthy people. What's needed for this if not a sufficient level of clinical experience, which has no connection with time or epoch? However, the treatment of patients still varies very much: for instance, feeding patients in a day care unit may become a very complex issue and not seen as something self-evident; conditions for going for a walk may be absent. According to V. Serbsky, it is important for physicians to know what the relationships between patients, so as to separate them, are sending in different places in time, or to make them change their minds. The abovementioned particular issues, of course, can be resolved through the optimal selection of medical staff.

More than 100 years ago, S.Korsakov, V. Serbsky wrote about the feasibility of establishing charities affiliated to psychiatric institutions. They should, if necessary, provide clothes for the patients, find them suitable occupation, and even provide monetary assistance. Today such ideas sound very true and their implementation is quite real - with the assistance of sponsors. So the sponsors are needed not only for occupational therapy and rehabilitation. In our view, diverse help is needed to mental patients both during the outpatient treatment, and at discharge from hospital. Of

course, the participation of the population in co-financing of health care can take many different forms [1, 2, 23].

N.Bazhenov [2] emphasized the importance of systematic observation of patients by physicians so that it would be possible to rapidly hospitalize patient into a clinic, call his/her relatives. However, today the level of readmissions to hospitals is no different from the level of 25 years ago. At present level of development of medicine this can not be considered a norm [15].

Due to the aging of the population as a whole today psychiatric care predominantly at home (home nursing with or without participation of relatives) becomes more and more important [23].

Historical background. Home nursing, patronage (from French "Patronage"- protection) – a special form of organization of prophylactic work at home, conducted by medical and prophylactic institutions. Provides follow-up care of patients in the family, in the workplace, including control of their adherence to regime. Patronage of mental patients first appeared in Geel (Belgium), and in the second half of the 19th century it spread throughout Western Europe in the form of "colonies of family care". In Russia, the patronage of mental patients was organized by N. Bazhenov in 1886, in Ryazan psychiatric hospital. The patronage was mainly concerned with single and elderly patients. The restless patients, patients dangerous to themselves and others, patients prone to vagrancy, weak patients, patients with severe physical or infectious diseases were not to be put into patronage (home nursing) (GSE, 1982.- V. 18.- pp. 1253-1254).

Also significant are various forms of "housing under the protection" (from hostels/dormitories to apartments for independent living) [8, 23]. The necessity to create "hospitals at home" was always motivated by clinical and social factors. Today it is believed, that it is mostly adequate for 3 nosologic groups (with schizophrenia spectrum disorders, organic mental disorders and mental disorders caused by epilepsy [8]). The social aspect of such a hospital is seen primarily in the normalizing patient's relationship with his/her neighbors and family, while local physician, psychologist and social worker can mutually provide care for the patient. The old stereotypical views regarding mental patients may lead to social isolation of these patients in case of patronage, intensive supervision, and that's why it is too early to stop ethical and deontological developments [23] find it important to create rehabilitation teams based on hospital outpatient departments, which would include psychiatrist, clinical psychologist, psychotherapist, social worker and medical nurse. They can provide comprehensive, complex care to actively monitored patients, those who violate the regime or therapeutic scheme, are often

hospitalized and are characterized by low social adaptation; as well as for their relatives, and to contact social services of the city.

However, the possibility of patronage (home nursing), living in a separate house with a permanent medical personnel and etc., for now mostly applies to the future of domestic psychiatry, due to the necessity to revise the economic costs, training of specialists and etc. At the same time, we should use the experience of other countries, especially Western Europe, given its "pros" and "cons", presented in detail in an analytical article by I. Gurovich et al (8). The literature discusses the possibility of "postponing" the need of a patient to be admitted in a psychiatric hospital. For such a purpose the so-called conserving-preventive rehabilitation is suggested – up to more frequent placements in a hospital, which naturally involves close contact in a system "patient – doctor – patient's close friends and relatives" [32]. Attention is paid to the effectiveness of such rehabilitation right after the first episode of endogenous disorder [12, 33]. Reduction of the frequency of hospitalization of the mental patients can be achieved by the interaction of relatives with district psychiatrist. After psychosocial training they would be able to earlier recognize the signs of the beginning of disorder exacerbation and take action to prevent its development, which would prevent the admittance of the patient into hospital. Psychosocial training also improves relations of the patient with his/her relatives, reducing the likelihood of conflicts, which relatives often solve by hospitalizing the patient [19,34].

Changes and achievements in the field of pharmacotherapy, occupational therapy and psychotherapy led to many fundamentally new conclusions, which created the possibility of more effective treatment of mental patients. Effectiveness is not limited to the release of patients out of the locked ward. The "key" problem is psychological: outside the hospital with optimal medical care, rehabilitation and good treatment many mental patients can speak and express themselves. The system of outpatient care should be developed not only as a requirement of humanism, but also as the means of recovery of consciousness in case of mental disorder. The aim of modern rehabilitation should be maximizing the return of the patient into society.

Analysis of literature, published in different years, can help to identify the main problems of the modern development of outpatient mental health care based on practical problems 1) Using one or more outpatient offices (psychiatric hospital branches) as a model, to examine the socio-demographic characteristics of the patients observed there (and define the share of different nosological categories, the proportion of elder age groups). 2) To develop criteria for selection of patients, treated by department, for therapy and rehabilitation in a day care unit, as well as methods for evaluating of the effectiveness of treatment (pharmacotherapy, psychotherapy, occupational therapy); 3) To reconcile day care unit as much as possible with

medical-rehabilitation department - if necessary, with the development of skills for independent life in patients, in case of loss of social connections by the patient; 4) To clarify the role of family in treatment and rehabilitation of mental patients in the outpatient unit setting (including organization of comprehensive medical and social events, clubs for patients); 5) To provide advice, psychiatric, psychotherapeutic, medical and psychological assistance, including for victims of emergencies, in order to prevent suicide and other dangerous actions, to organize "crisis hotline". Psychiatrist and psychologist (with knowledge regarding suicidology) should work in such an office of emergency help; 6) to organize outpatient forensic psychiatric examinations for long observed patients, when it comes to civil cases, in particular, the issues of legal capability, ability to conduct transactions and etc. 7) outpatient psychiatric department should have the necessary equipment for a quick medical examination and systematic treatment of its patients; should have standard medical information card for the evaluation of the effectiveness of therapy and rehabilitation; good nutrition unit (it is desirable to attract patients to work there). For this "Questionnaire for the Assessment of Social Functioning and Quality of Life of Mental Patients," "The Scales for Assessment of Emotional and Instrumental Support of Mental Patients," "The Scales for Assessment of Social Network of Mental Patients", "Estimates of the Level of Knowledge Regarding Mental Disorder and the Effectiveness of Group Psycho-Educational Program" [19, 37] and other forms of standardization of data obtained should be applied.

In the heyday of Zemsky (territorial) medicine, during the active work of the outstanding Russian psychiatrist V. Serbsky in some cases the abilities of psychiatry were significantly narrower, and in some cases - wider. The attitude to any patient was based on "being careful and loving human being", i.e. Humanism. In the most feeble-minded, degraded patient human qualities were seen and appreciated. Grieve was understood, both where the disease was and where there was no disease - in particular, in the relatives of the patient. This understanding is timeless and very important in the 21st century with its eternal rush of the big cities, the disunity of people and generations. It should be emphasized that these were Zemsky (territorial) physicians, who widely discussed the question of the organization of primary psychiatric care. Thus, V. Serbsky did not consider it right to deliver the patient into a psychiatric institution by means of fraud, stunning with sleeping pills or alcohol (the last three methods are sometimes discussed by relatives nowadays as well, which clearly contradicts human rights, freedom of human expression). He also noted that it is necessary to obtain the written statement from relatives or close friends of patient, requesting his medical examination, so that later this patient would not present any claims against doctors. V. Serbsky saw the desirability of the existence of public (state) and private psychiatric hospitals, which should differ only in the level of comfort,

but not **the quality of** treatment. Such approach seems to be of interest, but more as a reflection of the history of Russian medicine. It is important for the minimally possible comfort standards to be high enough, which today is not considered to be of significant importance in some psychiatric institutions.

Thus, many of the views of psychiatrists of 19th century regarding the prevention and treatment of mental disorders, interconnection between psychiatry and society, the patient and his/her relatives today did not lose their significance absolutely. Obviously, even during the past century the issues of outpatient care, including rehabilitation in the modern understanding of the word, are still not resolved completely, but may have a new understanding and solution based on a different level of development of psychiatry and society. Priority of outpatient psychiatric care is in many aspects similar to a new understanding of the principle of "non-restriction" of mental patient (but this time by hospital walls rather than chains or other methods of fixation).

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Sensory-Predominant Chronic Inflammatory Demyelinating Polyneuropathy in a Patient with Parainfectious Limbic Encephalitis (case report)

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ABSTRACT

We report a patient with chronic herpes infection, which manifested as parainfectious limbic encephalitis (PILE) and sensory-predominant chronic inflammatory demyelinating polyneuropathy (SP-CIDP). It is demonstrated that persisting herpes infection associated with immunodeficiency can facilitate two pathological processes: direct viral damage of limbic structures and autoimmune damage to myeline sheath of peripheral and cranial nerves. Description of the case includes clinical presentation and diagnosis of SP-CIDP and PILE. CIDP is an autoimmune disorder, characterized by damage of myelin sheath of peripheral and cranial nerves. It is thought that CIDP accounts for 20-50% cases of undiagnosed polyneuropathy. The contribution of Herpesviridae family to development of CIDP is a matter of debate. PILE associated with Herpesviridae infection is one of the most common forms of chronic herpetic encephalitis, characterized by abnormalities in function of limbic system (hippocampus and amygdala), with protracted course of disease and frequent exacerbations. Parainfectious limbic encephalitis is caused by direct viral damage to limbic structures.

We suggest a new diagnostic algorithm of SP-CIDP, which includes nerve conduction study, stabilometry with use of EU standard Rhomberg's test, computerized pallesthesiometry (CP) of distal parts of upper and lower extremities, computerized thermosensometry (CTS) for evaluation of thermoception and pain threshold for cold and hot stimuli. This algorithm can be used in the setting of outpatient clinic by neurologists and general practitioners. The diagnostic methods utilized in this algorithm, such as CP and CTS, are safe, simple, and non-invasive and may have broad application.

Keywords: chronic inflammatory demyelinating polyneuropathy (CIDP), parainfectious limbic encephalitis (PILE), vibroception, thermoception

Chronic inflammatory demyelinating polyneuropathy (CIDP) is an acquired autoimmune disease, characterized by loss of myelin sheath of peripheral nerves [4]. 20-50% of polyneuropathies of unknown cause are associated with CIDP [9]. CIDP is included in the group of dysimmuneneuropahies [6, 8, 14, 15]. A change in the immune status and the development of autoimmune process are the major contributing factors in the development of CIDP [10, 11, 17]. However, no specific antigens, which trigger the demyelination process, are identified. According to Kantimirova E.A. [1, 5], polymerase chain reaction (PCR) and enzyme-linked immunosorbent assay (ELISA), which were set to identify neurotrophicHerpesviridae family viruses in patients with CIDP, in 45% cases Hepres simplex virus 1 (HSV-1) was identified, 4,5% - cytomegalovirus (CMV) and Epstein-Barr virus (EBV), 13.6% cases were attributed to HSV-1 and EBV infection and in 9% CMV and EBV.

Clinical variants of CIDP include Lewis-Sumner syndrome (acquired multifocal demyelinating sensorimotor neuropathy), sensory-predominant CIDP (SP-CIDP), acquired distal demyelinating sensory neuropathy and CIDP with central nervous system involvement (CNS-CIDP) [15, 23, 26].

Acquired multifocal demyelinating sensorimotor neuropathy, also known as Lewis-Sumner syndrome, is characterized by multifocal lesions of sensory and motor nerve fibers, sometimes with asymmetrical presentation [22, 26] and slow progression of symptoms.

SP-CIDP is characterized by sensory symptoms: pain, imbalance (sensitive ataxia), paresthesia and dysesthesia. Neurophysiological evaluation reveals motor nerve fibers involvement, despite the absence of motor symptoms. Acquired distal demyelinating sensory neuropathy has slowly progressive course and is characterized by predominant involvement of sensory nerve fibers, which can be accompanied with moderate distal muscle weakness. The course of disease is slowly progressive. IgMparaprotein is often associated with the development of this kind of neuropathy [11, 12, 19].

CNS-CIDP is characterized by involvement of visual system, hyperreflexia and positive Babinski sign, with foci of demyelinization found on brain magnetic resonance imaging (MRI). Whether CNS-CIDP is a distinct nosological form or random combination of diseases is currently debatable.

Classic CIDP is defined by the predominance of motor symptoms over sensory, with motor weakness present in proximal or distal muscle groups, low or absent deep tendon reflexes. Motor variant of CIDP has more severe course [13, 19, 22]. Cranial neuropathy and bulbar symptoms develop in 10-20% cases [15, 20]. Sensory CIDP is more common variant and has following symptoms – loss of vibration and temperature sensitivity, as well as allodynia. This variant of CIDP is rarely diagnosed at the early stage in outpatient clinics, which burdens

following therapy and leads to relentless progression of the disease [12]. Modern diagnosis of CIDP includes nerve conduction study (NCS), nerve biopsy and cerebrospinal fluid test [8, 9, 20, 23, 28, 29]. Unfortunately, there is no consensus on pathological NCS results among authors [16, 18, 20]. There is a need for new electrophysiological method of SP-CIDP verification. We developed new algorithm for the diagnosis of SP-CIDP which includes computerized pallesthesiometry of distal parts of upper and lower extremities, stabilometry with utilization of EU standardized Rhomberg's test, nerve conduction studies and transcutaneous oximetry.

Parainfectious limbic encephalitis (PILE) associated with Herpesviridae infection is one of the most common variants of chronic herpetic encephalitis. It is defined by disturbances in limbic system (hippocampus and amygdala) functioning. The course of the disease is protracted with frequent exacerbations [6, 7, 21, 24, 25]. PILE is caused by direct damage of limbic system by infectious agent, usually HSV-1 [2, 3]. Clinical presentation includes cognitive impairment, seizures, sleep disturbances and mental disorders. PILE in patients with secondary immunodeficiency is characterized by covert course of disease which does not raise suspicion of this condition in doctors of outpatient clinic [25, 27, 30]. If diagnosed in timely manner, PILE has good prognosis. Otherwise, PILE can be complicated with mesial temporal sclerosis with the development of intractable parietotemporal epilepsy, emotional and cognitive impairment, as well as schizophrenia-like symptoms. All these complications severely hinder treatment and worsen prognosis.

Thus, chronic herpetic infection accompanied with immunodeficiency can lead to direct damage of the limbic system in form of PILE, while simultaneously activating autoimmune response and developing CIDP.

CASE REPORT

43-year-old patient came to Krasnoyarsk State Medical University's outpatient clinic with complaints of short-term memory disturbances, rare bouts of daytime sleepiness, speech problems, occasional tremor provoked by fatigue, unexplainable waking at 2 am and 5 am, overall fatigue and decreased performance.

Medical history: patient is regularly visiting immunologist for highly active chronic mixed herpevirus infection since 2009. Patient has frequent flare-ups of chronic herpetic infection manifesting with blisters on tongue, vermillion border and on the face with subsequent development of V1 and V2 trigeminal neuralgia, hyperesthesia in the right half of the face, muscle weakness in right arm, as well as paroxysmal tachycardia and dyspnea. Flare-ups were treated with T-cell stimulators, specific EBV immunoglobulin shots and other antiviral drugs, which usually resulted in remission up to 6 months. In January 2013 patient started to experience neurological symptoms, including tinnitus, blurred vision, emotional instability and irritability,

sudden daytime sleepiness with speech slurring and slowing, muscle weakness in right arm, and imbalance attacks. Patient's condition worsened in March 2013, when he noticed severe short-term memory problems, slurred speech in the morning; tremor triggered by fatigue, muscle jerks in the right half of the body, blood pressure instability with tendency to rise, irresistible paroxysms of daytime sleepiness during driving, myalgia and polyarthralgia, chronic tiredness and insomnia. This condition was accompanied with flare-ups of herpetic stomatitis every month. Patient underwent treatment prescribed by immunologist, but the duration of remission was short. On October 2013 patient went into spontaneous remission, with improvement in daytime sleepiness, hyperkinesia and memory loss. Relapsing orofacial herpes was still present.

It must be noticed, that the patient is the ENT doctor, thus frequently contacting with herpes patients. He is married, has 2 children. His wife has chronic HSV and EBV infection, as well as multiple sclerosis, controlled by glatiramer acetate. His children both have relapsing infectious mononucleosis and are infected by CMV.

At the time of observation patient's condition was stable. He was alert and mentally active. Skin was moderately moisturized with rare roseate nodular rash on the trunk and proximal part of upper extremities. No edema was present. There was a conjunctival redness with scant serous discharge. Patient had symmetrically swollen lymph nodes, which were tender in the right side. Enlarged tonsils were noticed upon oral cavity inspection with no adjacent redness of the pharynx. Patient was mentally alert and did not demonstrate any signs of mental disorder. Mood was slightly decreased. Interview revealed minor cognitive impairment due to short-term memory loss.

Neurological examination revealed diplopia during side gaze, convergence insufficiency in the left eye, tender points in trigeminal areas V1, V2 and V3. No muscle weakness was present, but mild spasticity in lower extremities was noted. Deep tendon reflexes elicited from upper extremities were normoactive and symmetrical. Knee and ankle reflexes were hyperactive and symmetrical. Mild sensitive ataxia was noted. Sensory symptoms in form of allodynia were present symmetrically at the elbow level and below in upper extremities, and in the knee level and below in lower extremities. Symptoms got progressively worse as they reached distal parts of extremities, presenting as hyperalgesia and dysesthesia. Bladder and bowel function were intact. No meningeal symptoms were observed.

Brain magnetic resonance imaging (MRI) with MR-spectrography confirmed chronic limbic encephalitis with lesions mainly located in the anterior and medial parts of right hippocampus with slight reduction of N-acetylacetate level. Other findings included chronic bilateral maxillary sinusitis, ethmoiditis, right nasal concha hypertrophy, and dysembryonic benign neoplasm in form of lipoma of medial parts of falx. Furthermore, chronic adenoiditis

without significant hypertrophy was found, with cystic inclusions in lymphoid tissue of the posterior wall of nasopharynx, sized 0.2-0.5 cm in diameter (Fig. 1-4).

Findings of visual evoked potentials (VEP) using reversal chess pattern were suggestive of moderate axonal/demyelinating lesion of optic nerves at pre- and postchiasmal level.

Brainstem auditory-evoked potentials (BAEP) revealed signs of bilateral initial decrease in I-III interpeak intervals, which is indicative of early signs of bilateral demyelinating lesions of auditory nerves, caused by chronic mixed type herpetic infection. Patient was referred to audiologist for tonal audiometry and further evaluation.

Polysomnography (PSG) revealed signs of secondary insomnia with significant deterioration of night sleep and shortening of its length, increased frequency of waking. 11 episodes of sleep apnea were registered, 10 of which were obstructive. Snoring was present only in supine position.

ELISA findings showed increased titer of anitbodies to Herpesviridae family viruses. Immune status test demonstrated decrease in T-helpers level, increased amount of T-cells, NK-cells and B-lymphocytes.

We developed new electrophysiological diagnostic algorithm for SP-CIDP, which includes computerized pallesthesiometry and thermosensometry of distal parts of upper and lower extremities, stabilometry (EU standard Rhomberg's test), upper and lower extremities nerve conduction study (NCS), and transcutaneous oxymetry. This algorithm was implemented in our patient, confirming the diagnosis of SP-CIDP with predominant involvement of lower extremities, peroneus profundus nerve being the most damaged.

NCS ("Neurosoft", Ivanovo, Russian Federation) showed markedly reduced nerve conduction in sensory fibers of bilateral median nerves, right peroneal nerves, which are indicative of axonal-demyelinating damage. Furthermore, mid axonal degeneration in motor fibers of both peroneal nerves were found.

Abnormalities in main posture of mixed cause with the involvement of proprioceptive and cerebellar system were found on stabilometry (EU standard Rhomberg's test) (MBN, Moscow, RF).

Computerized thermosensometry(CSM) (thermodynamic test with assessment of pain threshold to cold and hot) (MBN, Moscow, RF) of upper extremities found slightly reduced warmth sensation in both forearms, cold sensation was intact bilaterally. Moderate decrease in cold pain threshold was registered in both upper extremities, with warmth pain threshold being intact. CSM of lower extremities revealed mild decrease in warmth sensation bilaterally, more pronounced in feet, as well as mild reduction in cold sensation in distal parts of lower extremities. Cold pain threshold was moderately reduced bilaterally, warmth pain threshold was

intact. Cold dysesthesia was revealed. These findings are indicative of mild-to-moderate impairment of unmyelinated and thinly myelinated fibers of distal parts of extremities.

Computerized pallesthesiometry (CPM) (MBN, Moscow, RF) of styloid processes of ulna revealed reduced vibroceptionof high frequency vibration (250, 500 Hz) on the right, and 8, 16, 32 and 250 Hz on the left. These findings are compatible with mild damage to thickly myelinated fibers of Aβ type in distal parts of lower extremities (Fig. 5).

CPM of lateral malleoli revealed mild reduction of vibroception on frequencies 32-64 Hz and marked reduction with tendency to complete loss at frequencies 250 and 500 Hz. This is indicative of mild to moderate damage to thickly myelinated fibers of Aβ type in distal parts of extremities (Fig. 6).

Transcutaneous oxymetry ("Radiometer TCM4", Copenhagen, Denmark) revealed mild reduction of transcutaneous oxygen tension in soft tissues of dorsal part of right foot and lower one-third of right calf.

Homozygous carriage of high-productive polymorphic allelic variants of interleukin-1β gene in 3954 locus (C/C) and "wild" polymorphic allelic variant of interleukin-1β in 511 locus (G/G) were found on genetic testing. Risk factor stratification based on these findings positioned our patient in the moderate risk group for recurrent herpetic neuroinfection.

Final diagnosis considering aforementioned findings was as follows: Highly active chronic viral infection (EBV, HSV-1). Recurrent orofacial herpes, currently in frail remission. Slowly progressive type of chronic parainfectious limbic encephalitis with lesions mainly localized in mediobasal parts of right temporal lobe, moderate cognitive impairment (mainly anxiety-depressive syndrome), transient motor dysphasia, left side hyperkinetic syndrome. Multiple cranial neuropathy: newly revealed mild chronic inflammatory bilateral axonal-demyelinating optic neuropathy, mild chronic left trigeminal neuropathy, chronic oculomotor neuropathy (mild medial rectus muscle weakness of left eye resulting mild diplopia). Chronic inflammatory demyelinating polyneuropathy, sensorimotor variant with predominant mild to moderate impairment of distal parts of peroneal nerves, slowly progressive type with loss of proprio- and exteroception and mild sensitive ataxia.

Aforementioned condition was associated with secondary immunodeficiency with imbalance at the level of T-cell immunity and increase in levels of cytotoxic T-cells and natural killers with reduced function of humoral immunity. Chronic bilateral hyperplastic maxillary sinusitis with formation of cyst in right maxillary sinus. Chronic adenoiditis with formation of small cysts in pharyngeal tonsil. Chronic tonsillitis in remission. Nasal septum deviation, op-ed. Hypertrophy of right nasal concha. Rhonchopathy. Mild obstructive sleep dyspnea. Moderate secondary insomnia with the disturbances in sleep architecture and duration of night sleep.

Falxcerebrilipoma is unrelated to main disease.

After proper establishment of the diagnosis, intravenous immunoglobulin infusion and antiviral therapy with famcyclovir was carried out. Adjuvant therapy included antihistamines, alpha-lipoic acid, B vitamins and antioxidants.

CONCLUSION

Chronic herpetic infection is an actual health problem as demonstrated in presented case. Primary involvement of central nervous system in form of PILE was accompanied with secondary dysimmune neuropathy manifesting as SP-CIDP in the presence of genetically determined susceptibility to chronicity and relapse of herpes infection. Patients with chronic herpetic infection must be evaluated more thoroughly at the setting of outpatient clinic for possible primary and secondary neurological deficit. New algorithm for the diagnosis of SP-CIDP is simple and includes total evaluation of sensory system.

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Fig. 1. High-field brain magnetic resonance imaging of patient A., 43 years old (March 2014): hyperintensity in T1, T2-weighted images is found parasagitally in the medial parts of interhemispheric space, which is intimately confined to falxcerebri, the signal is suppressed in FLAIR images, with sharp and smooth edges, no perifocal reaction, sized The (?), which is structurally consistent with lipomaof falxcerebri.

Fig. 2. High-field brain MRI of the same patient: no significant changes in these images.

Fig. 3. Brain MRI of the same patient: insignificant local thickening and intense signal in T2 images in the cells of mucous membrane of ethmoid bone and both maxillary sinuses. Rhinosinusopathy. Cystic inclusions in the lymphoid tissue of nasopharynx, sized 0.2-0.5 in diameter.

Fig. 4. MR-spectrography of mediabasal parts of brain of the same patient: multivoxel spectroscopy (CSI_2D_TE30) revealed slight reduction of N-acetylaspartate level (neuronal marker) in anterior and medial parts of right hippocampus (compared to same parts of left hippocampus), which is also found in mediolateral part of left hippocampus. These findings are suggestive of neuronal dysfunction in these areas.

Fig. 5. Computerized pallesthesiometry of styloid processes of ulna of the same patient (Schneider N.A. et al. method): reduction of vibroception at 250 and 500 Hz in the right side and 8, 16, 32 Hz in the left side.

Fig. 6. Computerized pallesthesiometry of lateral malleoli of the same patient (Schneider N.A. et al. method): slight reduction of vibroception at 32-64 Hz and marked reduction with tendency to complete loss at 250 and 500 Hz.

Dysfunctional Disorders of the Biliary Tract in Children of the Republic of Sakha (Yakutia)

Ivanova O.N., Berezkina O.N., Molchanova G.M.

ABSTRACT

This article focuses on the actual problem of modern pediatrics - dysfunctional disorders of the biliary tract in children. It was revealed that dysfunctional disorders are more marked in children early switched to artificial feeding, underwent an intestinal infection and treated with antibiotics to two years. The authors studied the clinical efficacy of the drug hofitol in children with dysfunctional disorders of the biliary tract. It is found out that the use of the drug hofitol reduces pain and helps to normalize stool for 3-4 days of therapy.

Keywords: dysfunctional disorders, biliary system, gallbladder, biliary tract disease, pathology.

INTRODUCTION

Recent studies, based on the most modern and reliable methods for the examination of the gastrointestinal tract, indicate the prevalence of biliary tract disease in children [2, 5, 7, 9]. According to the observations of various researchers is not always possible to establish the primacy of the disease of any of the bodies gastrohepatic-pancreatoduodenal area, as between them are very complex functional relationships, especially evident in children [1, 3, 4, 6]. A number of authors have proved that to some extent the basis of disorders of function in diseases of the biliary system are different manifestations of the motor-evacuation changes of the gallbladder, biliary ducts and sphincter. To denote these States adopted the term "Dysfunctional disorders of the biliary tract" (the Rome consensus, 1999) [8, 10]. However, to date there is no unity of views on the essence of this problem, it is estimated ambiguously, as a rule, one-sided, and sometimes contradictory [1, 3, 4, 6]. Research concerning the study of the characteristics of dysfunctional disorders in children is relevant because there is no single approach to the diagnostic criteria of this disease.

MATERIALS AND METHODS

We made the analysis of 32 case histories of children on the basis of the gastroenterology Department at Republic hospital.

RESULTS

At admission, all patients complained of pain in the right hypochondrium of stabbing character (56%), nausea in the morning (34%), and abdominal pain (100%).

In the analysis of anamnestic data revealed that 56% of patients having complaints a year before seeking medical attention. In 40% of patients complaining of severe pain in the abdomen from early childhood, 67% of children complained of pain in the right hypochondrium, 45% of children complained of nausea, 50% of children worried about burping and 47% of children periodically felt a bitter taste in the mouth. The rest of the children (4%) had no complaints. From a medical history of complaints revealed that 50% of children artificial feeding was conducted one month, 35% from 3 months. In 38% of children were side effects allergies to foods. 75% of children had a history of intestinal infections up to 1 year. 100% of all surveyed children received antibiotic therapy in the first 2 years of life about SARS and intestinal infections.

In all children the state of admission in the Department was regarded as satisfactory. Physical development is age appropriate. Food in 76 % of children were regarded as low, 24% as normal. All the patients skin pink, elastic. Upon examination of the abdomen in 53% of patients: the volume is not increased, the stomach is painful to palpation. The gall bladder is painful to palpation at 45% of the surveyed children, positive symptoms Murphy, Kera, Ortner 67% of patients. 87% of all examined patients dysfunctional disorders of the biliary tract combined with acute and chronic gastritis. All children were conducted in the General clinical blood and urine tests, microscopic examination of feces, and ultrasound examination of abdominal cavity. 80% of the surveyed children changes in clinical tests were observed. In 20% was marked leukocytosis with neutrophilia and stab shift, accelerated ESR. At the biochemical analysis of blood in the examined children, significant changes are identified.

All patients had ultrasound examination of abdominal cavity organs, 45% identified strain of the gallbladder, 20% signs hipopotamo dyskinesia, 23% hypermotor dyskinesia. All patients were barium enema, pathological disorders in patients not identified.

Patients received Linex, smectite and 15 children assigned hofitol. Hofitol aqueous solution of fresh leaves of the artichoke with hepatoprotective action. The active components in this tool, causes a systemic effect hofitola: Cinnarizine with capreolinae acids has choleretic and hepatoprotective effect, flavonoids, selenium, manganese improves the redox processes in cells, insulin, ascorbic acid, carotene, b vitamins contribute to the normalization of metabolic processes in cells. Children over 6 years old it is recommended to take 1-2 tablets 3 times a day 30 minutes before meals.

Dynamics of symptoms of the biliary tract dysfunctional disorders in children who take hofitol (n=15), children not receiving hofitol (n=17) noted decrease in pain after eating, physical activity 3-4 days after onset of therapy after 7-8 days of treatment violations of the chair: loose stools or constipation normalization after 3 days of therapy 7-8 day of treatment.

Thus, the inclusion of the drug hofitol in the therapy of disorders of biliary tract reduces pain and promotes the normalization of stool already 3-4 days of therapy.

CONCLUSIONS:

1. Dysfunctional disorders often observed in children early transferred to artificial feeding, underwent an intestinal infection and treated with antibiotics for up to two years.
2. 2. 87 % of the children with dysfunctional digestive disorders marked acute and chronic gastritis.
3. The drug hofitol reduces pain and promotes the normalization of stool 3-4 days of therapy.

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