

ASJ

“ASJ”

№ (41) / 2020

Vol.3

Editor in Chief – Ivaschuk G. O., Doctor of Technical Sciences, Kiev Institute of Technology, Kiev, Ukraine

Assistant Editor – Stepanenko O.I., Doctor of Physical Sciences, Ternopol National Technical University, Ternopol, Ukraine

- Alfred Merphi - Doctor of Economics, University of Chicago, Chicago, United States
- Yen Lee - MD, wellness center «You Kang», Sanya, China
- Avital Gurvic - Doctor of Education, University of Haifa, Haifa, Israel
- George Perry - Doctor of Chemistry, Columbia College, New York, USA
- Isa Wright - Doctor of Sociology, Moraine Valley Community College, Chicago, USA
- Jessie Simmons - Doctor of Engineering Sciences, San Diego State University, San Diego, USA
- Nelson Flores - Doctor of Philology, Wheelock College, Boston, USA
- Andrey Chigrintsev - Doctor of Geographical Sciences, University of South Carolina, Columbia, United States
- Oleg Krivtsov - Doctor of History, National Museum of Natural History, Washington, USA
- Angelina Pavlovna Alushteva - Candidate of Technical Sciences, Institute of Computer Systems and Information Security (ICSiS), Krasnodar, Russian Federation
- Elena Dmitrevna Lapenko - Candidate of Law, Institute of Law, Volgograd, Russian Federation
- Aleksandr Ole - Doctor of Biological Chemistry, University of Stavanger, Stavanger, Norway
- Emily Wells - Doctor of Psychological Sciences, Coventry University, Coventry, England
- Leon Mendes - Doctor of Pharmaceutical Sciences, Universitat de Barcelona, Spain
- Martin Lenc - Doctor of Economics, Uni Köln, Germany
- Adel Barkova - Doctor of Political Sciences, Univerzita Karlova v Praze, Prague, Czech Republic
- Vidya Bhatt - Candidate of Medical Science, University of Delhi, New Delhi, India
- Agachi Lundzhil - Doctor of Law, The North-West University, Potchefstroom, South Africa
- Musaev Odil Rakhmatovich – prof. Department of Theory and Practice of Democratic State Building of the National University of Uzbekistan

Editor in Chief – Ivaschuk G. O., Doctor of Technical Sciences, Kiev Institute of Technology, Kiev, Ukraine

Assistant Editor – Stepanenko O.I., Doctor of Physical Sciences, Ternopol National Technical University, Ternopol, Ukraine

Alfred Merphi - Doctor of Economics, University of Chicago, Chicago, United States

Yen Lee - MD, wellness center «You Kang», Sanya, China

Avital Gurvic - Doctor of Education, University of Haifa, Haifa, Israel

George Perry - Doctor of Chemistry, Columbia College, New York, USA

Isa Wright - Doctor of Sociology, Moraine Valley Community College, Chicago, USA

Jessie Simmons - Doctor of Engineering Sciences, San Diego State University, San Diego, USA

Nelson Flores - Doctor of Philology, Wheelock College, Boston, USA

Andrey Chigrintsev - Doctor of Geographical Sciences, University of South Carolina, Columbia, United States

Oleg Krivtsov - Doctor of History, National Museum of Natural History, Washington, USA

Angelina Pavlovna Alushteva - Candidate of Technical Sciences, Institute of Computer Systems and Information Security (ICSiS), Krasnodar, Russian Federation

Elena Dmitrevna Lapenko - Candidate of Law, Institute of Law, Volgograd, Russian Federation

Aleksandr Ole - Doctor of Biological Chemistry, University of Stavanger, Stavanger, Norway

Emily Wells - Doctor of Psychological Sciences, Coventry University, Coventry, England

Leon Mendes - Doctor of Pharmaceutical Sciences, Universitat de Barcelona, Spain

Martin Lenc - Doctor of Economics, Uni Köln, Germany

Adel Barkova - Doctor of Political Sciences, Univerzita Karlova v Praze, Prague, Czech Republic

Vidya Bhatt - Candidate of Medical Science, University of Delhi, New Delhi, India

Agachi Lundzhil - Doctor of Law, The North-West University, Potchefstroom, South Africa

Musaev Odil Rakhmatovich – prof. Department of Theory and Practice of Democratic State Building of the National University of Uzbekistan

Layout man: Mark O'Donovan

Layout: Catherine Johnson

Consulting group "Education and Science"

Ukraine, Kiev, Peremogi, 56/1, office 115

Web-site: <https://american-issue.info>

E-mail: info@american-issue.com

Copies: 1000 copies.

Ukraine, Kiev, Peremogi, 56/1, office 115

СОДЕРЖАНИЕ

БИОЛОГИЧЕСКИЕ НАУКИ

- Kuliev T.X., Sulstonova K.R.,
Bakeev R.S., Ismoilova K.M.*
STATISTICAL BASIS FOR DETERMINATION OF
GENOTYPE TO ENVIRONMENTAL ADAPTATION4

МЕДИЦИНСКИЕ НАУКИ

- Hazarapetyan L.G.,
Grigoryan S.V., Sarksyán A.A.*
THE ROLE OF INFLAMMATION AND COAGULATION
CASCADE IN THE PATHOGENESIS OF ATRIAL
FIBRILLATION.8
- Vlasov Y.V., Ardatov S.V., Antipova T.A.,
Sineok E.V., Ardatova A.S., Gavrilov V.Yu.*
QUANTUM BIOPHYSICS IN CONVALESCENCE OF
NOSOLOGICAL FORMS (ON THE EXAMPLE OF
MULTIPLE SCLEROSIS). PREPARATION AND STORAGE
OF ENTANGLED STATES IN NONLINEAR CRYSTALS ...10
- Datskovsky I.(V.M.),*
DIAGNOSTIC TEST FOR CHILDREN'S PSYCHOPATHICITY
PCL-MYV19
- Кононков В.В.*26
- Rasulov R.I., Dvornichenko V.V.,
Nazarova D.V., Nurbekian G.V.*
PROSPECTS FOR NEOADJUVANT TREATMENT OF
AMPULLARY CANCER28
- Фомин А.М.*
ГЕМОПЕРФУЗИЯ ПРИ ОСТРОМ ОТРАВЛЕНИИ
ПСИХОТРОНЫМИ ПРЕПАРАТАМИ36

СОЦИОЛОГИЧЕСКИЕ НАУКИ

- Kazimi P.F., Mammadov M. A.*
ASSESSMENT OF THE LIBRARY INFORMATION
SERVICE (MODERN PROBLEMS OF LIBRARY AND
INFORMATION SERVICES)41
- Bočáková O., Kubičková D.*
SOCIO-HEALTH CONSEQUENCES OF THE RISKS OF
SENIORS44
- Bočáková O., Adamkovičová B.*
THE SELF-GOVERNING REGION OF TRENČIN IN THE
DIMENSIONS OF SOCIAL CARE AND SOCIAL HELP47

БИОЛОГИЧЕСКИЕ НАУКИ

STATISTICAL BASIS FOR DETERMINATION OF GENOTYPE TO ENVIRONMENTAL ADAPTATION

*Kuliev Tojiddin Xamdamovich**,
*Sultonova Kumush Ruzimurod kizi***,
*Bakeev Rifat Serverovich**,
*Ismoilova Karomatkhon Maxmudjonovna**

*Gulistan state University,
 **Samarkand State Veterinary Medical Institute

DOI: 10.31618/asj.2707-9864.2020.3.41.36

Abstract. This study is determined a level of correlation within nine traits, variation, coefficient of determination and similarity of matrixes in hairy vetch (*Vicia villosa* Roth) under control and salinity condition. It was found that a potential index of traits in salinity decreased by 5-17% compared to non-saline soil. The weight of the bean, the number of seed per bean and its weight were strongly determined and varied. Also, a similarity of the correlation matrixes shows as 91.6%. Our results suggests, a hairy vetch is a tolerant to salinity.

Key words: Correlation, determination, variation, saline soil, matrix of correlation, hairy vetch.

Introduction

The environment, especially the soil provides a useful macro and micro elements for plant growth and development. Plant traits are formed based on its genetic potentials. Therefore, a quantitative traits can vary among genotypes. A strong variation of quantitative traits still remained as a actual issues in genetics and breeding. Although quantitative traits have been studied for more than 150 years, their genetics has not been fully studied yet [1].

Using a modern technologies and innovations in biological research, it has been determined that environmental factors influences a systemic alteration of organisms. Therefore, it is recommended ecological, biological, eco-biological and genotypic trait-indicators [2].

The level of soil salinity is known to provide a stressful condition for the plant. In the saline soil, Na⁺ cations and Cl⁻ ions are toxic response. Under the influence of salts, the osmotic pressure of the soil solution increases, as a result, the root does not receive the required amount of water. Therefore, the plant productivity is significantly decreased [3,4].

Natural environmental conditions allow plants to adapt under salinity. It has been found that harvested cereals from dry climates are more tolerant to salinity than harvested from humidity conditions [5].

Along the salinity stress, there are other factors, such as an agronomic measures, including sowing rate and duration, amount of mineral fertilizers may also create a unfavorable conditions for plant growth and development. For instance, the level of variation of traits in sunflower plant were increased under stressfull condition than normal conditions. Also, it was noted that the degree of correlation between characters increased when winter wheat were planted a bit late and thick. In moderate salinity conditions, a bean weight and length of vetch is decreased by 25% and 4.8% respectively compared to weakly saline conditions [6,7].

The effect of steroids has been mainly studied as an increase of plant adaptation to soil salinity levels. In saline soil conditions, the coefficient of determination

was 0.8-0.11 without steroid treatment, while it was - 0.03-0.04 under the influence of compounds of steroids. This indicates that the compounds of a steroids can create suitable conditions for the growth and development of wheat under salinity [8].

In general, the external environment allows to survive of adaptive and specific genotypes. As an example, there are many halophytes and salt-tolerant plants that are common in the Mirzachul lands (highly saline area). Those plants may a crucial for breeding. However, there is no considerable criteria to determination of plant tolerance in terms of scientific methods so far. For this reason, the selection and creation of new genotypes as a stress tolerant remains one of the urgent tasks for current plant breeding. Our study provides some information to improve the methods for determining the tolerance of plants to salinity stress. The main purpose of the work is to study of statistical basis for determining the tolerance of hairy vetch to soil salinity levels.

Materials and methods

Plant Materials. The object of the experiment was a hairy vetch (*Vicia villosa* Roth) plant was used in this study. As a non saline soil treatment, hairy vetch collected from Zaamin district of Jizzakh region. As a saline soil treatment, hairy vetch collected from Mirzaabad district of Syrdarya region.

Data analysis. After harvesting of yield from saline and non-saline soils condition, the quantitative parameters of beans were measured. The data was statistically analyzed using the SPSS-14 program. It is included the correlation (r), determination (r^2) and coefficients of variability (Cv,%) [9]. A similarity of the correlation matrix was determined according to N.S. Rostova method [2].

Results and discussion

Our results shows that the level of soil salinity was affected to the bean features. The weight of bean was 0.18 g in non-saline soil conditions and 0.14 g in saline soil conditions. The difference between them was 19.1%. Similar results were observed at length of bean. A length of bean was 2.72 sm in non-saline soils and 2.28 sm in saline soils, the difference was 16.06%.

Other features such as width of bean, number of seed in legume, weight of seeds, and weight of 100 seeds were 5-11% lower in saline soil conditions than control. Non-pollinated bulbs was a higher percentage in saline than non saline condition, as 34.85% and a 16.99 % respectively. A grain yield (percentage of grain in legumes) was also higher than other features in saline soil conditions (Table-1).

Our biometrical analysis showed that the soil salinity levels affected to the variation of hairy vetch traits. This results stimulated to study the specific

features of trait variations. The data is shown in Figure-1. The weight of bean (1), the number of seeds per bean (5) and weight of seeds (6) were found as a strongly determined and varied. Such result was also observed in saline and non-saline soil conditions. It means that these traits are strongly associated with other traits. Therefore, this traits clearly depend both genotype and the external environment, which allows to determine adaptability. These traits can be called an eco-biological indicators.

Table-1.

Effect of levels of salinity stress on potential characters of legum.

Statistic characters	Weight of bean (g)	Length of bean (mm)	Width of bean (mm)	Thickness of bean (mm)	Number of seeds per bean	Weight of seed per bean	Harvest index,%	Weight of 1000 seeds (g),	Non pollinated bolts,%
Legum under control									
The arifmetic mean	0,18 ±0.01	2,72 ±0.03	0,71 ±0.01	0,52 ±0.01	3,20 ±0.15	0,12 ±0.01	63,57±1.35	3,71 ±0.12	34,85 ±2.76
Minimum	0,09	2,20	0,55	0,39	2,00	0,06	43,75	2,00	0,00
Maximum	0,34	3,30	0,90	0,65	6,00	0,24	87,50	6,33	60,00
r ²	0,34	0,08	0,03	0,22	0,33	0,40	0,21	0,10	0,28
Cv,%	27,7	8,37	10,7	14,0	32,8	37,4	15,1	23,4	56,2
Legum under saline soil									
The arifmetic mean	0,14 ±0.01	2,28 ±0.04	0,67 ±0.01	0,49 ±0.01	2,98 ±0.16	0,10 ±0.01	69,62 ±1.39	3,53 ±0.11	28,93 ±2.61
Minimum	0,06	1,50	0,51	0,39	1,00	0,03	40,00	2,00	0,00
Maximum	0,25	3,10	0,80	0,65	6,00	0,19	87,50	5,50	66,67
r ²	0,37	0,21	0,02	0,15	0,34	0,39	0,14	0,06	0,19
Cv,%	33,6	13,1	8,2	13,9	38	38,8	14,1	21,7	63,9
Effect,%	-19,1	-16,06	-5,04	-5,86	-6,87	-11,43	+9,51	-4,89	-16,99

Note: here, r²- determination, Cv,% coefficient of variation.

The length of bean (2), thickness of bean (4) weight of 100 seeds (7) were moderately determined and less variable. Although the variation of these traits are not independent, it can be called a biological indicators. Because, a multiple biological features are summed in genotype.

The width of bean (3) was less determined and less variable in both conditions (Table-1 and Figure-1). It means, this trait can variable independently and less variable to environmental responses. Therefore this trait is called a genotypic indicator.

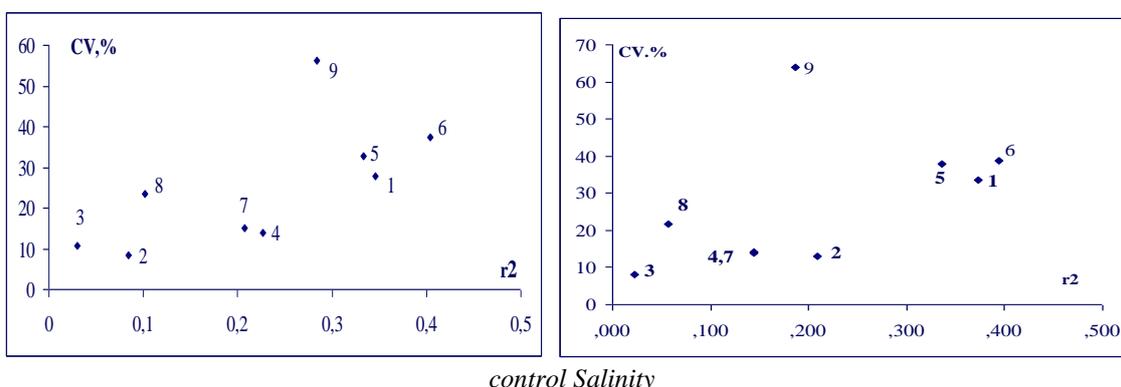


Figure-1. Effect of salinity to variation of traits(Cv,%) and determination (r²). Numbers mean a traits: 1- weight of bean; 2- length of bean; 3- width of bean; 4- tickness of bean; 5- number of seed per bean; 6- weight of seed per bean; 7- weight of 100 seeds; 8- harvest index; 9- non-pollinated bolts.

The soil salinity is not only affected to the quantitative traits, meantime, it also influence to the degree of correlational relationships. The average coefficient of determination was 0.08 and 0.21 in non-

saline and saline soil conditions respectively. It indicates that this trait is strongly influenced by soil salinity. The level of correlational relationships between quantitative traits also confirmed in Figure-2.

A strong correlation was observed between the weight of bean (1), the number of seeds per bean (5), and the weight of seeds per bean (6) in both conditions. The correlation coefficient between these characters was higher than $r = 0.7$. The correlation between weight of bean (1) and length of bean (2) and the number of seeds per bean (5) showed a weak determination ($r = 0.3$) in non-saline soil conditions. However, this trait was moderate value ($r = 0.61$) in saline soil conditions. Same results were observed between the number of seeds per bean (5) and the weight of 100 seeds (7). It is also found an inverse correlation between the number of non-pollinated bulbs (9) and the weight of bean (1), the length of bean (2), the thickness of bean (4), the number of seeds per bean (5), the weight of bean (6) weight of 100 seeds (7). It means, the weight of bean, a number of seeds and weight of seeds dropped when the

number of unpollinated bulbs are higher. The number of unpollinated bulbs increased in saline soil conditions.

The figure-1 shows that the level of soil salinity affected to the level of correlational relationships between the plant traits. But it is difficult to determine how they are similar or different. In this case, it is recommended to use the method of comparison of correlation matrixes. The results indicated that the similarity of the correlation matrixes was 91.6%. If the similarity of the matrixes is higher than 90%, it is called a highly similar matrixes [2]. Hence, the very similarity of the correlation matrixes suggests that the soil salinity levels did not strongly influence to vika traits. This indicates that the hairy vetch is a salt tolerance plant. The hairy vetch was also noted as a tolerant by other researchers [10].

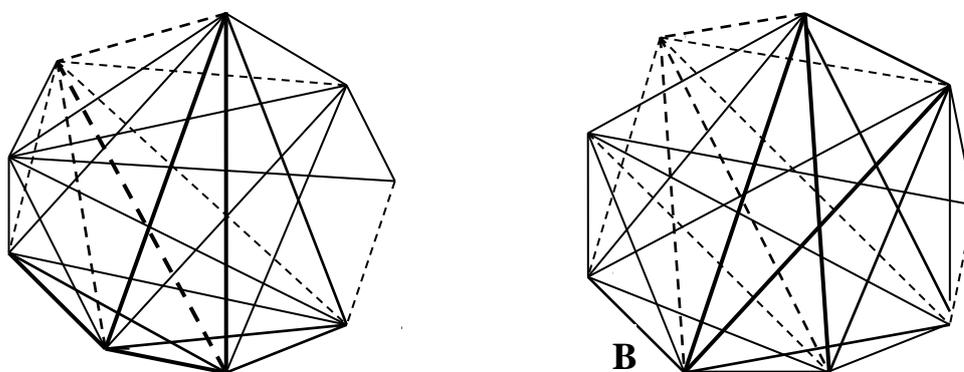


Figure-2. Level of correlation.

A-control; B-salinity.

Note: Numbers mean a traits and lines mean a level of correlation between traits:

$r=0.3-0.5$; $r=0.5-0.7$; $r=>0.7$; $r=-0.3-0.5$; $r=-0.5-0.7$



Conclusion

1. Approximately a 5–17% of quantitative features shows a lower value in salinity condition than in control condition.
2. A quantitative traits including a bean weight, number of grains in the bean and a weight of gain were strongly determined in both conditions.
3. The similarity of the correlation matrix was a 91.6%. It means a hairy vica is a tolerant to salt.
4. The method of comparing a correlation matrix can be used to compare genotypes.

References

1. Brach N.B. Razvitiy metodov izucheniya nasledovaniya kolichestvennix priznakov // Trudi po prikl.bot., gen., i sel.SPb.:VIR,2011.T.167.S.23-35
2. Rostova N.S. Korrelyatsii: struktura i izmenchivost . SPb.: Izd-vo S.-Peterb.un-ta, 2002. T.94.S.-308.
3. Geissler N., Hussin S., Koyro H.-W. Interactive effects of NaCl salinity and elevated atmospheric CO₂ concentration on growth. photosynthesis. water relations and chemical composition of the potential cash crop halophyte Aster tripolium L. // Environ. Exp. Bot. 2009. V. 65. P. 220–231.

4. Munns R. Comparative physiology of salt and water stress // *Plant Cell Environ.* 2002. V. 25. P. 239–250.
5. Koyro H.-W., Geissler N., Hussin S. Survival at Extreme Locations: Life Strategies of Halophytes // *Salinity and Water Stress* / Eds. Ashraf M., Ozturk M., Athar H.R. Netherlands: Springer Netherlands. 2009. P. 167–177.
6. Kuliiev T. Vika (VICIA VILLOSA ROTH) biometrik korsatkichlariga tuproq shorlanish darajasining tasiri // *Uzbekiston agrar fani xabornomasi.* Toshkent 2016. №1(63).2016. 60-66.b.
7. Kuliev T. Izmenchivost i determinirovannost priznakov podsolnechnika v usloviiah pochvennogo zasoleniya // *Naychnyi vestnik.* №1(3), 2015. Rossiia. 84-90 s.
8. Ismailova K. M. The impact of steroid nature compounds on the mutual connection level of overall indicators of winter wheat. *European Science Review.* Vienna. 2018. –P. 11-14.
9. Shishliannikova L.M. Matematicheskoe soprovozhdenie naychnoi raboty s pomoiy staticheskogo paketa SRSS for Windows 11.5.0 /Uchebno-metodicheskoe posobie M., 2005.S.105.
10. Trofimov I.T., Tolstov M.V., Bystrov A.V., Poriadin V.V. Vika mohnataia-tsennaia kormovaia kultura dlia kislyh i elochnyh pochv // *Vestnik Altaiskogo gosudarstvennogo universiteta.* 2010,-№ 8 (70).- S.-18-20.

МЕДИЦИНСКИЕ НАУКИ

THE ROLE OF INFLAMMATION AND COAGULATION CASCADE IN THE PATHOGENESIS OF ATRIAL FIBRILLATION.

*Hazarapetyan L.G.,
Grigoryan S.V.,
Sarkisyan A.A.*

*Yerevan State Medical University after M.Heratsy,
Research Institute of Cardiology, Armenia
DOI: 10.31618/asj.2707-9864.2020.3.41.32*

Abstract. Introduction: Atrial fibrillation (AF) is associated with prothrombotic or hypercoagulable states, various inflammation markers such as interleukin-6 (IL-6) and hsC-reactive protein (hsCRP) have also been associated with AF. The aim of this study is to investigate the relationship between inflammation markers and the prothrombotic state in the setting of AF and the impact on outcome in patients with AF.

Methods: We observed 141 patients with non-valvular AF. As a control group patients similar in gender and age without AF were examined. Clinical, instrumental and laboratory tests were performed on the observed patients. The markers of the coagulation cascade (TF and F) and of inflammatory markers (hsCRP and IL-6) were studied additionally by ELISA on the analyzer "Stat Fax 303 Plus". Studies were conducted using SPSS 13.0 and EXCEL-2013.

Results: The obtained results showed that compared to the control group, AF patients had significantly higher levels of IL-6 ($p = 0.043$), hsCRP ($p = 0.002$), TF ($p = 0.026$), and F ($p = 0.025$). Moreover, levels of hsCRP were higher among AF patients at "high" risk of stroke by CHA2DS2-VASc Score ($p = 0.003$). Besides, the levels of hsCRP and IL-6 were markedly elevated in patients with dilated left atrium ($p = 0.001$), poorly functioning left atrial appendage ($p = 0.023$) and longer duration of AF ($p = 0.002$).

Conclusion: We have demonstrated that the increased plasma levels of IL-6 and hsCRP are related to indices of the coagulation cascade and contribute to structural atrial remodeling in patients with AF.

Keywords: Atrial fibrillation; high sensitive C reactive protein; Interleukine-6; tissue factor; fibrinogen

Introduction: Atrial fibrillation (AF) is the most commonly sustained arrhythmia and at the same time the most heterogeneous arrhythmia with regard to the individual spectrum of resulting symptoms. AF is associated with atrial structural changes that may have an inflammatory basis [1, 2, 3, 4, 5, and 6]. The role of inflammation in the pathogenesis of AF has not yet been evaluated but inflammatory mechanisms may form a basis for new agents more likely to prevent recurrent episodes of AF. There has recently been much interest in the relationship between systemic inflammation and coagulation cascade in patients with AF [7, 8, and 9]. AF is also associated with a prothrombotic or hypercoagulable state and there is a plausible evidence linking inflammation to the initiation and perpetuation of AF and AF-related thrombosis. Several prothrombotic factors have been found to be elevated in AF, indicating abnormal thrombogenesis. Over the last years we suggested the link between inflammatory processes and development of AF. Classical markers of inflammation such as hsC-reactive protein (hsCRP) and proinflammation cytokine Interleukin -6 (IL-6) were found elevated in patients with AF. Tissue Factor (TF) is the principal initiator of the coagulation cascade. In this way TF promotes blood coagulation and is involved in inflammation and angiogenesis [10, 11, 12, and 13]. The aim of this study is to investigate the relationship between inflammation markers and the prothrombotic state in the setting of AF, including the impact of this interaction on clinical presentation and outcome in patients with AF.

Material and methods. We observed 141 patients with non-valvular AF. There were 84 males (59.2%), 57 females (40.8. %), mean age 59, 73 ± 6 , 49, the duration of AF is 14, 36 ± 12 7 months. Among the examined patients, 129 (92.4%) were diagnosed of ischemic heart disease, arterial hypertension was observed in 78 patients (56.1%). Heart failure (NYHA functional class I-II) was detected in 104 patients (76.4%) and NYHA (functional class III) - in 33 patients (23.6%). The exclusion criteria were: ventricular arrhythmia (more than 30 per hour by Lown) ventricular tachycardia, acute coronary syndrome, heart failure (functional class more than III by NYHA), bronchial asthma, diabetes, and acute inflammatory disease within the last 4 months, cardiomyopathy, myocarditis, valvular heart disease, the thyroid gland dysfunction. Clinical examination of patients included a study of medical history, physical, laboratory and instrumental examination. As a control group similar in gender and age composition 48 patients with IHD and AH without AF were examined. Clinical and instrumental characteristics of patients with AF were performed in Table 1.

The program of investigation included general clinical examination of patients: electrocardiogram, echocardiography and common biochemical blood tests. The level of the prothrombotic state, including markers of the coagulation cascade (TF and F) and levels of inflammatory markers (hsCRP and IL-6) were studied additionally and were determined by ELISA on the analyzer "Stat Fax 303 Plus». Studies were conducted on the basis of simple randomized protocols, using the universal statistical packages SPSS 13.0 and

EXCEL-2013. **Results:** The analysis of the data showed the significant differences between the levels of hsCRP and IL-6 among patients with AF and the control group (1.2 ± 0.60 vs. 5.7 ± 1.4 $p = 0.002$ and 1.2 ± 0.8 vs. 2.6 ± 1.1 $p = 0.043$ accordingly). HsCRP is an acute-phase protein that is why it is likely to react more quickly to the appearance of AF. In all likelihood the inflammation markers such as hsCRP and IL-6 markers of inflammation can be considered as risk factors for the occurrence and recurrence of AF. At the same time, the state of coagulation cascade of blood is of particular importance for the appearance of AF. Tissue Factor (TF), formerly known as thromboplastin, is the key initiator of the coagulation cascade. TF expression and activity can be induced in endothelial cells, vascular smooth muscle cells, and monocytes by various stimuli such as cytokines, growth factors, and biogenic amines. We revealed that in patients with AF, TF is improved as compared to the similar patients without AF (1300 ± 50 vs 600 ± 11.9 $p = 0.026$). The similar pattern was also observed when comparing the concentrations of fibrinogen F in AF patients with control group ($13. \pm 2.4$ vs 9.08 ± 1.4 $p = 0.025$). Moreover, we found a direct correlation between the activity of thromboplastin and the left atrium structural and functional changes ($r = 0.643$). Table 2 shows the results of concentration of some inflammatory markers and coagulation cascade agents in patients with AF and the similar patients without AF as a control group (table 2).

Thus, our obtained results showed that compared to the control group, AF patients had significantly higher levels of IL-6 ($p = 0.043$), hsCRP ($p = 0.002$), TF ($p = 0.026$), and F ($p = 0.025$). Moreover, plasma levels of hsCRP were higher among AF patients at "high" risk of stroke by CHA2DS2-VASc Score ($p = 0.003$). Besides the levels of hsCRP and IL-6 are markedly elevated in patients with dilated left atrium ($p = 0.001$), poorly functioning left atrial appendage ($p = 0.023$) and longer duration of AF ($p = 0.002$).

Conclusion: Thus, as a classic inflammatory marker hsCRP is the major acute phase protein and a sensitive indicator of inflammation. HsCRP elevation may be a non-specific response to any environmental stimulus, also it may be not directly or indirectly related to the pathogenesis of AF. Its synthesis by the liver is regulated to a large extent by the pro-inflammatory cytokine (such as IL-6), and probably acting on distance to the blood vessel wall to produce elevations in conventional cardiovascular risk factors and the coagulation cascade agents such as TF and F. That is why we have demonstrated that the increased plasma levels of IL-6 and hsCRP are related to indices of the coagulation cascade and may contribute to structural atrial remodeling in patients with AF.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

REFERENCES:

- [1]. Dernellis J, Panaretou M, Effect of C-reactive protein reduction on paroxysmal atrial fibrillation, *Amer.Heart J.* 2005, 4, 12-14.
- [2]. Grigoryan S.V., Adamyan K.G., Hazarapetyan L.G., Tumor necrosis factor as a prognostic marker of paroxysmal atrial fibrillation, ECAS Congress, Paris, France, April 19-21. 2009 Abstract 15-08.
- [3]. Maehama T, Okura H, Imai K et al., Systemic inflammation and left atrial thrombus in patients with non-rheumatic atrial fibrillation, *J Cardiol.* 2010,56, 118-124. <http://dx.doi.org/10.1016/j.jcc.2010.03.006>.
- [4]. Harada M, Van Wagoner, D.R., Nattel S., Role of inflammation in atrial fibrillation pathophysiology and management, *Circulation.* 2015, 79(3), 495–502.
- [5]. You-Jung Choi, Eue-Keun Choi, Kyung-Do Han et al., Increased risk of atrial fibrillation in patients with inflammatory bowel disease: A nationwide population-based study, *World J Gastroenterol.* 2019, 25(22), 2788-2798. doi: 10.3748/wjg.v25.i22.2788
- [6]. Sonmez, O, Ertem, F.U, Vatankulu M.A, Novel fibro-inflammation markers in assessing left atrial remodeling in non-valvular atrial fibrillation, *Med Sci Monit.* 2014, 20,463–470.
- [7]. Acevedo M., Corbalan R., Braun S. et al, C-reactive protein and atrial fibrillation: evidence for the presence of inflammation in the perpetuation of the arrhythmia, *Am J Cardiol.* 2006,108 (3), 326-331
- [8]. Adamyan K.G., Grigoryan S.V., Hazarapetyan L.G., The role of latent inflammation in the pathogenesis of atrial fibrillation, *Journal of Arrhythmology.* 2008, 54, 34-41 [Publ. in Russian]
- [9]. Cianfrocca C, Loricchio M.L, Pelliccia F, et al, C-reactive protein and left atrial appendage velocity are independent determinants of the risk of thrombogenesis in patients with atrial fibrillation, *Int J Cardiol.* 2010, 142, 22-28 <http://dx.doi.org/10.1016/j.ijcard.2008.12.052>
- [10]. Hayashi M., Takeshita K, Inden Y. et al, Platelet activation and induction of tissue factor in acute and chronic atrial fibrillation: Involvement of mononuclear cell-platelet interaction K, *Thrombosis Research.* 2011, 126, 6, e113-e118.
- [11]. Jesel L, Arentz T, Herrera-Siklody Cl., Trenk D, et al, Do Atrial Differences in Endothelial Damage, Leukocyte and Platelet Activation, or Tissue Factor Activity Contribute to Chamber-Specific Thrombotic Status in Patients with Atrial Fibrillation?, *Journal of Cardiovascular Electrophysiology.* 2014, 25, 3, 266–270.
- [12]. Reiffel J.A., Atrial fibrillation and stroke: epidemiology, *Am J Med.* 2014, 127(4), e15–e16.
- [13]. Li YG, Lee SR, Choi EK, Lip GY, Stroke Prevention in Atrial Fibrillation: Focus on Asian Patients, *Korean Circ J.* 2018, 48,665-684.

Tables

Table 1.

Characteristics of the average values of some parameters of patients with AF

Indices	Mean values+standards deviation
Age (years)	59,7 ± 6,49
Duration AF (months)	14,4 ± 12,7
LAD (mm)	42,28 ± 3,68
LVEDD (mm)	56, 69 ± 3, 84
EF (%)	46, 63 ± 5, 48
IVST (mm)	12.44 ± 2, 50

Note: LAD-left atrium diameters; LVEDD-left ventricular end-diastolic diameter; EF – ejection fraction; IVST - interventricular septum thickness;

Table 2.

The levels of inflammation markers and coagulation cascade agents in AF patients and the control group

Indices	Control group n=48	AF group n=141
TF pg/ml	600±11.9	1300± 50.* p = 0.026
IL-6 pg/ml	1.2± 0.8	2.6± 1.1* p = 0.043
hsCRP mg/l	1.2±0.60	5,7± 1.4* p = 0.002
F mgmol/l	9.08± 1.4	13. ± 2.4* p = 0.025

Notes: TF – tissue factor; F – fibrinogen; hsCRP – hsC reactive protein; IL-6 – cytokine interleukin -6.

Hazarapetyan L.G.

Grigoryan S.V.

**QUANTUM BIOPHYSICS IN CONVALESCENCE OF NOSOLOGICAL FORMS
(ON THE EXAMPLE OF MULTIPLE SCLEROSIS).
PREPARATION AND STORAGE OF ENTANGLED STATES IN NONLINEAR CRYSTALS**

Vlasov Yan Vladimirovich^{*1},
*Ardatov Sergey Vladimirovich*²,
*Antipova Tatyana Alexandrovna*³,
*Sineok Evgeniya Vitalyevna*⁴,
*Ardatova Anastasia Sergeevna*⁵,
*Gavrilov Vladimir Yurievich*⁶

¹ ORCID: 0000-0002-9471-9088

*Samara state medical University of the Russian Federation.
Professor of the Department of neurology and neurosurgery.
President of the "All-Russian public organization of disabled people with multiple sclerosis".*

² ORCID: 0000-0002-2644-5353

*Samara state medical University of the Russian Federation.
Associate Professor of the Department of traumatology,
orthopedics and extreme surgery named after academician A. F. Krasnov.
Head of the Department of traumatology and orthopedics №1 of SamSMU clinics.*

³ ORCID: 0000-0001-5499-2170

*Samara state medical University of the Russian Federation.
Associate Professor of the Department of medical physics,
mathematics and informatics.*

⁴ORCID:0000-0002-3390-0553

Samara state medical University of the Russian Federation.

Assistant of the Department of ophthalmology.

⁵ ORCID: 0000-0003-3329-9427

Samara state medical University of the Russian Federation.

Resident of the Department of medical rehabilitation,

sports medicine, physiotherapy and balneology.

⁶ ORCID: 0000-0001-6964-6086

Samara regional public organization of disabled people with multiple sclerosis.

Chief scientific adviser.

Corresponding member of the Academy of medical and technical sciences

of the Russian Federation.

*Corresponding Author: Yan V. Vlasov Samara state medical University of the Russian Federation.

Professor of the Department of neurology and neurosurgery.

President of the "All-Russian public organization of disabled people with multiple sclerosis".

Samara, Russia

DOI: 10.31618/asj.2707-9864.2020.3.41.33

Abstract. The principles discussed in this article are similar to the processes that occur every second in nature. They are the basis of the bionic model under consideration in the framework of nano -, bio -, info -, and cogno-convergence (nbic-convergence). This model is similar to the processes of quantum teleportation that occur in natural biogeocenoses and ecosystems. The article also discusses ways to "preserve" entangled states in crystals as optically active nonlinear media. The following is a method of hypothetical physiotherapy for modeling persistent remissions of multiple sclerosis due to the remyelination process. This method creates some forced conditions for the execution of the macroscopic quantum teleportation protocol. The considered hypothetical model can also be used for reconvalescence of a wide range of nosological forms.

Keywords: multiple sclerosis, physiotherapy, sound therapy, phototherapy (light therapy), preparation of entangled states, crystal optics, crystallography, acoustooptics, acoustoelectronics, teleportation of quantum information.

INTRODUCTION

The preparation of entangled (linked) states requires not only their correct preparation, but the long-term preservation of such states. This refers to conditions that simulate the necessary biochemical and biophysical processes in the body, usually inherent and occurring in the body against the background of appropriate pharmacotherapy. In this case, there is nothing else to do but create these states in vitro and store them in the form of diffraction gratings in crystals, followed by the use of these personal repositories for the needs of predictive medicine with an individual approach. The technology for preparing such entangled states in the form of a hypothetical model could look like this.

I. MODEL OF TECHNOLOGICAL SOLUTIONS FOR THE PREPARATION AND LONG-TERM STORAGE OF ENTANGLED STATES IN THE FORM OF DIFFRACTION GRATINGS

Previously, some aspects related to the long-term study of this issue and an extensive list of relevant original works related to the teleportation of information in macro systems, with appropriate references, were considered by the authors in [1, 2]. The model [3, 4] is based on the theory of crystals of crystallooptics and crystallography, acoustooptics and acoustoelectronics, describing the interaction between quasiparticles in crystals under the influence of electromagnetic radiation (including the light range) with the formation of periodic structures of plastic defects-dislocations ("diffraction gratings"), which carry complete information about the physical, chemical, biological and other properties of material

objects interacting in the "radiation — crystals — active substance" system, according to the physical mechanisms shown in diagrams (1) and (2) (figures 1 and 2, respectively). The model is based on a special method for processing crystals, semiconductors, and other active medium.

The technology must be divided into two conditional stages:

- The process of registering information about the physical properties of a material object (active substance) (figure 1).
- The process of reproducing and transmitting information about the physical properties of a material object (active substance) (figure 2).

A brief review of the content of the technological process on the example of crystals shown in the diagram (figures 1, 2).

- The process of registering information about the physical properties of a material object (active substance) — (figure 1).

1 — Coherent monochromatic pulsed radiation in the UV, visible and IR ranges. The pulse power for these active media (15) is $10 \cdot 10^7$ MW.

2 — IR radiation.

3 — Radiation in the visible range.

4 — UV radiation.

5 — Oscillations of atoms and (or) ions of the crystal lattice.

6 — Electrons of the periodic atomic lattice.

7 — Phonons of the crystal lattice.

8 — Frenkel Excitons (excitation of the electronic system of individual molecules).

9 — Non-destructive breakdown of the crystal by a giant laser pulse, causing shock ionization.

- 10 — Fluctuon (phase).
 11 — Shock wave resulting from shock ionization at the moment (12).
 12 — Phase transition to the plasma state.
 13 — Phonon generated when a shock wave passes into an acoustic one at a distance from the site of the phase transition.
 14 — The area of interaction of collective processes, fixed in the form of a plastic defect (dislocation).
 15 — Crystals (for example, sapphire Al_2O_3 with Fe admixture; iron-tritium garnet $\text{Y}_3\text{Fe}_5\text{O}_{12}$; quartz SiO_2 ; lithium niobate LiNbO_3 , etc.).
 16 — Active substance.

17 — Gap between the crystals.

Two mirror-displayed crystal (15) connected to the contact so that between them an air gap (17) of a width comparable with the wavelength of the incident radiation, is placed in a container filled with active substance (16), and exposed to coherent monochromatic light (1), and each face of one of the crystals is exposed to infrared (2), visible (3) and UV (4) ranges. Irradiation of each face is necessary due to the fact that the crystal has anisotropy and its physical properties in different directions are not identical. The crystal must be cut in such a way that any two of its faces are orthogonal.

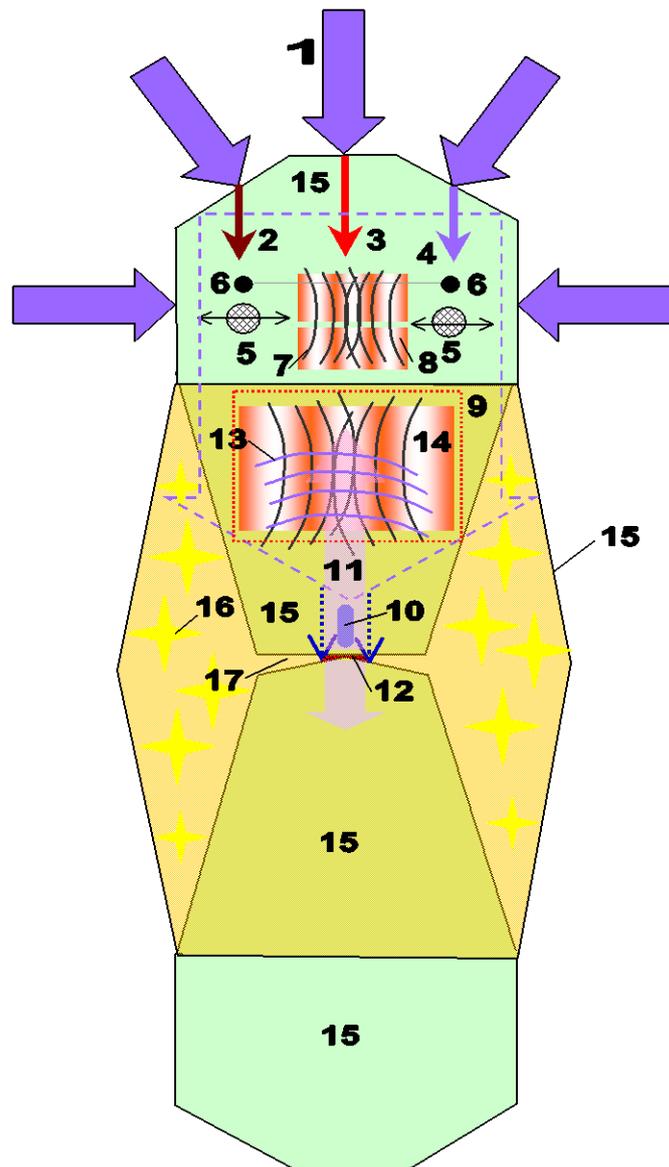


Figure 1. Technology of registration information about the physical properties of the active substance

When coherent monochromatic radiation of the infrared and visible optical range of a certain spectrum falls, waves of displacement of atoms (ions) and crystal molecules from the equilibrium position are excited in the crystal, accompanied by the formation of quasiparticles of phonons (7). Due to the chaotic directions of oscillations of atoms (ions) of the crystal

lattice, phonons can interfere with each other to form standing waves (7). According to the phenomenon of Mandelstam-Brillouin scattering, the incident light wave is modulated on a complex periodic structure formed by interfering phonons. The modulated light wave excites displacement waves, etc. As a result, a complex periodic structure is formed, which is fixed by

the formation of corresponding plastic defects. At these dislocations, the portion of quanta of the next pulse is dispersed and modulated. This is how the formation of increasingly complex periodic structures — defects that are fixed in the crystal in the form of dislocations, proceeds step by step.

When coherent monochromatic radiation of the ultraviolet optical range of a certain spectrum falls, electronic systems of individual molecules are excited in the crystal, migrating along the crystal, but not associated with the transfer of electric charge and mass, that is, quasiparticles called excitons (8), which interfere with each other to form complex periodic structures of a smaller scale.

Excitons, interacting with phonons, make structural corrections to the formation of complex periodic interconnected structures, the number of which increases with each subsequent step of new excitation. This complicates the picture of the formation and fixation of dislocations.

In addition, collective processes in crystals, semiconductors, and other active media make appropriate corrections for the following types of interactions that are not reflected in the description and diagrams:

- spin-orbit interaction;
- spin-phonon interaction;
- electron-phonon interaction;
- photon-phonon interaction;
- photon-exciton interaction;
- magnon-phonon and quantum interactions of particles and quasiparticles.

These interactions make additional corrections to the structural complexity of the plastic defects formed with each subsequent step.

When a non-destructive breakdown (9) of a crystal by a giant laser pulse in the gap between the crystals, the active substance jumps into another aggregate state (plasma (12)) with the appearance of a shock wave (11), the epicenter of which is located near the interface between the two crystals. As we move away from the epicenter, the quasiparticle of excitation (fluctuations-phonons (10)) turns into phonons (13) (acoustic waves). These waves, in turn, interfere with complex periodic structures (14) (excitations located near dislocations and described by quasiparticles called defectons) formed in the crystal earlier in the action process.

With the subsequent step of pulsed laser radiation, even more complex structures (plastic deformations (14)) are formed in the crystal, carrying information about the physical properties of the active substance (16). These structures are holograms inside the crystal,

carrying complete information about the physical, chemical, biological and other properties of the active substance (16), which do not depend on the aggregate state of the substance (16). In addition, after the laser breakdown, with the appearance of a shock wave, the sum of collective processes and the formation of defects increase avalanche-like. A certain sum of collective interactions is formed, which is neither possible nor necessary to describe correctly in this presentation.

After the final processing step, the crystal is ready for use as a device for transmitting complete information about the properties of the active substance (material object) — (16).

- The process of reproducing and transmitting information about the physical properties of a material object (active substance) (figure 2).

- 1 — Incoherent natural or artificial radiation.
- 2 — Radiation of the IR range (including the spectrum of incoherent radiation).
- 3 — Visible range radiation (including incoherent radiation spectrum).
- 4 — UV radiation (including incoherent radiation).

- 5 — Plastic defects (dislocations) organized as a periodic structure ("diffraction grating") that carries information about the physical, chemical, biological and other properties of the active substance and quasiparticles excited by the light flow-phonons, excitons, polarons, polaritons, etc.

- 6 — Phonons formed as a result of the interaction of incoherent radiation with plastic defects and are quanta of information about the physical, chemical, biological and other properties of the active substance.

- 7 — Material object.

- 8 — Hypersonic waves generated by phonons (6).

- 9 — Crystals (for example, sapphire Al_2O_3 with Fe admixture; iron-tritium garnet $\text{Y}_3\text{Fe}_5\text{O}_{12}$; quartz SiO_2 ; lithium niobate LiNbO_3 , etc.).

An incoherent natural or artificial electromagnetic wave (light) (1) falls on the prepared crystal (9) (see item 1). This wave contains the spectral components of the IR (2), visible (3) and UV (4) ranges. Wave (1), interacting with plastic deformation (5) (dislocation), containing full information about the active substance (16) — in scheme 1, and in fact being a registered hologram in the crystal, creates secondary acoustic waves (8) (hypersound), which interact with a material object (7), inducing the necessary information to initiate the corresponding processes.

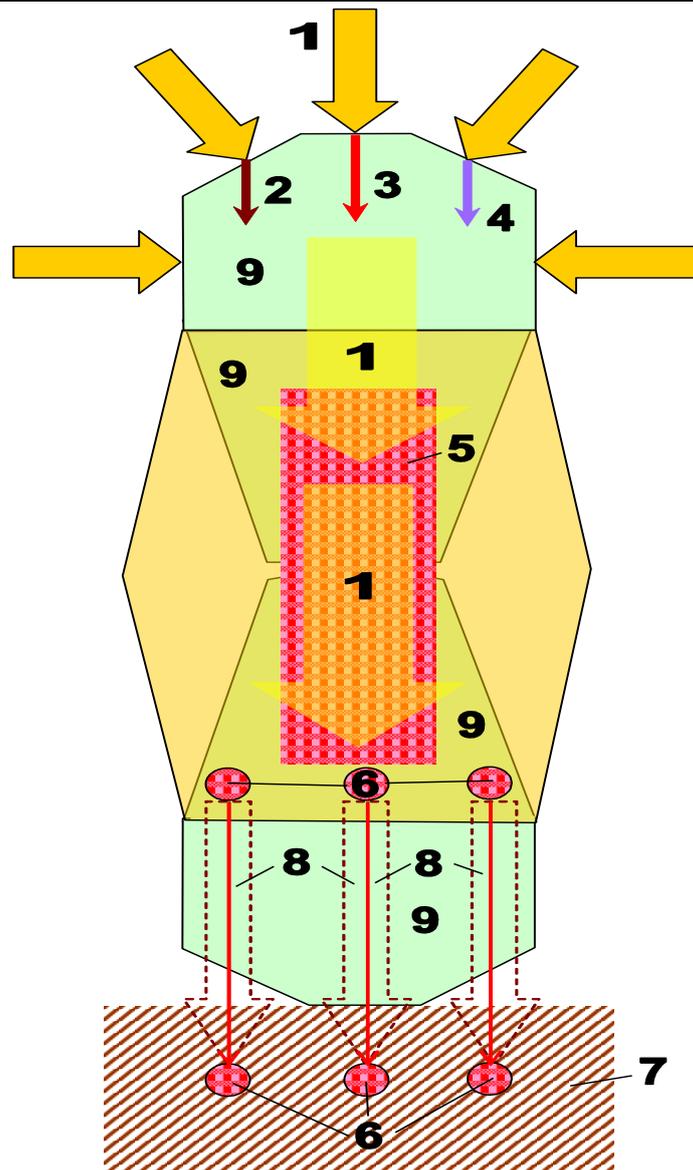


Figure 2. Playback technology and broadcasting information about the physical properties of the active substance

The mechanisms of reflection, scattering, absorption, and refraction excite significant cascades of collective interactions that occur in the crystal at the final processing step. At the moment of the phase transition of the active substance (16) – in the scheme (1) and the avalanche-like growth of collective processes, the sum of complex dislocations (5), when light rays diffraction on them, completely restores the wave front. This front is equal to the sum of the spectral composition patterns of all collective processes generated in the crystal at the moment of shock ionization of the active substance (16) in interaction with quasiparticles. These quasiparticles, in turn, were also the product of an exciting shock wave. They carry information about the physical, chemical, biological and other properties of the active substance (16) — in figure (1), in accordance with the spectral composition (16) – at the time of the phase transition.

Registration and restoration of the wave front is in full accordance with the principles of holography, with the only difference that the role of the reference wave is played by exciting radiation, and the object —

reflected, scattered and refracted waves of light rays in the crystal body. The role of the reference wave is also played by the spectrum of natural or artificial incoherent lighting modulated by collective processes in the crystal, thus forming a two-support mode of holographic technology, and the reference waves are also subject in this scheme.

Thus, the effect on a material object (7) occurs both by means of the restored wavefront of light waves of the corresponding range contained in the spectrum of natural and (or) artificial incident lighting (1) modulated by the spectrum of the final step of collective processes, and by means of secondary sound waves (8) modulating light waves.

Figuratively speaking, the crystal after processing, under the influence of light rays, reproduces a "musical composition with color music" on the theme set during the processing of the crystal and is perceived by organic semiconductors and biological crystals of living matter if the material object (7) is a biological object.

The technology can be applied to other active media, for example, semiconductors such as Si, Ge, as

well as compounds of the type — A_3B_5 — (In Sb), etc., as well as their various combinations. In these cases, the methods of processing and application, as well as the sum of the collective processes occurring in the materials in their interaction, will differ from those described above and presented in figures (1), (2).

The technology can be applied depending on the properties of the active substance interacting with the crystal, in all areas of practical activity related to the translation of information about physical, chemical, biological and other properties from one material object to another and is divided into 4 phases:

1. The phase of excitation of collective processes in the material (15) when the exciting radiation falls (1) is shown in figure (1).

2. The phase of excitation of collective processes in the active substance (16) at the laser breakdown (9), with the transition of the active substance to the plasma (shock ionization) — (12) and the appearance of a shock wave propagating into the crystal body — in figure (1).

3. The phase of transfer of information about properties of the active substance in the body of the crystal, due to the inclusion of phonon born shock wave (13), to the collective processes in the crystal and encoding this information in the structure of the plastic defects of crystal lattice — dislocations (14) — figure (1).

4. The phase of reading and translation of registered information in dislocations (5), in the form of hypersonic waves (8), to a material object (7), which occurs both by means of the restored wave front of light waves of the corresponding range contained in the spectrum of natural and (or) artificial incident lighting (1) modulated by the spectrum of the final step of collective processes, and by means of secondary sound waves (8) modulating light waves — in figure (2).

II. GENERAL SCHEME OF PHYSIOTHERAPEUTIC EFFECTS

A generalized scheme of physiotherapeutic effects based on new physical principles of action is shown in figure (3). Here the procedure for the object of influence (1) (patient) begins with the fact that the bone marrow (3) is taken from the bone (2). Further, a sufficient amount of this sample (4) is placed in the active nutrient medium (5), where after adding an

epidermal growth factor (EGF) and glial cell culture (6), the required regeneration stage will be formed, as a result of which, for the differentiation of oligodendrocytes, it is necessary that some of their mRNAs undergo a special modification known as m6A – methylation (that is, the addition of a methyl group to the sixth nitrogen atom of adenosine, which is part of the mRNA). This modification is necessary for proper splicing of mRNA encoding the protein neurofascin-155 – an important factor in the development of neuroglia cells. Further dynamics of the process continues until the desired stage is reached, namely, post-transcriptional modifications of mRNA in cells. And this is the covalent addition of a methyl group (-CH₃) to the nitrogen atom N₆ as part of the nitrogenous base of adenosine, known as m6A-methylation. Then the signal is registered using a multielectrode system (for example Multielectrode Arrays /MEA/ [5, 6]) in the developing dynamics of the process. Given system processes this signal in the form of a certain algorithm (8), through the amplifying equipment (7), for some time. Then, the received signal is sent to the modulator (9), which is irradiating the object with ultra short pulses (about 1 NS) of ultra-wideband (bandwidth of several gigahertz) electromagnetic radiation of the microwave range through the emitter (10). Emitter will generate a stimulating effect (11) [10-12 - figure (4)]. Feature of the new physical principle would be a favorable force conditions simulating natural geomagnetic background of the planet in the form of Schumann resonances [7 – 9] for exposure to electromagnetic field (12) produced in the affected area (16). A soft x-ray emitter (13) is required for creating a field of Louis de Broglie waves, as a source of bosons that are the carrier of useful information. The emitter (16) creates an electromagnetic field (17) with the frequency of Schumann resonances [8] in the area of influence (14) modeled by the device (15) [10 – 12 – figure (4)]. The universality of this exposure scheme is provided by the fact that the entire existing range of effects (from broadband microwave and EHF electromagnetic radiation to mechanical effects in the acoustic range) can be used for information transmission of the effect stimulating reparative treatment.

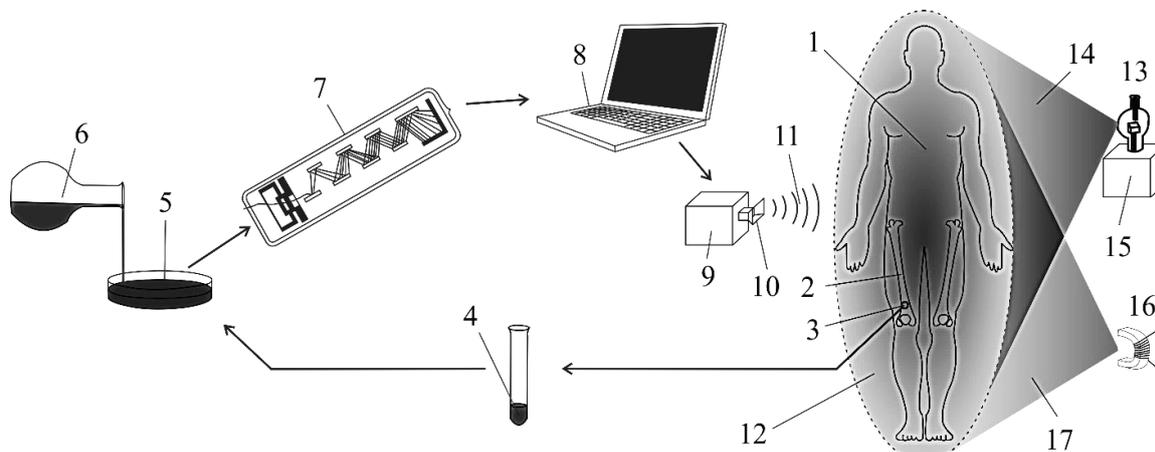


Figure 3. General scheme of stimulation based on new physical principles of action

III. OPTION FOR IMPLEMENTING OF PHYSIOTHERAPEUTIC EFFECTS

The principle of organizing physiotherapeutic influence, in the variant shown in figure (5), is implemented as follows. The object of influence (1) (in this case, the patient) is placed inside a certain device. The device is necessary to create a favorable electromagnetic environment that simulates the natural geomagnetic background of the planet in the form of a recreated permanent electromagnetic field of Schumann resonances (3) around the object of influence (1). It is necessary to create a favorable environment for decoherence inside the electromagnetic field simulating Schumann resonances, when information component is teleporting

to the object of influence (1). The role of this component is played by soft x-ray radiation (4), which is a carrier of Louis de Broglie waves [13-16], as a source of bosons. They are a component of a natural variant of the flow of unlikely events in the forced mode, which assumes a statistical quantum leap of events of low probability to events that are statistically more reliable [17,18]. The x-ray emitter (5) is controlled by a device (6). The stimulating effect (7) is carried out by means of an electromagnetic field radiated by a broadband emitter (8) [10-12 - figure (4)], whose operation is controlled by a modulator (9). Modulator puts into the radiation an information component obtained according to the scheme described earlier.

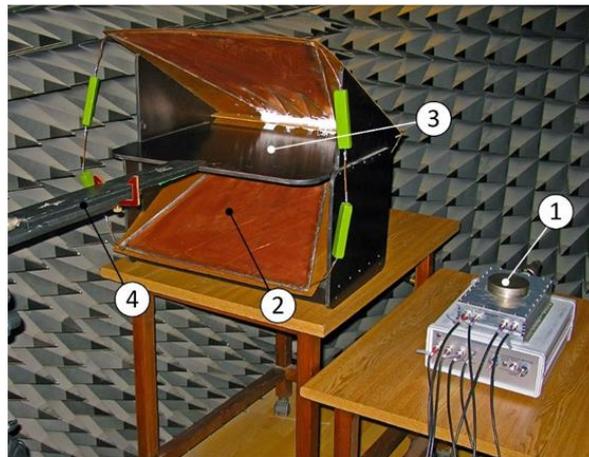


Figure 4. Generator of ultra-short-pulse (of the order of 1 NS) ultra-wide-band (band width of the order of several gigahertz) microwave electromagnetic radiation - according to works [10-12]

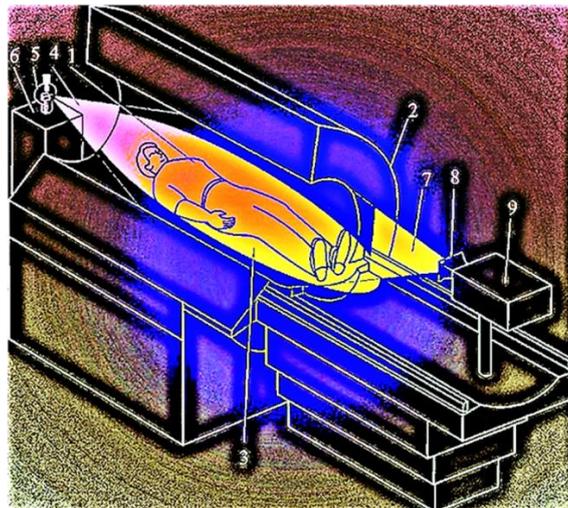


Figure 5. A variant of implementing a physiotherapeutic effect based on new physical principles of action

Portal for teleportation of information can be any receptor of the body or some combination of them. Such a portal for teleporting quantum information could well be a visual analyzer. This is clear and obvious in the example below.

It turns out that such a familiar phenomenon as navigation in birds is described by the laws of quantum mechanics. The ability to keep unpaired photoreceptor electrons entangled for a long time leads to the fact that

birds can see the magnetic field lines. Most likely, they are not the only ones. Perhaps the internal compass of many insects, migrating fish, and even some mammals works on the same principle [19]. The bizarre eye protein Cry4 belongs to a class of proteins called cryptochromes — these are photoreceptors sensitive to blue light that are found in both plants and animals. They also play a key role in the regulation of circadian rhythms — cyclic fluctuations in the intensity of

various biological processes associated with the change of day and night. We studied the vision of birds such as the Robin and Zebra Finch, and obtained data indicating that cryptochromes in the eyes of birds are responsible for the ability to navigate in flight by detecting magnetic fields. This process is called magnetoreception.

It is known that birds can sense magnetic fields if light waves of a certain length are available. In particular, studies have shown that avian magnetoreception seems to depend on blue light. This fact confirms that for birds, the mechanism for detecting magnetic lines is visual and based on cryptochromes, which can detect fields due to quantum coherence. Two teams of biologists set to work to find these cryptochromes. Researchers from Lund University in Sweden studied Zebra finches. Gene expression of three cryptochromes Cry1, Cry2, and Cry4, was measured in the finches' brains, muscles, and eyes. The hypothesis was that cryptochromes

associated with magnetoreception should maintain a constant perception of the magnetic field during the day. It was found that the circadian rhythms of cryptochrome Cry1 and Cry2 fluctuated throughout the day, while Cry4 was active constantly, making it the most likely candidate responsible for magnetoreception. As it turns out, cryptochrome Cry 4 clusters in an area of the retina that receives a lot of light, which makes sense for light-dependent magnetoreception [20,21]. The European Robin increases the expression of Cry 4 during the migration season, compared to non-migrating birds.

So what exactly does a bird see during flight when it adjusts its course to the earth's magnetic field? According to researchers in theoretical and computational Biophysics at the University of Illinois at Urbana-Champaign, the Cry4 protein automatically imposes a "filter" of magnetic lines over the bird's field of vision — as shown in the figure (6).

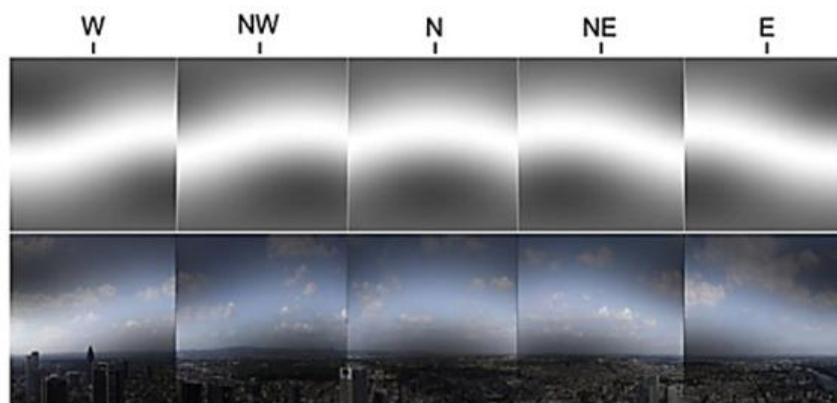


Figure 6. Illustration: Theoretical and Computational Biophysics/UofI

Thus, it is possible to use only acoustic - optical stimulation in the range of audible acoustic and visible light waves based on the diagrams in figures (3) and (5).

It is not difficult to change the nature of the sources of useful signals accordingly. Namely, using conventional acoustic systems and a low-intensity broadband white laser - instead of designations 9, 10, 11, 12, 13, 14, 15, 16, 17 – in figure (3) and 5, 6, 7, 8, 9 – in figure (5). These sources can be replaced by geophysical backgrounds of Schumann resonances and soft x-rays of natural origin. Moreover, the scheme can be simplified to use a conventional incoherent radiation source instead of a laser source. The sources must repeat the rhythm and spectrum of the useful signal pattern. But this will be a less forced and effective mode of influence.

Luc Montagnier, the 2008 Nobel prize winner who previously discovered that HIV causes AIDS, made a statement. From his point of view, there is every reason to believe that DNA is able to send "ghost" electromagnetic imprints of itself to distant cells and fluids. And enzymes can mistake these prints for real DNA and start copying them to reproduce the original. In fact, this is quantum teleportation of DNA, reported in [22, 23].

The mathematical apparatus for the above topic is presented in [24].

To implement quantum teleportation of useful information, which initiates processes in the material environment with which this information is entangled, it is necessary to have two participants in this game: microscopic and macroscopic, as well as some mesoscopic intermediary. A microscopic player is the sum of non-local fields of some configuration. A macroscopic player is a material environment that represents a certain matrix of biochemical and biophysical processes. And the mesoscopic intermediary is a tracing paper of non-local interferences that form a holographic "cast" of the modulated classical process or their sum. The method is published as a Preprint in [25].

CONCLUSION

In preparation for the above-described physical therapy, information about such effects can be prepared and stored in crystals in the form of stable deformations of the crystal lattice. Information is stored in crystals as a multi - and quasi - partial diffraction grating of "preserved" entangled states, which then reproduces the holographic picture in the form of an information matrix of the modeled process at the impact stage. The modeled process occurs as follows:

- epidermal growth factor and glial cell cultures form the required stage of regeneration, which results in the differentiation of oligodendrocytes;

- some of their mRNAs undergo a special modification known as m⁶A-methylation (that is, the addition of a methyl group to the sixth nitrogen atom of adenosine, which is part of the mRNA);

- this modification is necessary for proper splicing of mRNA encoding the protein neurofascin-155 – an important factor in the development of neuroglia cells;
- further dynamics of the process continues until the required stage is reached, namely, post-transcriptional modifications of mRNA in cells;

- this is the covalent addition of a methyl group (-CH₃) to the nitrogen atom N₆ in the nitrogenous base of adenosine, known as m⁶A-methylation.

Then, apparently, the process of remyelination of nerve fibers will be initiated, which, under favorable circumstances, will lead to a possible remission of one or another degree of duration and persistence.

[1] Gavrillov V. Y., Antipova T. A., Vlasov Y. V., Ardatov S. V. and Ardatova A. S., TELEPORTATION OF SARS-COV-2 INFORMATION AND QUANTUM ENTANGLEMENT OF THE COVID-19 PANDEMIC PROCESS (SOME PHYSICAL MEANINGS), PREPRINTS.RU: 3112047, <https://doi.org/10.24108/preprints-3112047> (2020).

[2] Antipova T. A., Ardatov S. V., Ardatova A. S., Vlasov Ya. V. and Gavrillov V. Yu., Review of some interdisciplinary approaches to the study of quantum information teleportation in macro- and ecosystems of the biogeosphere, Modern scientific research and innovation, **3**, 91665, <http://web.snauka.ru/issues/2020/03/91665> (2020).

[3] Gavrillov V. Yu., Neganov V. A., Osipov O. V., Pryanikov I. V. and Savransky V. V., Technology for recording and broadcasting information about the physical properties of material objects, based on a special method for processing crystals, semiconductors, etc. active media, Certificate of registration and Deposit of the work - the object of copyright (related) rights №300. Registered in the Register for No. 1100300 of 07.02.2007 by Law firm Gorodissky and Partners (2007).

[4] Ardatov S. V., Ardatova A. S., Vlasov Ya. V., Gavrillov V. Yu. and Shchankina A. V., Concept of creating functional 4 D holographic loci of a new type of non-volatile memory - as a carrier and storage of various modes of preserved entangled quantum states, Modern scientific research and innovation, **5**, 89228, <http://web.snauka.ru/issues/2019/05/89228> (2019).

[5] Boven K-H, Fejtł M, Möller A, Nisch W, Stett A. On Micro-Electrode Array Revival. In: Baudry M, Taketani M, eds. Advances in Network Electrophysiology Using Multi-Electrode Arrays. New York: Springer Press; 24-37 (2006).

[6] Mukhina I. V., Physiology and Biophysics of excitable systems, Lobachevsky state University of Nizhny Novgorod, Nizhny Novgorod, <http://www.unn.ru/pages/issues/aids/2007/31.pdf> (2007).

[7] Kristian Schlegel, Martin Füllekrug, Weltweite Ortung von Blitzen: 50 Jahre Schumann-Resonanzen, Physik in unserer Zeit, **33**(6), 256 (2002).

[8] Schumann, W. O., On the radiationless natural vibrations of a conducting sphere surrounded by a layer of air and an ionosphere shell, **7a**, 149 (1952).

[9] B. P. Besser, Synopsis of the historical development of Schumann resonances, Radio Science, **42**, RS2S02, 20 (2007).

[10] Sokolov A. A., Sakharov K. Yu, Mikheev O. V., Turkin, V. A. and Aleshko A.I., Proceedings of the Third International Conference on Ultrawideband and Ultrashort Impulse Signals, Sevastopol, 203 (2006).

[11] Device for input of high-voltage voltage pulses into the TEM-horn antenna: Patent 2185012 Russian Federation. No. 2001111370/09; application no. 26.04.01; publ. 10.07.02, bul. no. 19 - 5 p.

[12] Sakharov K. Yu., Turkin V. A., Mikheev O. V., Dobrotvorskyy M. I. and Sukhov A. V., Picosecond pulsed electric field strength measuring transducer, Measurement Techniques, **2**, 201 (2014).

[13] Shirokov Yu. M., Yudin N. P. Nuclear physics, Moscow: Nauka, 17-18 (1972).

[14] Feynman R., Leighton R., Sands M., Feynman lectures on physics, **3-4**, 221-222, 412 (1976).

[15] Louis de Broglie, The Reinterpretation of Wave Mechanics, Foundations of Physics, **1**, 1 (1970).

[16] Martinson L. K., Smirnov E. V., Experimental confirmation of the de Broglie hypothesis, Quantum physics, Moscow: Bauman Moscow state technical University, **5**, 2.2, 496 (2004).

[17] Baretto Lemos G., Borish V., Cole G. D., Ramelow S., Lapkiewicz R. and Zeilinger A., Quantum imaging with undetected photons, Nature, **512**, 409 (2014).

[18] Zakharov A. V., Vlasov Ya. V., Poverennova I. E., Khivintseva E. V. and Antipov O. I., Features of postural disorders in patients with multiple sclerosis, Journal of neurology and psychiatry named after C. C. Korsakov, **2**, 55 (2014).

[19] Manuela Zapka, Dominik Heyers, Christine M. Hein, Svenja Engels, Nils-Lasse Schneider, Jörg Hans, Simon Weiler, David Dreyer, Dmitry Kishkinev, J. Martin Wild and Henrik Mouritsen, Visual but not trigeminal mediation of magnetic compass information in a migratory bird, Nature, **461**, 1274 (2009).

[20] Atticus Pinzon-Rodriguez, Staffan Bensch and Rachel Muheim, Expression patterns of cryptochrome genes in avian retina suggest involvement of Cry4 in light-dependent magnetoreception, Journal of the Royal Society Interface, **15**, 0058, <https://doi.org/10.1098/rsif.2018.0058> (2018).

[21] Anja Günther, Angelika Einwich, Emil Sjulstok, Karl-Wilhelm Koch, Ilija A. Solov'yov and Henrik Mouritsen, Double-Cone Localization and Seasonal Expression Pattern Suggest a Role in Magnetoreception for European Robin Cryptochrome 4, Current Biology, **28**, 2017.12.003, <https://doi.org/10.1016/j.cub.2017.12.003> (2018).

[22] Coghlan A., Scorn over claim of teleported DNA, *NewScientist*, LIFE, <https://www.newscientist.com/article/mg20927952-900-scorn-over-claim-of-teleported-dna/?ignored=irrelevant> (2011).

[23] Montagnier L., Aïssa J., Ferris S. et al., Electromagnetic signals are produced by aqueous nanostructures derived from bacterial DNA sequences, *Interdiscip Sci Comput Life Sci*, **1**, 81, <https://doi.org/10.1007/s12539-009-0036-7> (2009).

[24] Bo-Sture K Skagerstam, Karl-Erik Eriksson and Per K Rekdal, Causality in quantum field theory with classical sources, *Journal of Physics Communications*, **8**, 082001, 10.1088/2399-6528/ab3c1c (2019).

[25] Vlasov Y. V., Ardatov S. V., Antipova T. A., Sineok E. V., Ardatova A. S. and Gavrilov V. Y., Preparation of entangled states for performing convalescence of nosological forms (on example of multiple sclerosis), *PREPRINTS.RU*: 3112071, <https://doi.org/10.24108/preprints-3112071> (2020).

UDC 159.9:616.89-071

DIAGNOSTIC TEST FOR CHILDREN'S PSYCHOPATHICITY PCL-MYV

Israel (Vladimir Modestovich) Datskovsky,
Ph.D

Cabinet of Clinical Psychology and Pathopsychology
Rival str. #3, apt. 2, Beit Shemesh 9908188, State of Israel

Abstract. The introduction notes the difficulties and limitations in the diagnosis of child psychopathy, especially as part of an expert approach that requires a thorough study of the patient's entire previous life. The second part of the article is devoted to the available tests, questionnaires and diagnostic scales and the difficulties of their use for children are noted. The third part of the article is devoted to neuropsychological methods for diagnosing psychiatry in children and the difference in the perception of emotionally charged samples in healthy and psychopathic children is noted. The fourth part considers the world's most famous tool for diagnosing psychopathy in children as part of an expert approach – a List of psychopathic traits – a youthful version of R. Hare and K. Kiehl and highlights its shortcomings when it is extended to younger, pre-adolescent age of the subjects. The fifth part is devoted to the PCL-MYV test, which is proposed for the diagnosis of psychopathy in children before any physical signs of puberty appear (6-12 years) as part of an expert approach and the rules for working with it. This tool, as well as the Youthful version of the Psychopathy Checklist, is designed to be completed by specially trained professionals.

Keywords: psychopathy, list of psychopathic traits, phenomenological approach, expert approach.

1. Introduction

The field of child psychopathies, despite a sufficient number of printed sources on this topic, is still a relatively poorly researched area both as part of child psychiatry and as part of psychiatry of borderline states. In our opinion, this situation is primarily associated with the difficulty of distinguishing states related to the field of psychopathies of childhood from other mental states, especially taking into account the fact that, as shown in our previous article (Datskovsky I., 2019 [B]), the very concept of psychopathy is ambiguous and there are two significantly different approaches to diagnosis, operating with the same name for the condition – psychopathy.

In addition, it is quite reasonable that in childhood a diagnosis of psychopathy is not made at all due to the inseparability of congenital (nuclear) psychopathy, early brain injury (trauma, intoxication) and the results of the psycho-traumatic (psychopathic?) influence of the environment and upbringing at an early age, although a number of cases described in the literature clearly indicate the diagnosis. This is due to the uncertainty of the correctness of such a serious diagnosis, which lays a heavy imprint on a person's entire life, since there are many cases of becoming a normative person growing out of a child who manifested many symptoms of psychopathy in childhood. Even the compromise diagnosis of F60 in

the ICD-10 ("Specific personality disorders") is generally not given to children, even as comorbid ones, and the diagnosis of accentuations of character accepted in the Russian literature (A.E. Lichko, 2016), by definition, describes preclinical conditions. That is, on the one hand, there is a well-founded fear of overdiagnosis of psychopathy. On the other hand, "as the signs of social distress become more persistent, we no longer have the luxury of ignoring psychopathy in certain children." (R. Hare, 2007).

In this text, we will continue to call psychopathies by psychopathies (from ancient Greek *ψυχή* (psychi) "spirit; soul; consciousness; character" + from Greek *πάθος* (pathos) "suffering, pain, illness" – a suffering soul, however, it is not noticed that psychopaths noticeably suffer from their psychopathy, from their temperament, but the environment of psychopaths suffers from their psychopathy very significantly), although in the modern trend of replacing medical terms that have penetrated into general speech and carry a negative, sometimes offensive connotation in it, this term is being replaced by more neutral "personality disorder", (to be distinguished from personality changes), although there is no tendency to return to the old, rather accurate terms "moral dullness", "emotional underdevelopment".

The main objective of this article is the development of a test for the diagnosis of child

psychopathicity as part of an expert approach to the diagnosis of psychopathies (Datskovsky I., 2019 [B]) in the age group of the school stage of psychophysical development from 6 to 12 years old for taking appropriate adequate measures of both socio-pedagogical and medical spectra.

2. Psychological tests, questionnaires, scales

Since the end of the 19th century, various numerous tests and questionnaires, in addition to differently structured (clinical) interviews, are one of the main methods of studying the psyche. These methods have proven themselves very well, the number of tests is multiplying exponentially, the Internet has led to an explosive increase in the number of such tests, however, not all of them are sufficiently well tested (or not tested at all) and adapted to the tasks they are designed to solve and to the target population group, for which they should especially show the properties of validity and reliability. There are texts both universal, designed to solve many problems of general and clinical psychology, and more specific tests that solve the problems of specific differential diagnosis. Simple and short screening tests and questionnaires have the least specificity.

Nevertheless, in the area under consideration (child psychopathy), there are numerous sensitive points in comparison with the ability to make or refute other diagnoses. "Assessing and predicting which children will become psychopaths is a difficult task. Some consider that scientists should not even make such attempts, because if a similar diagnosis is made to children, it can become a stigma for them for life. Moreover, such stigmatization can be a self-fulfilling prophecy. According to others, if parents are told that their child is a psychopath, this may further alienate them from their child... Scientists working in this field go to all sorts of tricks, just not to use the term *psychopathy* when discussing children. Most often they speak of traits of *callousness and indifference*." (K. Kiehl, 2015).

Varieties of questionnaires are used to solve this problem. Among the universal tests, the first are questionnaires TAT (Thematic Apperception Test – a projective psychodiagnostic technique developed in the 1930s. The purpose of this technique was to study the driving forces of the personality – internal conflicts, drives, interests and motives. After the Second World War, the test became widely used by psychoanalysts and clinicians to work with disorders in the emotional sphere of patients) and MMPI (Minnesota Multiphasic Personality Inventory – a personality questionnaire developed in the late 30s – early 40s at the University of Minnesota, the most studied and one of the most popular psychodiagnostic techniques, designed to study individual characteristics and mental states of a person. MMPI is widely used in clinical practice. This technique was based on a quantitative comparison of the responses of representatives of the normative group with typical responses of patients, whose picture of clinical disorders clearly demonstrated the predominance of one or another syndromic complex: hypochondria, depression, hysteria, psychopathy, psychasthenia, paranoia, schizophrenia, hypomania.

There are Russian-language adaptations of MMPI: MMPI technique modified by F.B. Berezin et al. and SMIL (standard methodology for the study of personality) modified by L.N. Sobchik).

However, universal questionnaires are fundamentally nonspecific, therefore, for a more accurate diagnosis of child psychopathy, more specific questionnaires have been developed and continue to be developed and tested. One of the widespread questionnaires in Russia for the diagnosis of character accentuations and psychopathies in adolescence is the Pathocharacterological Diagnostic Questionnaire for adolescents, PDQ, developed by A.E. Lichko (Ivanov N.Ya., Lichko A.E., 1995).

In Canada and the United States, more recently, a notable range of questionnaires that are specific to assessing the traits of callousness and indifference in children have been developed.

The first and most common self-report tool for assessing callousness and indifference traits in children is the Childhood Psychopathy Scale (CPS), developed by Dr. Don Lyman of Purdue University. It includes questions about the children's relationship with others, about what is important to them, whether they are very angry, etc. The University of New Orleans has developed several scales for assessing the traits of callousness and indifference for parents and teachers, including the Antisocial Process Screening Device (APSD). In parallel, Dr. Frick developed the Inventory of Callous-Unemotional Traits (ICU) with options for parents, teachers and the child (there are also options for preschool and primary school children). Hare's Psychopathy Checklist: Youth Version (PCL: YV); Youthful Psychopathic Traits Inventory (YPI); Child Problematic Traits Inventory (CPTI) may also be named.

Research has even shown that traits of callousness and indifference in boys aged 7-12 predict their psychopathic score at age 19 (for example, Burke J. D., Loeber R. & Lahey B. B. Adolescent Conduct Disorder and Interpersonal Callousness as Predictors of Psychopathy in Young Adults. [Research Support, N.I.H., Extramural]. Journal of Clinical Child Adolescent Psychology, no. 36 (3), 2007, pp. 334–346 and also Lynam D. R., Caspi A., Moffit T. E., Loeber R. & Stouthamer-Loeber M. Longitudinal Evidence that Psychopathy Scores in Early Adolescence Predict Adult Psychopathy. Journal of Abnormal Psychology, no. 116 (1), 2007, pp. 155–165).

However, such questionnaires have their drawbacks and limitations. Moreover, some drawbacks are exacerbated when trying to assess the features of callousness and indifference in young children. Thus, many children at risk, whose callousness and indifferent traits we want to assess, are simply unable to read or listen to questions and answer them on the CPS, MMPI or other questionnaires.

Another disadvantage of self-reporting in psychology is that it requires patient cooperation. It is very easy to spoil the results if the patient lies (consciously or unconsciously), answers questions at random, or simply refuses to fill in the questionnaires.

This greatly limits the usefulness of questionnaires when the patient is hostile or unable to cooperate with the psychologist. In addition, in the field of research on psychopathies, especially in childhood and adolescence, a negative feature of conventional psychological approaches has been revealed. It lies in the fact that, on the one hand, tests and questionnaires filled in by children (if the children are not angry, agree to cooperate and know how to read or at least listen and answer clearly), questionnaires filled in by parents (if the parents are adequate in their assessments and do not specifically give false answers, for example, when their child is threatened with isolation in special pedagogical systems) about the same children and, on the other hand, a professional expert assessment of objective materials and independent assessments about this child and a focused clinical interview to fill in the Expert Youth Version of the Psychopathy Checklist (PCL: YV – R. Hare, 2007) give very different assessments of the psychopathic properties of the child. Finally, and perhaps the most important flaw in self-report questionnaires for assessing callousness and indifference is that children with these traits may simply not be able to talk about their emotional world in detail. They do not understand themselves, and this can prevent the researcher from assessing these traits in them. Therefore, the main emphasis in the diagnosis of psychopathy or psychopathic temperament has to be done precisely on the expert assessment of a specialist.

3. Neuropsychological methods

"In addition to using tests, questionnaires, scales, and other tools to measure callousness and indifference, psychologists and neuropsychologists have developed tasks or games to study the brain systems associated with these symptoms. One such task or game used by researchers is a task of making *an emotional lexical decision*. It actually kind of reminds of spelling dictation. Chains of letters quickly appear on the computer screen, and the subject must decide whether the letters constitute a real word, or it is gibberish or a word written with a mistake. When letters form an emotional word ("hate," "kill," "die"), people react faster than to a neutral word ("chair", "table", "hand"). Emotional word processing employs a brain system that makes us recognize them very quickly. Today, it has been fairly reliably found that, unlike ordinary people, psychopaths do not respond to emotional words faster than neutral ones. This proved that psychopaths "know the words, but not the melody." In other words, psychopaths know the meaning of the words "love", "hate", "murder", but they *do not feel* the affective influence conveyed by these words." (K. Kiehl, 2015).

After these discoveries, studies have shown that children and adolescents with traits of callousness and indifference are worse at solving emotional vocabulary and other similar tasks. The use of many studies and tasks developed in recent years suggests that children and adolescents with callousness and indifference (as well as adults with psychopathy in terms of an expert approach) are characterized by deficiencies in the quality and speed of processing emotional stimuli.

However, the methods of neuropsychology, just like traditional test methods, provide researchers and

doctors with only indirect tools for assessing the psychopathic characteristics of children and adolescents and, when applied, require the active participation of the subjects.

4. Expert approach

In section 3 "Phenomenological approach" of the article (Datskovsky I., 2019 [B]), we have already indicated that the issue of child psychopathy was already raised by P.B. Gannushkin (1933). However, it remained (and in many respects remains today) within the framework of an approach based on clinical-descriptive criteria, which remain both subjective and eclectic. Today, the presence of child psychopathy (and early accentuations of character) is widely recognized, the corresponding chapters (within the framework of the phenomenological approach) are included in many child psychiatry books (V.V. Kovalev (1979), I.V. Makarov (2019), B.V. Voronkov (2017) and many others), however, we believe that the real breakthrough in the diagnosis of child psychopathy is precisely the expert approach (Datskovsky I., 2019 [B]) and the objective diagnostic methods that have been further brought to clinical use, especially those that do not require the active participation of the child under study. At the same time, other characterological deviations in the state and thinking of a child (and an adult), considered in the framework of the phenomenological approach to psychopathies, are not denied in any way. Consider the expert approach to the diagnosis of child psychopathy proposed by Dr. K. Kiehl (2015) and propose a modified tool that is more suitable for younger children (6-12 years old).

K. Kiehl (2015) provides a corresponding Psychopathy Checklist for children and adolescents, which is a modification of R. Hare's Psychopathy Checklist (2007) for adults. The traits and behavior inherent in this disorder (child psychopathy) are assessed by an expert (trained specifically for such an assessment of the data by a specialist) using this checklist based on collecting as much information as possible about the child's previous life (anamnesis vitae). Just as when using the adult version of the questionnaire, for each item the expert gives the child a score from the series 0, 1, 2, and children who scored 30 or more points are considered psychopathic.

"List of Psychopathic Traits for Children and Adolescents:

- 1) Introducing oneself in society (external)
- 2) Exaggerated sense of self-esteem (internal)
- 3) Desire for arousal
- 4) Pathological deceit
- 5) Manipulation for personal gain
- 6) Lack of remorse
- 7) Affective flattening
- 8) Callousness/lack of empathy
- 9) *Parasitic orientation*
- 10) Anger
- 11) **Impersonal sexual relations**
- 12) Early behavioral problems
- 13) Lack of goals
- 14) Impulsivity
- 15) Irresponsibility
- 16) Failure to take responsibility

17) Unstable interpersonal relationships

18) ***Major infractions***

19) ***Serious violations of the conditions of release***

20) ***Variety of criminal activities***".

Since in this paper we are discussing children between the ages of 6 and 12, a number of features cited by Dr. K. Kiehl is irrelevant or requires a change in the wording for this age group (and often for a group of older children). We have marked these characteristics in Dr. K. Kiehl's Checklist in ***underlined italics***. However, among these signs there are two, which, although infrequently, appear in the examined children and very clearly (obligatory) indicate the presence of psychopathy. We marked these features in ***highlighted underlined italics***, and in the proposed test, we highlighted them in a separate group of features (table 2).

5. Psychopathy Checklist – Modified Youth Version (PCL-MYV)

Often, the problems of psychopathic development of the child's character become noticeable to parents and educators, as a rule, from 3-4 years old (and sometimes even earlier), but it is obvious that it is impossible to diagnose such a difficult diagnosis based on only recently noticed problems. And a child of primary school age (from 6-7 years old) is already a fairly mature personality with clearly distinguishable character traits that can already be diagnostically analyzed, although the actual diagnosis of psychopathy cannot be made even before any physical signs of puberty appear, or even until late adolescence (for avoidance of labeling, when the diagnosis can greatly interfere with the child's socialization and thereby turn out to be a self-fulfilling prophecy). However, even the diagnosis "established" by the points scored in the pre-pubertal age should be recorded only in documents that are closed from outsiders (except for a professional-specialist) and explained to parents in Aesopian language, with euphemisms in the form of recommendations for correctional, educational and, if this is indicated, for medical measures.

For the needs of early diagnosis of child psychopathy (in terms of an expert approach), we have clarified the Psychopathy Checklist for children and adolescents (in fact, by proposing PCL-MYV – Psychopathy Checklist – Modified Youth Version), removing irrelevant items and adding items that are absent in the original Checklist, but important from our point of view, or changing the wording of some items from the Checklist of R. Hare – K. Kiehl.

In addition, we have made the scoring a little more difficult. Although this list is in no way a test or a questionnaire for a small patient and it is also not a questionnaire for the environment of the child being checked (parents, educators, teachers, neighbors, etc.), but is a professional tool of a trained professional psychologist or psychiatrist, nevertheless, if you use the method of R. Hare – K. Kiehl, to give a score of 2 points, you need to have a very vivid picture of this deviation, which is often very difficult to collect, given the limited materials on the characteristics of the behavior of a small patient, and a score of 1 point is often does not give a sufficiently adequate

characterization of the child. Therefore, we mitigated the difficulty of assessing a particular characteristic of a child by introducing not a three-position (0-1-2), but a four-position assessment (0 (absent) – 1 (present in a mild form) – 2 (present in a highly developed form) – 3 (striking feature of the child's personality)). We understand that in most cases it will not be easy to give a score of 3 for most characteristics (as well as a score of 2 in the R. Hare – K. Kiehl approach), therefore, we left the main scoring at the level of the third column (the characteristic is in a very developed form), giving the relatively rare characteristics that received a point in the fourth column to slightly increase the total score and thereby slightly strengthening the validity of the psychopathic diagnosis.

It was also noted that some characteristics from the modified children's list of psychic traits are almost always found in children with psychopathic problems and characterize their personality much more clearly than other characteristics. Moreover, such characteristics are absent or poorly expressed in non-psychopathic children. To account for this phenomenon, we introduced the concept of important characteristics (some semblance of obligate symptoms in psychiatry) and ordinary characteristics (some semblance of facultative symptoms in psychiatry), provided that important characteristics received a double number of points (scale 0-2-4-6).

Moreover, there is a third group of characteristics, which includes only two characteristics (in a modified formulation), marked by us in the list of K. Kiehl in ***highlighted underlined italics***. These characteristics (highlighted in Table 2) receive points in the same way as the characteristics in Table 1, but these characteristics were NOT entirely included in the total score when setting the boundary values of points (like the points in the fourth column), but were included in the score points given to this child. This leads to the fact that scores other than zero in this table noticeably shift the result towards the diagnosis of psychopathy.

We do not consider parabolic or more complex scales of increasing points within one PCL-MYV item (for example, instead of a scale of 0-1-2-3 points, introducing a scale of 0-1-3-6 points with an increase in the difference in points when moving up the scale), as to substantiate such an approach, we need a fairly large statistical sample WITH TRACED CATAMNESIS at least up to the upper limit of adolescence (18 years), which we do not have.

We also refrained from highlighting some characteristics that do not strongly affect the child's image into the fourth, one-half, less significant scale with score values of 0-0.5 – 1-1.5 in order not to multiply entities (Occam's razor) without a sufficiently long and massive statistical study on numerous children with psychopathic problems.

Since the collection of full-fledged, complete information about a fairly short life of a young patient is very difficult, we tried to compensate for this problem with more detailed, consisting of a larger number of characteristics than in the original. This also mitigates the influence of each given score on the final diagnostic result.

We shall note that adult psychopaths usually have a history of late (after the age of 5 years) enuresis. However, it is impossible at this stage of diagnosis to accept this symptom as a predictor of psychopathy – according to modern concepts, enuresis can be caused by abnormalities in one of the four neural pathways, but it seems that only one of them, passing through the amygdala, to some extent indicates psychopathic development. Apparently, those suffering from enuresis due to the pathology or underdevelopment of other neural pathways do not become psychopaths, and they often even have late enuresis spontaneously or with some treatment, although later than most children.

We also note that in psychopathy, deviating personality traits should be total, that is, be manifested everywhere and always, in any situation and circumstances. "They should be present almost everywhere – at home, at work, at school, in communication with family, friends and neighbors." (K. Kiehl, 2015). "A teenager with psychopathy

discovers his/her type of character in the family and school, with peers and with elders, in school and on vacation, in work and play, in the ordinary and familiar, as well as in the most emergency situations." (A.E. Lichko, 2016). But the opposite is also true: "A tyrant at home and an exemplary student at school, a quiet child under harsh authority and an unbridled bully in an atmosphere of connivance, a fugitive from a home where an oppressive atmosphere reigns or a family is torn apart by contradictions, who can get along well in a good boarding school – they all should not be counted to psychopaths, even if adolescence passes under the sign of impaired adaptation." (A.E. Lichko, 2016).

The test was constructed according to a scheme similar to the scheme of the Modified Detailed Infantilism Test – DIT-M, previously published (Datskovsky I., 2019 [A]).

The proposed revised list of PCL-MYV (Psychopathy Checklist – Modified Youth Version) consists of three tables (scales) and looks as follows:

1. Important characteristics

Item No.	Characteristic	Absent 0 points	Present in mild form 2 points	Present in a highly developed form 4 points	Striking personality trait of a child 6 points
1	Early behavioral problems				
2	Affective flattening				
3	Lack of empathy				
4	Lack of remorse				
5	Callousness				
6	Indifference				
7	Pathological deceit				
8	Aggressiveness				
9	Conflict, numerous fights, often on their own initiative without sufficient reason				
10	Systematic cruelty to animals, insects and even children and adults that does not pass even after many explanations and punishments. Unexplained disappearances and deaths of animals				
11	Intriguery				
12	Seeking arousal to perform inappropriate actions / susceptibility to boredom				
13	Lack of fear				
14	Apparent ineffectiveness of punishments				
	Column scores				
	Total score for important characteristics				

2. Rarely found important characteristics

Item No.	Characteristic	Absent 0 points	Present in mild form 3 points	Present in a highly developed form 3 points	Striking personality trait of a child 9 points
1	Active sexual behavior beyond age (up to the normal age of puberty)				
2	Major infractions, often with violent behavior				
	Column scores				
	Total score for rarely found important characteristics				

3. Ordinary characteristics

Item No.	Characteristic	Absent 0 points	Present in mild form 1 point	Present in a highly developed form 2 points	Striking personality trait of a child 3 points
1	Pompous introducing of oneself in society for both adults and children (external)				
2	Exaggerated sense of self-esteem (internal)				
3	Loquacity / superficial charm (ability to speak convincingly, fluently, interesting, streamlined)				
4	Manipulation for personal gain				
5	Envy				
6	Anger even for minor reasons, or even for no apparent reason				
7	Impulsiveness				
8	Lack of goals even in normal activities (play, study, etc.)				
9	Lack of idea even about the immediate results of their own actions				
10	Lack of idea about the feasibility and reality of the goal of the performed actions (even without taking into account possible obstacles in achieving the goal)				
11	Lack of both close and more distant plans				
12	Unstable interpersonal relationships (both with adults and in the children's team)				
13	Irresponsibility				
14	Failure to take responsibility				
15	Inability to study regularly, even with good intelligence				
16	Inability to control expenses, excessive and unnecessary spending, debts that are not even planned to be paid				
17	Cheating in games, during tests				
18	Inappropriate behavior against the background of their age group				
19	Non-participation in collective actions (games and other actions), striving for individual activity				
20	Lack of cooperation (separation of functions in collective actions) and lack of understanding of the need to share in games and other actions				
21	Pyromania				

22	Difficulties with abstract concepts: abstract description of objects in mathematics, metaphors, proverbs, fables in the humanities				
23	Impaired learning ability (not school, but life), even from their own experience (not to mention the experience of children from their age group or gleaned from literary or folklore sources)				
24	Imperviousness to moral ideas and rules (including inferences from literary or folklore sources)				
25	Nasty things (verbal (name-calling, curses) and actions), often in an underhand way, without witnesses				
	Column scores				
	Total score for ordinary characteristics				
	Total score for the test				
	Conclusion				

The total score for the third column (the characteristic is present in a highly developed form) for both tables – scales (tables 1 and 3) is 106 points (without points for table 2). Following Dr. R. Hare and K. Kiehl, we will establish the conclusion about the presence of psychopathy at the level of overcoming 75% of the mark, that is, 80 points and above. However, for a more differential diagnosis, we will introduce two more scoring ranges:

- 54-79 points (51-75%) – psychopathic character formation;
- 36-53 points (36-50%) – suspected psychopathic character formation;
- 35 or less points – no psychopathic tendencies.

We shall notice that, since we have proposed the calculation of the sums of points according to the sum of points in the third column, it is theoretically possible that some especially pronounced psychopaths who scored points in the fourth column for several characteristics or received points other than zero according to Table 2 will exceed 106 points. The theoretical maximum is 159 points (167 points taking into account the points in Table 2).

6. Conclusion

Therefore, in this article we have proposed the PCL-MYV test (Psychopathy Checklist – Modified Youth Version), which is a sufficiently distant relative of the Psychopathy Checklist (PCL) for children and adolescents, proposed by R. Hare (2007) and K. Kiehl (2015), but, like it, drawn up in the framework of an expert approach. The proposed test has a completely different, more complex and branched structure in relation to the Psychopathy Checklist (PCL) for children and adolescents and is more focused on children aged 6-12 years (pre-pubertal age).

An attempt is made to introduce the boundaries of various preclinical stages of psychopathy, separating them from the indicators of healthy children, determined by the same test.

Although it is clear to us that the expert and phenomenological approaches to the diagnosis of psychopathies and preclinical psychopathic states are

not very compatible with each other, nevertheless, an attempt has been made to draw some analogies in assessing the severity of a psychopathic state between these approaches.

In addition, the traits of the character and behavior of children are considered, which at a certain stage of ontogenesis may be similar to some psychopathic traits, but require careful attention to themselves in order to avoid unreasonable overdiagnosis of psychopathic states.

References:

1. Aleksandrovsy Yu.A. Borderline Mental Disorders: A Guide for Physicians. Moscow, 2000, 496 p. Available at: https://www.koob.ru/alexandrovskij_u_a/pogranichnie_psyhicheskie_rasstrojstva (accessed on 10 July 2019).
2. Voronkov B.V. Psychiatry of Children and Adolescents. Saint Petersburg, Nauka i Tekhnika Publ., 2017, 288 p.
3. Datskovsky I. Modified Detailed Infantilism Test – DIT-M. *Vostochno-Yevropeyskiy nauchnyy zhurnal – East European Science Journal*, no. 47 (07.2019 [A]), part 1, pp. 41-50, article in Russian. Available at: https://eesa-journal.com/wp-content/uploads/EESA_-JULI_47_part_1.pdf (accessed on 29 August 2019).
4. Datskovsky I. Two Approaches to the Diagnosis of Psychopathies. *Klinicheskaya i meditsinskaya psikhologiya: issledovaniya, obucheniye, praktika: elektronnyy nauchnyy zhurnal – Clinical and medical psychology: research, training, practice: electronic scientific journal*, 2019 [B], vol. 7, no. 4 (26) Available at: http://medpsy.ru/climp/2019_4_26/article06.php (accessed on 18 February 2020).
5. Kiehl K.A. Psychopaths. A Reliable Story about People Without Pity, Without Conscience, Without Remorse. Moscow, Tsentrpoligraf Publ., 2015, 360 p.
6. Kovalev V.V. Child Psychiatry (a Guide for Physicians). Moscow, Meditsina Publ., 1979, 608 p.

7. Kozlovskaya Galina Vyacheslavovna. Mental Disorders in Young Children (Clinic, Epidemiology and Habilitation Issues). Extended Abstract of Thesis for a Habilitation Degree in Medicine, 1995. Available at: <http://www.psychiatry.ru/cond/0/diss/1995/94> (accessed on 30 June 2019).

8. Lichko A.E. Types of Accentuations of Character and Psychopathies in Adolescents. Moscow, IOI Publ., 2016, 336 p.

9. Makarov I.V. (ed.) Pediatric Psychiatry. A Guide for Physicians. Saint Petersburg, Nauka i Tekhnika Publ., 2019, 992 p.

10. Ivanov N.Ya., Lichko A.E. Pathocharacterological Diagnostic Questionnaire for Adolescents. Moscow, Folium Publ., 1995, 64 p.

11. Tiganov A.S. Pathology of Mental Development. Available at: <http://drlev.ru/book/tiganov4.pdf> (accessed on 30 June 2019).

12. Hare R. Without Conscience: The Disturbing World of the Psychopaths Among Us. Williams, 2007.

Кононков Валерий Васильевич

DOI: 10.31618/asj.2707-9864.2020.3.41.31

Абстракт. Общая анестезия является методом выбора у пациентов подвергающихся обширным оперативным вмешательствам. Иногда данная анестезия может комбинироваться с эпидуральной анестезией. Однако комбинирование обоих методик имеет множество ограничений и побочных эффектов. Здесь мы предоставляем случай пациентки, у которой была выполнена срединная лапаротомия по поводу острого холецистита осложненного холедохолитиазом и синдромом билиарной гипертензии. Сопутствующая патология: ишемическая болезнь сердца, постинфарктный и атеросклеротический кардиосклероз, атеросклероз аорты и коронарных артерий, Н2А, последствия перенесенного ОНМК. Коронавирусная двухсторонняя полисегментарная пневмония, тяжелое течение ДН2.

Интра- и послеоперационное ведение данной пациентки требовало адекватного обезболивания с минимальным количеством наркотических анальгетиков. Адекватная анестезия была достигнута путем комбинирования общей анестезии и интратекального введения низких доз тяжелого бупивакаина и морфина. Данная комбинация позволила снизить количество введенных опиоидов и миорелаксантов во время операции и отказаться от использования наркотических анальгетиков в послеоперационном периоде, что позволило быстрее активизировать пациентку в раннем послеоперационном периоде и избежать осложнений характерных для пациентов с данным коморбидным фоном.

Введение

Общая анестезия – метод анестезии который наиболее часто применяется у пациентов подвергающихся лапаротомным вмешательствам. Однако у пациентов с сопутствующей кардиальной патологией, последствиями перенесенного ОНМК и коронавирусной пневмонией желательнее применение Fast truck методик и использование меньшего количества опиоидных анальгетиков в послеоперационном периоде. Рутинная комбинация комбинированной анестезии с применением эпидурального обезболивания сопровождается гемодинамическим дисбалансом и требует жесткого контроля показателей свертывания крови при стоянии эпидурального катетера, так при лечении COVID пневмонии требуется введение терапевтических доз гепаринов.

Учитывая заболевание пациентки, сопутствующую патологию, ограничение ресурсов в условиях эпидемии COVID 19 была выбрана комбинированная анестезия с использованием интратекального введения низких доз бупивакаина и морфина в виде единичного введения. Используя этот метод мы добились хорошего уровня интра- и послеоперационного обезболивания с минимальным количеством опиоидов, ранней экстубации и активации, возможность раннего перевода в общесоматическое отделение с последующей выпиской из стационара.

Презентация случая

Мы проводили анестезию пациентке, у которой был диагностирован острый калькулезный

холецистит, холедохолитиаз, синдром билиарной гипертензии. Пациентке оказывалась помощь в специализированном стационаре т.к. у нее была диагностирована двухсторонняя полисегментарная коронавирусная пневмония. Исходное состояние оценивалось как тяжелое ЧД – 28 SpO2 95 с подачей увлажненного кислорода через носовые канюли со скоростью потока, 7л/мин. Содержание кислорода в артериальной крови составило 67 mmHg. Респираторный индекс 250 Среднее АД было несколько выше нормы и колебалось в пределах 95-100 мм рт ст. По данным РКТ грудной клетки от с обеих сторон более выражено слева, по всем легочным полям, больше в нижних отделах перибронхиально и субплеврально определяются участки снижения пневматизации по типу матового стекла. С участками утолщения интерстиция.

Сопутствующая патология включала ишемическую болезнь сердца, постинфарктный и атеросклеротический кардиосклероз, атеросклероз аорты и коронарных артерий, Н2А, последствия перенесенного ОНМК.

Пациентке была выполнена операция: лапаротомия, холецистэктомия. Реконструктивная операция на желчевыводящих путях, трансдуоденальная папиллосфинктеропластика, дренирование холедоха по Холстеду.

В качестве анестезиологического пособия мы выбрали комбинированную анестезию с использованием интратекального введения низких доз бупивакаина и морфина в виде единичного введения в комбинации с тотальной внутривенной анестезией с ИВЛ.

Методика анестезии: за 15 минут до начала операции по стандартной методике, на боку была выполнена люмбальная пункция иглой 25G карандашной заточки на уровне L3-L4 интратекально введена комбинация тяжелого бупивакаина 5 мг и морфина спинала 150 мкг. Далее наклонили головной конец кровати. В положение Тренделенбурга пациент находился 5 минут. За это время местный анестетик распространяется вверх и блокирует болевую чувствительность в зоне операции без развития моторного блока и значимых нарушений гемодинамики. Затем проводятся пробы определяющие зоны утраты чувствительности. Целевым уровнем сенсорного блока является Th4-Th 5. Уровень моторной блокады по Bromage составляет 0 балл. Данная комбинация анестетиков позволяет проводить анестезию при длительных операциях с использованием меньшего количества наркотических анальгетиков и релаксантов, что позволяет ускорить восстановление мышечного тонуса и произвести более раннюю экстубацию, а в раннем послеоперационном периоде обеспечивает обезболивание в течение суток, быстрое восстановление и двигательную активность.

Индукция анестезии проводилась пропофолом 200 мг, фентанилом 100 мкг и дитилин 140 мг. Поддержание анестезии закись азота и кислород в соотношении 2 к 1, пропофол 7 мг/кг, миорелаксант - тракриум. Интраоперационный мониторинг включал электрокардиограмму, мониторинг SpO₂, неинвазивные оценки давления крови (BP) каждый 5 минут, механику дыхания. Предоперационные тесты легочной функции показали умеренную рестриктивную картину, поэтому для поддержания нормокапнии или легкой гиперкапнии была запланирована стратегия вентиляции по давлению с ограничением дыхательного объема до 6 мл/кг. Вентиляция проводилась аппаратом ВИАН МК 1-2. В течение операции контролировали драйвенное давление, оно не превышало 14-15 мбар.

Операция длилась 2,5 часа, в течение которых у пациента не развилось каких-либо серьезных гемодинамических изменений, требующих применения вазоконстрикторов или инотропных препаратов. За это время доза введенного фентанила составила 300 мкг, а тракриума 40 мг. Кроме того, она не нуждалась в введении жидкости, который был больше рассчитанного объема. За двадцать минут до завершения операции вводили 30 мг кеторолака внутримышечно и 8 мг ондансетрона внутривенно. Наконец, пациентка была экстубирована, когда она достигла адекватного восстановления мышечного тонуса через 10 минут после окончания самой операции.

В течение первых 48 часов после операции пациентка оценивала свою боль по числовой шкале оценки ВАШ каждые 6 часов как 2-3 из 10 и не требовала дополнительной анальгезии.

Дискуссия

Эффект от интратекального введения местных анестетиков известен более ста лет и основан на блокаде натриевых каналов проводящих путей спинного мозга, возможность терапевтического применения методом интратекального введения опиоидов основана на экспериментальных наблюдениях (Yaksh, Rudy, 1976) (Wang, 1977) и (Bromage et al, 1980) описавших опиоидные рецепторы задних рогов спинного мозга. Длительность эффекта опиоидов зависит от их липофильности. На этом основано применение относительно гидрофильного морфина как средства для длительного контроля боли. Известно, что для подавления гипервозбудимости спинальных нейронов требуются большие дозы морфина. Однако если малые дозы морфина назначать непосредственно перед повреждающей стимуляцией, то триггерная центральная гипервозбудимость никогда не формируется (Woolf, Wall, 1986). В настоящее время стало ясно, что предварительное лечение позволяет предупредить сильную послеоперационную боль (Wall, Melzack, 1994) Использование низких доз бупивакаина в сравнении с обычными ассоциируется с большей гемодинамической стабильностью [Saudi J Anaesth. 2019 Jul-Sep; 13\(3\): 208–214](#) [Marta J. Cenkowski, Doug Maguire,¹ Stephen Kowalski,¹ Fahd A. Al Gurashi,² and Duane Funk](#) Комбинацию интратекального введения низких доз морфина и бупивакаина с общей анестезией мы используем у пациентов с высокой потенциальной частотой побочных эффектов опиоидов: пациентов с ожирением, ХОБЛ, а так же пациентов требующих жесткого гемодинамического контроля: пожилых пациентов с сопутствующей патологией со стороны сердечно сосудистой системы.

В данном случае мы использовали комбинацию по причине необходимости выполнения обширной лапаротомной операции пациентке с коронавирусной двухсторонней полисегментарной пневмонией, страдающей к тому же ишемической болезнью сердца, постинфарктным и атеросклеротическим кардиосклерозом, атеросклерозом аорты и коронарных артерий, H2A, последствиями перенесенного ОНМК. Целью анестезии было обеспечить надежный интра и послеоперационный контроль боли, гемодинамическую стабильность в сочетании с возможностью ранней экстубации и активизации пациентки. Всего этого мы добились уменьшив количество системных наркотических анальгетиков как интра так и в послеоперационном периоде. А так же за счет минимизации интраоперационного применения мышечных релаксантов.

PROSPECTS FOR NEOADJUVANT TREATMENT OF AMPULLARY CANCER

**Rasulov R.I.¹,
Dvornichenko V.V.^{1,2},
Nazarova D.V.²,
Nurbekian G.V.²**

¹Department of Oncology,
Branch of the Russian Medical Academy of Continuing Professional Education,
Ministry of Health of the Russian Federation,
64049, Irkutsk, Yubileiny microdistrict, 100.

²SBHI "Regional Oncological Dispensary", 664035, Irkutsk, Frunze str., 32

DOI: 10.31618/asj.2707-9864.2020.3.41.34

Abstract. Objective: to study the possibilities of preoperative radiation therapy in a radical treatment regimen for glandular ampullary cancer.

Materials and methods. In 2001-2019, 21 cases of pancreatic-biliary type of ampullary cancer underwent radical treatment, including preoperative RT, extended GPDR and adjuvant chemotherapy according to indications (experimental group), 48 cases of pancreatic-biliary type of ampullary cancer underwent expanded GPDR and adjuvant chemotherapy according to indications (control group), and 43 cases of intestinal type of ampullary cancer underwent extended GPDR and adjuvant chemotherapy according to indications.

Results. Radiation therapy caused radiation injuries in 28.6% of patients: grade 1 erythema (19.1%), grade 1 leukopenia (4.75%), and grade 2 leukopenia (4.75%). Postoperative complications, mortality of the experimental group and the control group, respectively, amounted to 28.6% and 50.0% ($p = 0.09$) and 4.8% and 6.3% ($p = 0.8$). The overall 5-year survival rate, the average life expectancy of the experimental group and the control group, respectively, were 50.7% and 9.8% ($p = 0.01$) and 74.8 ± 12.58 months and 21.7 ± 6.11 months ($p = 0.0008$). The overall 5-year survival rate, the average life expectancy of the group with intestinal ampullary cancer, were 61.3% and 60.5 ± 9.15 months, respectively. Relapse-free survival of patients with glandular ampullary cancer ($n = 112$) who received treatment according to the radical regimen was: 1-year - 77.8%, 3-year - 51.0%, 5-year - 35.2%, average life expectancy - 44.7 ± 5.44 months

Conclusion. Radiation injuries were stopped by conservative measures and did not increase the duration of the preoperative period. Preoperative RT in the radical treatment regimen for pancreatic-biliary type of ampullary cancer neither changed the nature nor increased the incidence of postoperative complications. Combined treatment significantly improved long-term survival in cases with pancreatic-biliary type of ampullary cancer.

Keywords: ampullary cancer, pancreatic-biliary type, preoperative radiation therapy.

Information about authors

Rodion Ismagilovich Rasulov - Ph.D. Medicine, Professor, Professor of the Department of Oncology, Branch of the Russian Medical Academy of Continuing Professional Education, Ministry of Health of the Russian Federation.

Viktoriiia Vladimirovna Dvornichenko - Ph.D. Medicine, Professor, Head of the Department of Oncology, Branch of the Russian Medical Academy of Continuing Professional Education, Ministry of Health of the Russian Federation, Chief Physician of SBHI "Regional Oncological Dispensary".

Daria Vladimirovna Nazarova - senior resident of the oncology unit No. 7 of SBHI "Regional Oncological Dispensary".

Grigorii Valerievich Nurbekian - resident physician of oncology unit No. 7 of SBHI "Regional Oncological Dispensary".

For correspondence: Rodion Ismagilovich Rasulov

Address: 32 Frunze Street, Irkutsk, 664035

tel.: 89246209670

Introduction

Treatment of cancer of the ampulla of Vater is one of the most complex and yet unresolved problems in oncology. Many tactical and technical issues have remained controversial and far from being addressed.

Currently, the range radical surgical techniques is represented by transduodenal papillectomy and pancreatoduodenal resection (PDR). The indications for transduodenal papillectomy are strictly limited. This range of surgical aid is an alternative in the surgeon's arsenal for patients with severe concomitant pathology, which excludes the use of PDR.

The surgical standard for treatment of ampullary cancer remains PDR with lymphadenectomy.

Postoperative complications account for 22-67%, mortality – 0-9% [1, 2, 3]. Overall survival in observations where the R0 operation was performed: median - 30.1-113 months, 1-year - 75-86.7%, 3-year - 57.3-69.4%, 5-year - 20-88% [4, 5, 6, 7, 8].

To improve long-term results, radical surgery should be integrated into multimodal treatment.

Currently, the data on the effectiveness of the use of adjuvant therapy in the radical regimen for the treatment of ampullary cancer are contradictory. A number of fairly large studies have shown that adjuvant therapy did not improve long-term treatment results. In particular, clinical studies of ESPAC-1 (1997) and EORTC (1999) of pancreatic head cancer and

peripapillary cancer did not reveal the effectiveness of adjuvant chemoradiation therapy (CRT) [9, 10]. As a result, the role of CRT in the radical treatment of pancreatic head cancer requires clarification. I. Nassour et al. (2018) noted that in 2004-2013 the treatment of pancreatic head cancer made a shift from adjuvant chemotherapy to chemotherapy (CT), which increased from 9% to 32%. However, adjuvant chemotherapy in peripapillary cancer in the ESPAC-3 study (2012), and in ampullary cancer in the ESPAC-3 study (v2, 2016) did not increase life expectancy [12, 13]. Subsequently, Z. Jin et al. (2018), M. Al-Jumayli et al. (2019), B.L. Ecker et al. (2019) did not find a significant increase in long-term survival of patients with ampullary cancer receiving adjuvant treatment.

According to other studies, adjuvant therapy is a promising direction in the combination treatment of ampullary cancer. A meta-analysis of ten retrospective studies, including 3361 observations, showed that adjuvant chemoradiotherapy was associated with a lower risk of death (HR = 0.75; P = 0.001) compared to surgery alone [17]. Analysis of a large sample of NCDB (National Cancer Database) showed that adjuvant chemotherapy significantly increased life expectancy in the group with the T3/T4 index, and adjuvant chemotherapy significantly increased life expectancy in the group with metastatic lymph node lesions [11].

Thus, there are still no randomized controlled trials proving the effectiveness of adjuvant chemotherapy and radiation therapy (RT) for ampullary cancer. Until now, neither the national clinical

guidelines, nor the recommendations of RUSSCO, ESMO, NCCN provide indications and modes of adjuvant chemotherapy in the program of radical treatment of ampullary cancer.

Randomized controlled trials on the neoadjuvant treatment of ampullary cancer are also absent. There is no definitive consensus recommendation for the use of neoadjuvant chemotherapy and radiotherapy for ampullary cancer; in general, treatment is individualized and/or based on regional inpatient protocols.

In conclusion, the issue of neoadjuvant treatment of ampullary cancer remains open. The issue of adjuvant treatment of ampullary cancer has not yet been closed (there are no indications and regimens for adjuvant chemotherapy), and morphological heterogeneity of ampullary cancer determines a large spread in long-term survival rates (5-year from 20% to 88%), which requires the study of prognostic factors, considering the latter, and the development of radical treatment regimens.

Objective: to study the possibilities of preoperative radiation therapy in a radical treatment regimen for glandular ampullary cancer.

Materials and methods

In 2001-2019, 116 patients with glandular ampullary cancer received treatment in the Irkutsk Regional Oncological Dispensary. Of these, 63 (54.3%) were men and 53 (45.7%) - women. Most of the patients were aged 51-70 years (86 - 74.1%); the average age was 59.1 ± 0.83 years (Table 1).

Table 1

Grouping by sex and age

age	sex		total
	men	women	
30-40	2 (1.7%)	-	2 (1.7%)
41-50	10 (8.6%)	7 (6.0%)	17 (14.7%)
51-60	27 (23.3%)	17 (14.7%)	44 (37.9%)
61-70	21 (18.1%)	21 (18.1%)	42 (36.2%)
over 70	3 (2.6%)	8 (6.9%)	11 (9.5%)
	63 (54.3%)	53 (45.7%)	116 (100%)
total	116 (100%)		

Ninety-one (78.4%) of 116 patients with ampullary cancer were admitted to the dispensary with obstructive jaundice. At the pre-specialized stage, the following bile diversion techniques were performed: cholecystostomy by projection access - 12 (13.2%), laparoscopic cholecystostomy - 15 (16.5%), endoscopic stenting of extrahepatic bile ducts - 44 (48.3%), external drainage of the common bile duct - 7 (7.7%), formation of biliodigestive anastomoses - 4

(4.4%), cholecystostomy under ultrasound navigation - 1 (1.1%), and endoscopic papillosphincterotomy - 8 (8.8%) cases.

At the diagnostic stage, pancreatobiliary type of cancer was found in 71 (61.2%) cases, and intestinal type of cancer in 45 (38.8%) cases.

Grouping of the patients by morphology and stage of the tumor process is shown in Table 2.

Table 2

Grouping of the patients by morphology and stage of the tumor process			
signs	pancreato-biliary type	intestinal type	total
1. stage of the tumor process			
- IA	9 (12.7%)	8 (17.8%)	17 (14.7%)
- IB	10 (14.1%)	10 (22.2%)	20 (17.2%)
- IIA	12 (16.9%)	6 (13.3%)	18 (15.5%)
- IIB	17 (23.9%)	6 (13.3%)	23 (19.8%)
- III	2 (2.8%)	6 (13.3%)	8 (6.9%)
- IV	21 (29.6%)	9 (20.0%)	30 (25.9%)
total	71 (100%)	45 (100%)	116 (100%)
2. tumor differentiation degree			
- severe	5 (7.0%)	22 (48.9%)	27 (23.3%)
- moderate	53 (74.7%)	17 (37.8%)	70 (60.3%)
- low	13 (18.3%)	6 (13.3%)	19 (16.4%)
total	71 (100%)	45 (100%)	116 (100%)

Stage II of the tumor process (40.8%) and a moderate degree of tumor differentiation (74.7%) prevailed in the pancreatic-biliary type of ampullary cancer. In the intestinal type, stage I of the tumor process (40.0%) and severe tumor differentiation (48.9%) prevailed.

In the structure of ampullary cancer, stage I was in 31.9% of cases, stage II - 35.3%, stage III - 6.9%, and stage IV - 25.9%. Severe tumor differentiation was found in 23.3% of cases, moderate - in 60.3% and low - in 16.4%.

Sixty-nine of 71 cases of pancreatic-biliary type of ampullary cancer received radical treatment; in 2 cases during the operation, metastatic lesions of the liver and carcinomatosis of the abdominal cavity were detected. Forty-three of 45 cases of intestinal ampullary cancer received radical treatment; in 2 cases during the operation, metastatic lesions of the liver and carcinomatosis of the abdominal cavity were detected.

In 21 cases of the pancreatic-biliary type, treatment was started with remote RT (main group), in 48 (control group) - with radical surgery.

Remote RT was started 4 weeks after biliary decompression. Topometry was performed on a multispiral computed tomograph. For better visualization of the tumor and a landmark, X-ray contrast marks were applied, and the introduction of a X-ray contrast agent was also used. Computed tomograms were performed with an interval of 2.5-5 mm, with the scanning level from the upper edge of the liver Th10-11 to L3-4. The second stage was the contouring of the scans obtained as a result of topometry. Planning and dosimetric calculations were performed on a 3-dimensional planning system "Eclipse" (3D) with the exclusion of critical organs (kidney, spinal cord, liver, spleen, small intestine) from the irradiation zone. RT was performed using the classical mode of fractionation ROD-2Gy 5 times a week to SOD-50Gy for 5 weeks.

In 112 (96.5%) cases, a radical volume of the operative manual was completed (Table 3). This group included 21 observations, where treatment was started with remote RT and 91 observations, where treatment was started with radical surgery.

Table 3

Grouping of patients by the extent of surgical aid	
extent of surgical intervention	number
extended gastropancreatoduodenal resection	91 (78.4%)
+ right hepatic artery resection	1 (0.9%)
<i>total</i>	92 (79.3%)
extended gastropancreatoduodenal resection with mesenteric-portal venous segment resection	12 (10.3%)
+ right hepatic artery resection	1 (0.9%)
<i>total</i>	13 (11.2%)
total pancreatoduodenal ectomy	5 (4.3%)
transduodenal papillectomy	2 (1.7%)
explorative laparotomy	3 (2.6%)
hepaticojejunostomy, gastrojejunostomy	1 (0.9%)
<i>total</i>	116 (100%)

Ninety-one (78.4%) cases underwent extended gastropancreatoduodenal resection (GPDR), 12 (10.3%) cases - extended GPDR with resection of the mesenteric-portal venous segment (MPVS), 1 (0.9%) - expanded GPDR with resection of the right hepatic artery, 1 (0.9%) - extended GPDR with resection of the MPVS and the right hepatic artery, 5 (4.3%) - total duodenopancreatotomy, 2 (1.7%) - transduodenal

papillectomy, in 3 (2.6%) - trial laparotomy, and 1 (0.9%) - hepaticojejunostomy, gastrojejunostomy.

Currently, neither the national clinical guidelines, nor the recommendations of RUSSCO, ESMO, NCCN provide indications and modes of adjuvant chemotherapy in the program of radical treatment of ampullary cancer. Therefore, in order to determine the indications for adjuvant chemotherapy, the relationship

between long-term survival and morphological features was studied. Based on the data obtained, the indications for adjuvant chemotherapy were determined: the growth of the ampullary tumor into the pancreas head, metastatic lesions of regional or juxta-regional lymph nodes, the presence of tumor emboli in the lymphatic or blood vessels. Based on the results of the ESPAC-3 study, Mayo regimen and gemcitabine monotherapy were adopted as medication regimens.

Four-six weeks after radical surgery, the following chemotherapy regimens were used: in 17 cases - Mayo regimen (5-fluorouracil 425 mg / m² i.v., jet + leucovorin 20 mg/m² i.v., jet, on the 1st - 5th days of the 28-day cycle, 6 cycles), in 30 cases - monotherapy with gemcitabine (1000 mg/m² on the 1st, 8th, 15th day with a break of 2 weeks, 4-6 courses).

Results

To assess the neoadjuvant treatment of pancreatic-biliary ampullary cancer, patients were grouped as follows – experimental group (n = 21) or control group (n = 48). In the experimental group, combined treatment was carried out, including preoperative remote RT, extended GPDR and adjuvant chemotherapy according to indications. In the control group, extended GPDR and adjuvant chemotherapy were performed according to indications. The groups studied postoperative complications, mortality, overall survival, average life expectancy.

The analysis of the studied groups showed no significant differences: sex (p = 0.5) and age (p = 0.6) distribution of patients, ECOG functional state (p = 0.8), ASA physical status (p = 0.3), the stage of the

tumor process (p > 0.05), the extent of surgical aid (p > 0.05), the type of anastomosis between the pancreas stump and the intestinal tube (p > 0.05), the duration of the operation (p = 0.9), intraoperative blood loss (p = 0.9), regimens of adjuvant chemotherapy (p = 0.9), i.e. the studied groups are identical.

In the experimental group, at the stage of RT, radiation injuries occurred in 6 (28.6%) cases: erythema in 4 (19.1%) cases, and leukopenia in 2 (9.5%) cases. Considering the table of acute radiation injuries (RTOG, 1995), grade 1 erythema was determined in all 4 cases. On average, erythema occurred on day 20.9 ± 1.84 (14-32) from the start of RT. To relieve itching and inflammation, the area of radiation damage was treated with mild steroid creams. On average, erythema disappeared without skin pigmentation in 6.8 ± 0.61 (4-10) days after the end of RT. Leukopenia developed in 2 cases at the RT stage. Considering the table of acute radiation injuries (RTOG, 1995), grade 1 leukopenia and grade 2 leukopenia were established in 1 case. Grade 1 leukopenia developed during the first sessions of external RT and persisted throughout the entire course of RT. This leukopenia was not specifically corrected. Grade 2 leukopenia developed after the fourth RT session. In order to correct leukopenia, a single injection of prednisolone 30 mg intramuscularly was performed. There was a positive dynamics and recovery of leukocytes within the laboratory norm before discharge (one day after the end of RT).

Postoperative complications in the groups are presented in Table 4.

Table 4

Postoperative complications in the groups

postoperative complications based on the Clavien-Dindo grades	experimental group, n=21	control group, n=48	intestinal type, n=43	total, n=112
<u>grade I</u>				
- wound suppuration	-	-	1 (2.33%)	1 (0.9%)
- hemorrhagic gastritis	-	-	1 (2.33%)	1 (0.9%)
- bilateral pneumonia	-	-	1 (2.33%)	1 (0.9%)
<u>grade IIIa</u>				
- pancreatic fistula, class A according to ISGPF	3 (14.3%)	7 (14.6%)	5 (11.6%)	15 (13.4%)
- pancreatic fistula, class AB according to ISGPF	-	3 (6.3%)	2 (4.65%)	5 (4.4%)
- liver abscess	-	1 (2.08%)	-	1 (0.9%)
- abscess of the abdominal cavity	2 (9.5%)	-	1 (2.33%)	3 (2.7%)
p=0.9				
<u>grade IIIb</u>				
- pancreatic fistula, class AC according to ISGPF	-	1 (2.08%)	-	1 (0.9%)
- hepaticojejunostomy failure	-	-	1 (2.33%)	1 (0.9%)
- bilious peritonitis	-	1 (2.08%)	-	1 (0.9%)
- perforation of the small intestine	-	-	1 (2.33%)	1 (0.9%)
- acute intestinal obstruction	-	1 (2.08%)	-	1 (0.9%)
- biliary fistula	-	1 (2.08%)	-	1 (0.9%)
- abscess of the abdominal cavity	-	1 (2.08%)	-	1 (0.9%)
- subcutaneous eventration	-	-	1 (2.33%)	1 (0.9%)
p=0.1				
<u>grade IVa</u>				
- arrosive bleeding	-	3 (6.3%)	1 (2.33%)	4 (3.6%)
- intra-abdominal bleeding	-	1 (2.08%)	-	1 (0.9%)
- TELA	-	1 (2.08%)	-	1 (0.9%)

	p=0.1			
<u>grade V</u> - arrosive bleeding - postoperative peritonitis	1 (4.8%) -	- 3 (6.3%)	1 (2.33%) 2 (4.65%)	2 (1.8%) 5 (4.4%)
	p=0.8			
total	6 (28.6%)	24 (50.0%)	18 (41.9%)	48 (42.9%)
	p=0.09			

A retrospective analysis of the immediate results of surgical treatment of the main group and the group of clinical comparison showed that postoperative complications occurred in 6 (28.6%) and 24 (50.0%) cases, respectively.

Postoperative complications in the experimental group and control group were distributed as follows: grade IIIa complications, respectively 5 (23.8%) and 11 (22.9%; $p = 0.9$), grade IIIb complications - 0 and 5 (10.4 %; $p = 0.1$), grade IVa complications - 0 and 5 (10.4%; $p = 0.1$), grade V complications - 1 (4.8%) and 3 (6.3%; $p = 0.8$) observations. There were no significant differences in the structure and frequency of postoperative complications of the studied groups ($p = 0.09$).

Forty-eight (42.9%) of 112 cases radically operated for ampullary cancer developed complications

(Table 4). Analysis of the structure of postoperative complications showed that in the overwhelming majority they are represented by evasion of pancreatic secretion from the zone of pancreatojejunostomosis and complications arising against the background of this evasion - pancreatic fistula (18.7%), arrosive bleeding (5.4%), postoperative peritonitis (4.4%) and abdominal abscesses (3.6%).

A retrospective analysis of the immediate results of surgical treatment of the main group and the group of clinical comparison showed that mortality in the study groups was 4.8% (1 case) and 6.3% (3 cases, $p = 0.8$), respectively.

The causes of deaths in the groups are presented in Table 5.

Table 5

The causes of deaths in the groups

Cause of death	experimental group, n=21	control group, n=48	intestinal type, n=43	total, n=112
hemorrhagic shock	1 (4.8%)	-	1 (2.3%)	2 (1.8%)
multiple organ failure	-	3 (6.3%)	2 (4.7%)	5 (4.4%)
total	1 (4.8%)	3 (6.3%)	3 (7.0%)	7 (6.2%)
	p=0.8			

Seven (6.2%) of 112 cases radically operated for ampullary cancer died.

In 2 (1.8%) cases, the cause of death was hemorrhagic shock against the background of arrosive bleeding. Of these, in 1 case arrosion of the splenic artery wall was established and in 1 case - the left gastric artery. In 5 (4.4%) cases, the cause of death was

multiple organ failure associated with postoperative peritonitis. Of these, in 3 cases, the cause of postoperative peritonitis was pancreatic fistula of class C according to ISGPF and in 2 cases - recurrent perforation of the intestinal tube.

The overall survival rate of the groups is shown in Table 6.

Table 6

The overall survival rate of the groups

survival	intestinal type	experimental group	p	control group	ductal pancreatic head cancer, data of IROD*
1 year	100%	94.2%	0.004	51.9%	51.8%
2 years	93.3%	88.3%	<0.001	23.0%	19.8%
3 years	81.9%	82.2%	<0.001	13.1%	14.4%
5 years	61.3%	50.7%	0.01	9.8%	5.2%
7 years	42.5%	44.4%	0.01	6.5%	5.2%
10 years	42.5%	35.5%	0.05	6.5%	2.6%
average survival, months	60.5±9.15	74.8±12.58	0.0008	21.7±6.11	15.5±1.65

Note: * - data of the clinical material of the Irkutsk Regional Oncological Dispensary for 2006-2016 published in *Practical Oncology*. 2018; 19(4): 408-418. doi: 10.31917/1903408

Table 6 includes column No. 6 (in dark) with long-term survival rates for ductal cancer of the pancreas head (operable observations, where extended GPDR and adjuvant chemotherapy were performed).

The overall survival of the experimental and control group, respectively, was: 1 year - 94.2% and 51.9% ($p = 0.004$), 2 year - 88.3% and 23.0% (p

<0.001), 3 year - 82.2% and 13.1% ($p < 0.001$), 5 year - 50.7% and 9.8% ($p = 0.01$), 7 year - 44.4% and 6.5% ($p = 0.01$), 10 year - 35.5% and 6.5% ($p = 0.05$), average life expectancy - 74.8 ± 12.58 months and 21.7 ± 6.11 months ($p = 0.0008$).

A notable fact is that the traditional treatment regimen (radical surgery and adjuvant chemotherapy

according to indications) in patients with pancreatic-biliary type of ampullary cancer (control group) showed unsatisfactory long-term survival results, which are almost identical to the long-term survival results in pancreatic ductal cancer (see Table 6). The inclusion of preoperative radiation therapy in the radical treatment regimen made it possible to significantly increase the long-term survival rate in

pancreatic-biliary type of ampullary cancer (experimental group), which became commensurate with the long-term survival rate of radically treated intestinal type of ampullary cancer.

Relapse-free survival of patients with glandular ampullary cancer (n = 112) who received radical treatment in 2001-2019 in the Irkutsk Regional Oncological Dispensary is presented in Table 7.

Table 7.

Relapse-free survival of patients with glandular ampullary cancer who received radical treatment in 2001-2019.

survival	Stage I	Stage II	Stage III	Stage IV	All stages
1 year	90.0%	78.2%	81.9%	60.0%	77.8%
2 years	86.4%	57.8%	54.6%	23.5%	59.1%
3 years	78.7%	46.2%	54.6%	17.6%	51.0%
5 years	59.0%	33.7%	54.6%	0	35.2%
7 years	43.3%	33.7%	27.2%	0	27.4%
10 years	43.3%	33.7%	0	0	25.6%
average survival, months	79.2±11.86	37.7±7.37	28.2±15.20	14.5±4.89	44.7±5.44

Relapse-free survival was: 1 year - 77.8%, 2 years - 59.1%, 3 years - 51.0%, 5 years - 35.2%, 7 years - 27.4%, 10 years - 25.6%, average life expectancy - 44.7 ± 5.44 months.

Discussion

Ampullary cancer is a relatively rare heterogeneous malignant neoplasm, occurs in 6 cases per 1 million population, accounts for 0.2% in the structure of cancer of the digestive tract and 16.4% in the structure of cancer of the bile ducts.

Due to the anatomical features of the ampulla of Vater, the course of the disease and the development of the clinical picture, ampullary cancer is usually diagnosed at an early stage. Therefore, in more than half of the observations of primary treatment, it is possible to carry out a radical treatment regimen.

PDR is a standard surgery for ampullary cancer.

The data of the morphological study of our own clinical material show that the choice of the extent of the surgical aid (the depth of dissection) directly depends on the histological type of ampullary cancer. In the intestinal type and resectable tumor process, the standard PDR is a radical volume; three (7.1%) of 42 cases of intestinal type had metastases to juxta-regional lymph nodes detected. In the pancreatic-biliary type, various combinations of morphological signs (tumor growth in the MPVS, metastatic lesions of juxta-regional lymph nodes, perineural invasion, the presence of tumor emboli) amounted to 27 (39.7%) of 68 cases. Thus, the radical volume of the operation in the pancreatic-biliary type must be recognized as the extended GPDR.

Since half of all ampullary cancers recur after radical primary intervention, it is of paramount importance to identify and manage (appropriately) the features associated with the risk of disease recurrence. Currently, a group of unfavorable morphological signs has been identified and constantly revised, these are growth into surrounding organs and tissues, perineural invasion, metastatic lesions of lymph nodes, low tumor differentiation, etc., which determine an early relapse of the disease and a low life expectancy. The overwhelming majority of these prognostically unfavorable morphological signs are inherent in the

pancreatic-biliary type of ampullary cancer, i.e. histological type of ampullary cancer is an independent predictor of long-term survival; the overall 5-year survival rate for pancreatic-biliary and intestinal types is 27.5-53.3% and 61-73%, respectively. In our study, we compared long-term survival in the groups of pancreatic-biliary and intestinal types, where the radical treatment regimen included extended GPDR without neoadjuvant therapy. The overall 5-year survival rate and average life expectancy in the studied groups, respectively, were 9.8% versus 61.3% (p < 0.001) and 21.7 ± 6.11 months against 60.5 ± 9.15 months (p = 0.0007).

The high relapse rate is a strong argument for considering multimodal treatment for ampullary cancer.

Currently, the data on the effectiveness of the use of adjuvant therapy in the radical treatment regimen for ampullary cancer are contradictory.

ESPAC-1 (1997) of cases with R0 resection revealed the median survival in groups with and without adjuvant chemotherapy equal to 15.9 months against 16.9 months, respectively. According to the results of EORTC-40891 (1999), the 2-year survival rate for ampullary cancer in the control group and the group of adjuvant chemotherapy was 63% and 67%, respectively (p = 0.737). ESPAC-3 (v2, 2016), for ampullary cancer, revealed the median survival in the control group and the combination treatment group, respectively, equal to 34 months and 57 months, respectively. According to B.L. Ecker et al. (2019) regardless of the stage of the tumor process, the severity, the presence/absence of tumor cells at the edge of the resection, the presence/absence of metastatic lesions of the lymph nodes, histological type, adjuvant therapy does not play any role in improving overall survival in patients with FS cancer. According to M. Al-Jumayli et al. (2019) adjuvant therapy did not change relapse-free and overall survival rates. The 5-year survival rate was 22.7%.

Analysis of a large sample of NCDB showed the following. Group with adjuvant chemotherapy and without adjuvant chemotherapy: median overall survival was 47.2 and 35.5 months, 1-year survival - 90% and 85%, 3-year - 57% and 49%, 5-year - 44% and 38%, respectively. It was stated that adjuvant chemotherapy significantly increased life expectancy in the group with the T3/T4 index. Group with adjuvant chemotherapy and without adjuvant chemotherapy: median overall survival was 38.1 months, respectively. versus 31.0 months, 1-year survival rate - 88% versus 83%, 3-year survival rate - 51% versus 45%, 5-year survival rate - 40% versus 35%. Adjuvant CRT significantly increased life expectancy in the group with metastatic lymph node involvement. A recent series from the Mayo Clinic (2018) demonstrated the benefit of adjuvant chemotherapy in stage IIB or higher. According to the data obtained, a 55% reduction in the risk of death was noted in patients with advanced disease receiving adjuvant therapy [HR: 0.45, (95% CI: 0.22–0.93), P = 0.03]. Similar encouraging results were obtained in another retrospective series, which collected data from the National Database, including 4190 patients with ampullary cancer. There was a 18% reduction in the risk of death [HR: 0.82, (95% CI: 0.71–0.95)], which is typical for large tumors and advanced stages. In our study, we used two modes of adjuvant chemotherapy (based on the results of the ESPAC-3 study): Mayo and gemcitabine monotherapy. We do not consider these chemotherapy regimens to be successful for ampullary cancer. Probably, in the future, chemotherapy regimens for the pancreatic-biliary type will be represented by various combinations of 5-FU, gemcitabine and capecitabine; for the intestinal type, the FOLFOX regimen is possible.

Neoadjuvant treatment is represented by single observations in the form of retrospective reports (Yeung R.S. et al., 1993; Hoffman J.P. et al., 1998; Palta M. et al., 2011). Randomized controlled trials are absent. Nevertheless, the authors noted a high frequency of grade 4 treatment pathomorphosis (80–100%) in the removed specimens, partial (67%) and complete (28%) tumor response. Considering the above and agreeing with the opinion of C.G. Willett et al. (1993) that preoperative RT will reduce the risk of dissemination of cancer cells during surgery, we conducted a single-center retrospective prospective study to evaluate the combined treatment of pancreatic-biliary type of ampullary cancer. The overall 5-year survival rate and average life expectancy in the groups of combined treatment (preoperative RT and extended GPDR) and extended GPDR without preoperative RT, respectively, were 50.7% versus 9.8% ($p = 0.01$) and 74.8 ± 12.58 months versus 21.7 ± 6.11 months ($p = 0.0008$). The relatively small number of observations with the discussed nosology did not allow us to compare the long-term survival rate taking into account the stages of the tumor process.

The above studies of neoadjuvant treatment of ampullary cancer pay little attention to the damage to

radiation therapy, methods of control and drug correction of these pathological conditions. R.S. Yeung et al. (1993) reported that the diagnosed toxicity was represented by febrile neutropenia (in 2 cases), biliary sepsis (in 2 cases), nausea and vomiting. One patient died of biliary sepsis prior to completion of CRT. J.P. Hoffman et al. (1998) the problem of the safety of neoadjuvant therapy was not discussed, probably due to the small number of observations. M. Palta et al. (2012) bypassed the topic of chemotherapy toxicity, noting only the disadvantages - the preoperative time interval during which the patient's condition may worsen, the disease progresses, which excludes subsequent surgical intervention. In our study, during remote radiotherapy, radiation injuries occurred in 28.6% of cases: grade 1 erythema - in 19.1%, grade 1 leukopenia - in 4.75%, and grade 2 leukopenia - in 4.75% of cases. The above-mentioned injuries of radiation therapy were arrested against the background of conservative therapy for a short period of time, in particular, erythema within 4–10 days from the moment of completion of radiation therapy, leukopenia - one day after completion of radiation therapy, and did not increase the duration of the preoperative period.

To finalize the discussion we should say that there are no malignant neoplasms insensitive to radiation therapy. Achievement of therapeutic effect requires selecting correctly the type of ionization radiation, the method and dose of energy supply to the focus, the sequence for combined treatment. The same applies to drug therapy, it is necessary to choose the right chemotherapy regimen. As for the contradictory data regarding the effectiveness of the above therapy, the reason probably lies in the study protocol itself and its components, namely, the retrospective nature of the study, a small number of observations in ongoing studies (due to the rarity of the discussed nosology), the heterogeneity of the compared groups by histological type of ampullary cancer and disease neglect (patients who received adjuvant therapy after PDR have more advanced disease), lack of proper control of chemotherapy regimens, differences in the volume of operations (mainly due to the depth of dissection), etc. For correct conclusions, a multicenter randomized controlled trial is required.

Intestinal and pancreatic-biliary types of ampullary cancer are two different tumor processes with different tumor biology, local manifestations, drug sensitivity and disease prognosis. The pancreatic-biliary type is morphologically, immunohistochemically and clinically similar to ductal cancer of the pancreas and assumes the same type of treatment regimen represented by neoadjuvant therapy and appropriate chemotherapy regimens. The intestinal type is morphologically and clinically similar to colorectal cancer, showing tropism for similar drugs. This is the second strong argument for starting a multicenter randomized controlled trial to confirm these claims.

Abbreviations	
GPDR	- gastropancreaticoduodenal resection
RT	- radiation therapy
MPVS	- mesentrico-portal venous system
PDR	- pancreaticoduodenal resection
P	- pancreas
rLa	- right liver artery
AV	- ampulla of Vater
CT	- chemotherapy
CRT	- chemoradiotherapy

References

- Dorandeu A, Raoul JL, Siriser F, Leclercq-Rioux N, Gosselin M, Martin ED, Ramée MP, Launois B. Carcinoma of the ampulla of Vater: prognostic factors after curative surgery: a series of 45 cases. *Gut*. 1997 Mar;40(3):350-5. PubMed PMID: 9135524; PubMed Central PMCID: PMC1027085.
- Casaretto E, Andrada DG, Granero LE. [Results of cephalic pancreaticoduodenectomy for ampullary carcinoma. Analysis of 18 consecutive cases]. *Acta Gastroenterol Latinoam*. 2010 Mar;40(1):22-31. Spanish. PubMed PMID: 20446393.
- Zhou J, Zhang Q, Li P, Shan Y, Zhao D, Cai J. Prognostic factors of carcinoma of the ampulla of Vater after surgery. *Tumour Biol*. 2014 Feb;35(2):1143-8. doi: 10.1007/s13277-013-1153-9. Epub 2013 Sep 12. PubMed PMID: 24026886.
- Balachandran P, Sikora SS, Kapoor S, Krishnani N, Kumar A, Saxena R, et al. Long-term survival and recurrence patterns in ampullary cancer. *Pancreas*. 2006;32:390-395. doi: 10.1097/01.mpa.0000220864.80034.63.
- Junrungsee S, Kittivarakul E, Ko-iam W, Lapisatepun W, Sandhu T, Chotirosniramit A. Prognostic Factors and Survival of Patients with Carcinoma of the Ampulla of Vater after Pancreaticoduodenectomy. *Asian Pac J Cancer Prev*. 2017 Jan 1;18(1):225-229. doi: 10.22034/APJCP.2017.18.1.225. PMID: 28240523; PMCID: PMC5563104.
- Murakami T, Matsuyama R, Ueda M, et al. High-Mobility Group Box 1 expression predicts survival of patients after resection of adenocarcinoma of the ampulla of Vater. *World J Surg Oncol*. 2019;17(1):140. Published 2019 Aug 9. doi:10.1186/s12957-019-1675-8.
- Sato Y, Hara T, Takami Y, et al. Conversion surgery for initially unresectable carcinoma of the ampulla of Vater following pathological complete response to chemotherapy: a case report. *Surg Case Rep*. 2019;5(1):122. Published 2019 Jul 30. doi:10.1186/s40792-019-0680-z.
- Zimmermann C, Wolk S, Aust DE, Meier F, Saeger HD, Eehalt F, Weitz J, Welsch T, Distler M. The pathohistological subtype strongly predicts survival in patients with ampullary carcinoma. *Sci Rep*. 2019 Sep 3;9(1):12676. doi: 10.1038/s41598-019-49179-w. PubMed PMID: 31481741; PubMed Central PMCID: PMC6722235.
- Neoptolemos JP, Kerr DJ, Beger H, Link K, Pederzoli P, Bassi C, Dervenis C, Fernandez-Cruz L, Laçaine F, Friess H, Büchler M. ESPAC-1 trial progress report: the European randomized adjuvant study comparing radiochemotherapy, 6 months chemotherapy and combination therapy versus observation in pancreatic cancer. *Digestion*. 1997;58(6):570-577. doi:10.1159/000201503.
- Klinkenbijn JH, Jeekel J, Sahnoud T, van Pel R, Couvreur ML, Veenhof CH, Arnaud JP, Gonzalez DG, de Wit LT, Hennipman A, Wils J. Adjuvant radiotherapy and 5-fluorouracil after curative resection of cancer of the pancreas and periampullary region: phase III trial of the EORTC gastrointestinal tract cancer cooperative group. *Ann Surg*. 1999;230(6):776-784. doi:10.1097/00000658-199912000-00006.
- Nassour I, Hynan LS, Christie A, Minter RM, Yopp AC, Choti MA, Mansour JC, Porembka MR, Wang SC. Association of Adjuvant Therapy with Improved Survival in Ampullary Cancer: A National Cohort Study. *J Gastrointest Surg*. 2018 Apr;22(4):695-702. doi: 10.1007/s11605-017-3624-6. Epub 2017 Nov 10. PMID: 29127604; PMCID: PMC5890432.
- Neoptolemos JP, Moore MJ, Cox TF, Valle JW, Palmer DH, McDonald AC, Carter R, Tebbutt NC, Dervenis C, Smith D, Glimelius B, Charnley RM, Lacaine F, Scarfe AG, Middleton MR, Anthony A, Ghaneh P, Halloran CM, Lerch MM, Oláh A, Rawcliffe CL, Verbeke CS, Campbell F, Büchler MW; European Study Group for Pancreatic Cancer. Effect of adjuvant chemotherapy with fluorouracil plus folinic acid or gemcitabine vs observation on survival in patients with resected periampullary adenocarcinoma: the ESPAC-3 periampullary cancer randomized trial. *JAMA*. 2012 Jul 11;308(2):147-56. doi: 10.1001/jama.2012.7352. Erratum in: *JAMA*. 2012 Nov 14;308(18):1861. PubMed PMID: 22782416.
- Neoptolemos JP, Moore MJ, Cox TF, Valle JW, Palmer DH, McDonald A, Carter R, Tebbutt NC, Dervenis C, Smith D, Glimelius B, Coxon FY, Lacaine F, Middleton MR, Ghaneh P, Bassi C, Halloran C, Olah A, Rawcliffe CL, Büchler MW. Ampullary cancer ESPAC-3 (v2) trial: a multicenter, international, open-label, randomized controlled phase III trial of adjuvant chemotherapy versus observation in patients with adenocarcinoma of the ampulla of Vater. *J Clin Oncol*. 2016;29:LBA4006.
- Jin Z, Hartgers ML, Sanhueza CT, Shubert CR, Alberts SR, Truty MJ, Muppa P, Nagorney DM, Smyrk TC, Hassan M, Mahipal A. Prognostic factors and benefits of adjuvant therapy after pancreatoduodenectomy for ampullary adenocarcinoma: Mayo Clinic experience. *Eur J Surg Oncol*. 2018 May;44(5):677-683. doi:

10.1016/j.ejso.2018.02.008. Epub 2018 Feb 16. PMID: 29506768.

15. Al-Jumayli M, Batool A, Middiniti A, Saeed A, Sun W, Al-Rajabi R, Baranda J, Kumer S, Schmitt T, Chidharla A, Kasi A. Clinical Outcome of Ampullary Carcinoma: Single Cancer Center Experience. *J Oncol*. 2019 May 2;2019:3293509. doi: 10.1155/2019/3293509. PMID: 31186632; PMCID: PMC6521487.

16. Ecker BL, Vollmer CM Jr, Behrman SW, Allegrini V, Aversa J, Ball CG, Barrows CE, Berger AC, Cagigas MN, Christein JD, Dixon E, Fisher WE, Freedman-Weiss M, Guzman-Pruneda F, Hollis RH, House MG, Kent TS, Kowalsky SJ, Malleo G, Salem RR, Salvia R, Schmidt CR, Seykora TF, Zheng R, Zureikat AH, Dickson PV. Role of Adjuvant Multimodality Therapy After Curative-Intent Resection of Ampullary Carcinoma. *JAMA Surg*. 2019 Aug 1;154(8):706-714. doi: 10.1001/jamasurg.2019.1170. PMID: 31141112; PMCID: PMC6547142.

17. Kwon J, Kim BH, Kim K, Chie EK, Ha SW. Survival Benefit of Adjuvant Chemoradiotherapy in Patients With Ampulla of Vater Cancer: A Systematic Review and Meta-analysis. *Ann Surg*. 2015 Jul;262(1):47-52. doi:

10.1097/SLA.0000000000001182. Review. PubMed PMID: 25775067.

18. Rasulov RI, Zemko MV, Ushakova IV, Songolov GI. Ductal cancer of pancreatic head neoadjuvant treatment: close and results. *Practical oncology*. 2018; 19(4): 408-418. doi: 10.31917/1903408.

19. Hoffman JP, Cooper HS, Young NA, Pendurthi TK. Preoperative chemotherapy of adenocarcinoma of the pancreas and ampulla of Vater. *J Hepatobiliary Pancreat Surg*. 1998;5(3):251-4. Review. PubMed PMID: 9880771.

20. Palta M, Patel P, Broadwater G, Willett C, Pepek J, Tyler D, Zafar SY, Uronis H, Hurwitz H, White R, Czito B. Carcinoma of the ampulla of Vater: patterns of failure following resection and benefit of chemoradiotherapy. *Ann Surg Oncol*. 2012 May;19(5):1535-40. doi: 10.1245/s10434-011-2117-1. Epub 2011 Nov 2. PubMed PMID: 22045467; PubMed Central PMCID: PMC4155936.

21. Willett CG, Lewandrowski K, Warshaw AL, Efid J, Compton CC. Resection margins in carcinoma of the head of the pancreas. Implications for radiation therapy. *Ann Surg*. 1993 Feb;217(2):144-8. doi: 10.1097/0000658-199302000-00008. PMID: 8094952; PMCID: PMC1242753.

УДК 13058
ГРНТИ 76.29

ГЕМОПЕРФУЗИЯ ПРИ ОСТРОМ ОТРАВЛЕНИИ ПСИХОТРОНЫМИ ПРЕПАРАТАМИ

Фомин Александр Михайлович

Ведущий научный сотрудник

*ГБУЗ МО «МОНИКИ им. М.Ф.Владимирского»,
Москва, Россия.*

HEMOPERFUSION IN ACUTE PSYCHOTROPIC POISONING

Fomin Aleksander Mikhailovich

Moscow Regional Research and

Clinical Institute (MONIKI), Moscow, Russia.

DOI: 10.31618/asj.2707-9864.2020.3.41.35

Аннотация. Представлено комплексное лечение пациентки с острым отравлением амитриптилином и циклодолом с применением энтеросорбции, кишечного лаважа и гемосорбции на новой колонке с синтетическим сорбентом. Для гемосорбции использована колонка с двухслойным синтетическим полимером, разработанная для селективной сорбции цитокинов методом прямой гемоперфузии. Количественные определения уровней амитриптилина и циклодола до колонки и после колонки, а также до гемосорбции и после гемосорбции показали высокую эффективность сорбента по удалению токсиканта из крови. Применение 6 часовой гемосорбции позволило снизить уровень амитриптилина от исходного более чем в 4 раза и уровень циклодола - более чем в 3 раза до терапевтических уровней и получить выраженный положительный клинический эффект в комплексном лечении пациентки с тяжелым отравлением.

Summary. Presented is a complex treatment of a patient with acute amitriptyline and cyclodole poisoning using enterosorption, intestinal lavage and hemosorption on a new column with a synthetic sorbent. For hemosorption, a column with a two-layer synthetic polymer was used, developed for selective sorption of cytokines by direct hemoperfusion. Quantitative measurements of levels of amitriptyline and cyclodole before and after the column, as well as before haemosorption and after haemosorption, showed a high effectiveness of the sorbent in removing toxicant from the blood. The use of 6-hour hemosorption allowed to reduce the level of amitriptyline from the initial by more than 4 times and the level of cyclodole by more than 3 times to therapeutic levels and obtain a pronounced positive clinical effect in the complex treatment of a patient with severe poisoning.

Ключевые слова: острое отравление, амитриптилин, циклодол, гемосорбция.

Key words: acute poisoning, amitriptyline, cyclodole, hemosorption.

Введение. Из числа госпитализированных в стационары пострадавшие с суицидальными отравлениями, протекающими в наиболее тяжелой форме, составляют 27-30% от всех острых отравлений. Острые отравления лекарственными средствами, как причина смертельных исходов не входят в число лидеров, но составляют 1 случай на 100 тысяч населения и 2,8% от общего числа острых отравлений [1]. Сочетанное применение энтеросорбции и кишечного лаважа при острых пероральных тяжелых отравлениях психофармакологическими средствами составляют основу интенсивной терапии [2]. В токсикогенной стадии тяжелых острых отравлений наиболее эффективными на сегодняшний день являются экстракорпоральные сорбционно-диализные методы детоксикации с использованием искусственных полимерных или естественных полупроницаемых мембран и неселективных угольных сорбентов, позволяющие в короткие сроки ликвидировать летальный уровень токсиканта [3]. В связи с этим, проведение научных исследований в комплексной детоксикации при острых отравлениях, основу которой составляют методы искусственной детоксикации организма с использованием новых гемосорбентов является актуальным направлением [4].

Материалы и методы. Представляем лечение пациентки Л., 55 лет, и/б №9824-с. Клинический диагноз: Острое суицидальное отравление психотропными препаратами (амитриптилином и циклодолом) тяжелой степени. Шизофрения параноидальная, эпизодический тип течения на фоне нарастающего эмиционально-волевого дефекта (F20.01). Гипертоническая болезнь II ст., риск ССО 3. Пациентка более 20 лет страдает шизофренией, состоит на учете у психиатра. По назначению психиатром получает лечение: трифтазин 5 мг вечером, циклодол 1 табл. х 2 раза в сутки, афобазол 1 табл., амитриптилин 1 (25 мг) табл., мелипрамин 1(25 мг) табл., сибазон 1 табл. Со слов родственников 11.04.2019 года около 8 часов 30 минут с суицидальной целью в быту могла принять около 100 таблеток амитриптилина и 50 таблеток циклодола. Пострадавшая сообщила родственникам о приеме таблеток. Родственники, мать и брат, вызвали скорую медицинскую помощь. Врачи реанимационной бригады скорой медицинской помощи произвели интубацию трахеи и начали ИВЛ, инфузионную терапию, установили назогастральный зонд и провели промывание желудка. Пациентка была доставлена в реанимационное отделение Дзержинской городской больницы. При поступлении состояние пациентки тяжелое. Кома (3-4 балла по шкале комы Глазго). Арефлексия. На ИВЛ. Тоны сердца ритмичные, приглушены. Артериальное давление 110/68 мм.рт.ст. Частота сердечных сокращений (ЧСС) 133 удара в минуту. ЭКГ в динамике: синусовая тахикардия, горизонтальное положение ЭОС; изменения в миокарде желудочков; урежение

синусового ритма с 133 до 88-81 удара в минуту. Рентгенография органов грудной клетки без особенностей. Больной продолжена инфузионная терапия, промывание желудка, введен активированный уголь 50 г. В анализах: эритроциты $4,3 \times 10^{12}$ Ед/л, гемоглобин 123 г/л, лейкоциты 10×10^9 Ед/л тысяч, амилаза 25 Ед/л, глюкоза крови 8,2 ммоль/л, мочевины 5,3 ммоль/л, креатинин 47,6 ммоль/л, общий белок 61,5 г/л, билирубин 3,4 ммоль/л, АЛТ 12,4, калий 3,9 ммоль/л, натрий 136 ммоль/л, хлор 102 ммоль/л. Взята кровь для проведения химико-токсикологических исследований.

Для проведения специализированного лечения 11.04.2019 года в 19 часов 09 минут больная была доставлена в отделение реанимации и интенсивной терапии ГБУЗ МО МОНИКИ им.М.Ф.Владимирского. При поступлении состояние тяжелое. Повышенного питания. Вес около 108 кг. Температура тела 36,3. Без сознания. Кома 3-4 балла по Глазго. Зрачки D=S. Кожный покров и видимые слизистые бледно-розовые, чистые. На ИВЛ в режиме SIMV PCV с параметрами Pressure controle – 14, РЕЕР -3, FiO₂-40%, при этом Vt до 650 мл, F общ. до 18 в мин. Аускультативно дыхание жесткое, ослабленное в нижних отделах, хрипов нет. Тоны сердца приглушены, ритмичны. Артериальное давление 114/61 мм рт ст, поддерживается введением норадреналина 0,15 мкг/кг/мин. Пульс 112 ударов в минуту. ЦВД 70 мм в д.ст. Живот увеличен в объеме за счет подкожно-жировой клетчатки, при пальпации мягкий. Притупления в отлогих местах живота нет. Печеночная тупость сохранена. Печень и селезенка не пальпируются. Перистальтические шумы ослаблены. Диурез достаточный. Темп диуреза 1,2 мл/мин. В крови и моче обнаружены амитриптилин и его метаболиты, циклодол и гидроксированный метаболит циклодола.

Пациентке начата комбинированная детоксикационная терапия, включающая энтеросорбцию, кишечный лаваж и гемосорбцию на колонке «Цитосорб». Для этого по желудочному зонду введено 50 г активированного угля. Подготовлен солевой энтеральный раствор для кишечного лаважа. Фракционный кишечный лаваж проводился по методике разработанной Маткевич В.А и соавторы [2]. Для проведения кишечного лаважа использовали солевой энтеральный раствор - «СЭР» производства «Внешпромфарм» (Россия), катионно-анионный состав и pH (5,5–5,8) которого были близкими характеристикам химуса тонкой кишки человека [5]. Пропись СЭР: натрия фторноокислого однозамещенного - 2,5 г; натрия хлористого - 3,43 г; натрия уксусноокислого - 2,88 г; калия хлористого - 1,54 г; магния серноокислого 25% раствора - 5 мл; кальция хлористого 10% раствора - 15 мл; воды дистиллированной – до 1 л. Всего было приготовлено 25 литров СЭР. Дыхательные пути пациентки уже защищены установленной интубационной трубкой с манжетой

для ИВЛ. По назогастральному двуканальному зонду, перфузионный канал которого присоединяли к гравитационной системе емкостью 1,5–2 л, при возвышенном положении верхней половины тела пациентки, вводили порциями по 150-200 мл через каждые 5 мин подогретый до 37 градусов Цельсия солевой энтеральный раствор. После введения 2,5 л раствора на 42-45 минуте появился жидкий стул. Кишечный лаваж продолжался до момента выделения из прямой кишки прозрачной жидкости без примеси кала. В общей сложности в желудочный зонд было введено 20 литров солевого энтерального раствора в течении 6,5 часов.

Для проведения гемосорбции в правую подключичную вену установлен двухходовой диализный катетер диаметром 12Fr «Arrow» (США). Гемосорбция проводилась с применением гемопротессора «АК-10» фирмы «Gambro» (Швеция). Использовали стандартный набор диализных кровопроводящих магистралей и колонку для гемосорбции «Цитосорб» производства «CytoSorbents Inc» (США). Колонка «Цитосорб» представляет собой устройство одноразового применения для прямой гемоперфузии с биосовместимыми высокопористыми синтетическими полимерными гранулами для адсорбции токсичных субстанций. Корпус колонки имеет длину 180 мм, внешний диаметр 60 мм. Объем контейнера с адсорбентом составляет 300 мл. Колонка «Цитосорб» разработана для сорбции цитокинов крови у пациентов при различных критических состояниях, в частности при септическом шоке. Поры гранулы сорбента адсорбента способны улавливать цитокины молекулярным весом 5-55 кДа. Площадь гранул, которая может эффективно удалять цитокины из крови составляет около 40000 квадратных метров.

Перед подключением колонка промывалась 2000 мл физиологического раствора. Антикоагуляция обеспечивалась введением гепарина, перед процедурой введено 10 тысяч Ед гепарина, через 3 часа дополнительно введено 5 тыс Ед гепарина. Контроль антикоагуляции осуществлялся по уровню активированного частичного тромбопластинного времени (АЧТВ), 60 – 80 сек является достаточным для гемосорбции.

Гемосорбция проводилась в течении 6 часов. Скорость экстракорпорального кровотока составила 200 мл/мин. Гемодинамических реакции при подключении и проведении гемосорбции не было. Артериальное давление было стабильным, исходное давление было 114/61 мм рт ст, далее 114/69, 134/90, 132/89, 139/67 и 131/62 мм рт ст после окончания процедуры. Доза вазопрессорной поддержки была снижена с 0,15 до 0,05 мкг/кг/мин. ЧСС колебалась от 112 до 91 удара в минуту. ЦВД до комбинированной терапии 70 мм в д ст и 80 мм в д ст после. Температура тела оставалась стабильной – 36,4 градуса по Цельсию. На фоне проведенной терапии наблюдалось восстановление сознания и через 14 часов от момента поступления

пациентка экстубирована. Осмотрена неврологом, острой неврологической симптоматики не выявлено. Консультирована психиатром. Рекомендован перевод в психо-неврологический диспансер для дальнейшего лечения.

Результаты и обсуждение.

Амитриптилин является трициклическим антидепрессантом. При тяжелых острых отравлениях наиболее значимы поражение центральной нервной системы (ЦНС), вплоть до развития комы, сердечно-сосудистой системы (ССС) с развитием аритмий и нарушений внутрисердечной проводимости, в том числе и остановки сердечной деятельности, угнетение дыхания. Симптомы развиваются через 4 ч после передозировки, достигают максимума через 24 ч и длятся 4-6 суток. Время достижения максимальной концентрации после приёма внутрь составляет 2.0-7.7 ч. Период полувыведения из плазмы крови длительный - 10-26 ч для амитриптилина и 18-44 ч для его метаболита - нортриптилина. Выводится почками - 80%, главным образом в виде метаболитов, за 2 недели, частично печенью. Препарат имеет высокий объем распределения в организме – 5-10 л/кг. Связь с белками плазмы составляет 96%, поэтому гемодиализ, перитонеальный диализ и форсированный диурез при остром отравлении амитриптилином не эффективны [8].

Циклодол является противопаркинсоническим средством, действующим веществом является тригексифенидил. Характер смертельных осложнений, так же как и у амитриптилина, связан с воздействием на ЦНС, ССС и дыхание. Период выведения циклодола составляет около 5-10 часов, выводится преимущественно почками в неизменном виде [8].

Учитывая эти особенности фармакокинетики токсикантов в комплекс лечения входят энтеросорбенты, методики очищения желудочно-кишечного тракта и сорбционные методы экстракорпоральной гемокоррекции.

Колонки «Цитосорб» применяются при септическом шоке и ряде других критических состояниях, а её применение при остром отравлении основано на исследовании Koertge A. «in vitro», продемонстрировавшее хорошие сорбционные свойства по отношению к амитриптилину [7]. Для оценки адсорбционной способности колонки через 2-3 минуты от начала проведения гемосорбции брали кровь пациентки до поступления в колонку и сразу после выхода из колонки. При химико-токсикологическом исследовании крови, поступающей в колонку, обнаружены: амитриптилин в концентрации 0,95 мг/л и его метаболиты, циклодол в концентрации 0,4 мг/л и гидроксильированный метаболит циклодола. При химико-токсикологическом исследовании крови, вытекающей из колонки, обнаружены амитриптилин и циклодол в следовом количестве. После 6 часов гемосорбции на колонках «Цитосорб» в сыворотке крови при химико-токсикологическом исследовании

обнаружен амитриптилин в концентрации 0,22 мг/л и его метаболиты, циклодол в концентрации 0,13

мг/л и гидроксированный метаболит циклодола (рис.1).

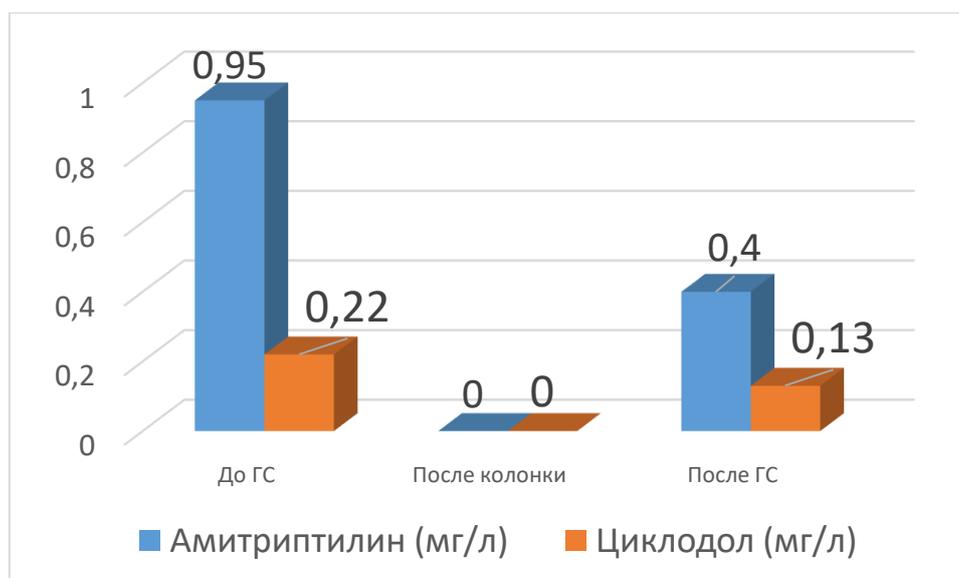


Рис. 1. Динамика уровня амитриптилина и циклодола при гемосорбции на колонке «Цитосорб» при остром отравлении.

По данным Anthony С. Moffat [8] терапевтическая концентрация амитриптилина в сыворотке обычно составляет 01,-0,2 мг/л, летальная концентрация амитриптилина в крови составляет от 0,55 до 16,12 мг/л. Терапевтическая концентрация циклодола в сыворотке составляет 0,05-0,2 мг/л, токсическая концентрация циклодола составляет 0,5 мг/л. Таким образом, на момент проведения гемосорбции в крови имелась летальная концентрация амитриптилина и токсическая концентрация циклодола. При проведении гемосорбции на колонке «Цитосорб» в первый временной промежуток происходит практически 100% удаление амитриптилина и циклодола из крови, что свидетельствует о хороших сорбционных свойствах колонки по отношению к амитриптилину и циклодолу. За 6 часов гемосорбции удалось снизить уровень амитриптилина от исходного более чем в 4 раза и уровень циклодола - более чем в 3 раза. В результате гемосорбции на колонке «Цитосорб» концентрации токсикантов снизились до терапевтического уровня. Сохраняющийся уровень токсикантов через 6 часов процедуры можно объяснить снижением сорбционной емкости колонки и перераспределением в кровь, токсикантов имеющихся большой объемом распределения, из других жидкостных секторов. Для более точного объяснения ситуации необходимы дополнительные исследования.

В соответствии с инструкцией по эксплуатации колонка «Цитосорб» разработана и рекомендуется для проведения гемосорбции в течение длительного времени – до 24 часов. Осложнения в связи с применением колонок возможны в виде реакций гиперчувствительности и аллергических реакций на материал колонки и экстракорпорального контура

(полистерол/дивинилбензол, поликарбонат, полипропилен, силикон, полиэстер), но данные реакции встречаются крайне редко. Противопоказанием к применению колонки является гепарин-индуцированная тромбоцитопения и тромбоцитопения менее 20000 ед/мкл. В нашем случае неблагоприятных событий в связи с проведением гемосорбции на колонке «Цитосорб» при остром отравлении амитриптилином и циклодолом не было. Клинических признаков кровоточивости не установлено. Показатели гемостаза до проведения процедуры составили АЧТВ 29,9 с (референсная норма 25,4-39,9 с), протромбиновая активность по Квику 94% (норма 70-140%), МНО 1,09 (норма 0,9-1,2), тромбоциты $182 \cdot 10^9/\text{л}$. После проведения гемосорбции спустя 3-4 часа показатели гемостаза составили: АЧТВ 49,4 с (референсная норма 25,4-39,9 с), протромбиновое время 13,1с (норма 9,4-12,5 с), протромбиновое отношение 1,1 (норма 0,9-1,2), протромбиновая активность по Квику 85% (норма 70-140%), МНО 1,09 (норма 0,9-1,2), протромбиновое время 24,8 с (норма 15,8-24,9), антитромбин III активность 76% (норма 83-123), фибриноген по Клауссу 2,82 г/л (норма 2-3,93). Тромбоциты $279 \cdot 10^9/\text{л}$. Таким образом, гемосорбция на колонках «Цитосорб» не оказывала отрицательного влияния на показатели гемостаза и уровень тромбоцитов. Удлинение АЧТВ связано с воздействием гепарина.

Заключение. Гемосорбция на колонках «Цитосорб» в комплексном лечении острого отравления амитриптилином и циклодолом является высокоэффективной процедурой, позволяющей снизить концентрации токсикантов с токсического уровня до терапевтического и получить хороший клинический эффект.

Список литературы.

1. Остапенко Ю.Н., Ковалев А.В., Гасимова З.М., Зайковский В.В. Токсикологическая помощь населению Российской Федерации: состояние и проблемы // Токсикологический вестник. 2014. №3. С.2-8. [Ostapenko Ju.N., Kovalev A.V., Gasimova Z.M., Zajkovskij V.V. Toxicological assistance to the population of the Russian Federation: state and problems. Toksikologicheskij vestnik. 2014; (3): 2-8. In Russ].]
2. Маткевич В.А., Лужников Е.А., Рожков П.Г., Белова М.В. Сочетанное применение энтеросорбции и кишечного лаважа при острых пероральных отравлениях психофармакологическими средствами // Токсикологический вестник. 2012. №1. С.26-8. [Matkevich V.A., Luzhnikov E.A., Rozhkov P.G., Belova M.V. The combined use of enterosorption and intestinal lavage in acute oral poisoning with psychopharmacological agents. Toksikologicheskij vestnik. 2012; (1):26-8. (in Russ).]
3. Лужников Е.А., Гольдфарб Ю.С., Бадалян А.В. Детоксикационная терапия острых отравлений химической этиологии на современном этапе // Токсикологический вестник. 2014. №3. С.9-7. [Luzhnikov E.A., Gol'dfarb Ju.S., Badaljan A.V. Detoxification therapy of acute poisoning of chemical etiology at the present stage. Toksikologicheskij vestnik. 2014; (3):9-7. (in Russ).]
4. Лужников Е.А., Гольдфарб Ю.С., Кабанова С.А., Маткевич В.А., Остапенко Ю.Н., Богопольский П.М. Нормативно-правовая база применения методов искусственной детоксикации при острых отравлениях химической этиологии // Токсикологический вестник. 2015. №2. С.2-9. [Luzhnikov E.A., Gol'dfarb Ju.S., Kabanova S.A., Matkevich V.A., Ostapenko Ju.N., Bogopol'skij P.M. The legal framework for the use of artificial detoxification methods for acute poisoning of chemical etiology. Toksikologicheskij vestnik. 2015; (2):2-9. (in Russ).]
5. Баклыкова Н.М. Состав и приготовление сред для внутрикишечного введения при перитоните // Метод. рекомендации. М: Московский городской НИИ скорой помощи им. Н.В.Склифосовского. 1986. С.1-19. [Baklykova N.M. Composition and preparation of media for intrainestinal administration in peritonitis. Method.recommendations. M: N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Healthcare Department; 1986: 1-19. (in Russ).]
6. Толмачева Е.А. // Справочник Видаль. Лекарственные препараты в России 2018. 1240 с. [Tolmacheva E.A. Reference Vidal. Left drugs in Russia; 2018: 1240. (in Russ).]
7. Koertge A, Mitzner S, Wasserkort R. Removal capability of cytosorb hemadsorption columns for selected prescription drugs frequently related to drugs overdose. ESAO congress; 2017. Available at: http://cytosorb-therapy.com/wpcontent/uploads/2018/02/2017_Koertge_Poster_ESAO.pdf
8. Anthony C. Moffat Clarke's Analysis of Drugs and Poisons: In pharmaceuticals, body fluids and postmortem material, London: Pharmaceutical Press, 2004; 2-628.

СОЦИОЛОГИЧЕСКИЕ НАУКИ

ASSESSMENT OF THE LIBRARY INFORMATION SERVICE (MODERN PROBLEMS OF LIBRARY AND INFORMATION SERVICES)

Kazimi Parviz Firudin Oglu

*Baku State University, Associate Professor, Doctor of Philosophy,
+994553704141*

ORKID: - Parviz Kazimi4[0000-0001-5577-4773]

Mammadov Mehmanali Akbar Oglu

Baku State University, Associate Professor, Doctor of Philosophy

ОЦЕНКА БИБЛИОТЕЧНО-ИНФОРМАЦИОННОЙ СЛУЖБЫ (СОВРЕМЕННЫЕ ПРОБЛЕМЫ БИБЛИОТЕЧНО-ИНФОРМАЦИОННОГО ОБСЛУЖИВАНИЯ)

Аннотация. Известно, что ценовая политика в маркетинговой деятельности включает базовую цену, цену контракта, переменную цену, цену сделки, текущую цену, цену со скидкой и т. Д. совмещает методы ценообразования. Библиотеки могут использовать все методы ценообразования в зависимости от общей среды информационного рынка.

Цены на платные библиотечные и информационные услуги, в первую очередь, объем и интенсивность спроса на соответствующие услуги, качество и эффективность услуг (оперативность, полнота, актуальность и др.), Стоимость их разработки, общий размер затрат на рекламу, особенности рынка услуг, цены на других конкурентных рынках. , затраты на стимулирование труда, износ оборудования и, наконец, доход, прибыль и т. д. определяется с учетом факторов. Известно, что такие же затраты возникают и при неоплачиваемых услугах.

Несомненно, формирование цен зависит от технологии подготовки соответствующих услуг в каждой библиотеке и библиотечной системе, профессионального уровня сотрудников и общего состояния материально-технической базы библиотеки. По этим причинам пока невозможно установить единую цену на одну и ту же услугу для всех библиотек.

В настоящее время наиболее широко используемым методом ценообразования в библиотеках является метод «средняя стоимость + прибыль». Размер прибыли при таком методе ценообразования можно рассчитать от 20% до 50% от средней стоимости. Этот метод восходит к советским временам и не отвечает современным требованиям.

С этой точки зрения необходимость разработки единой методики оценки библиотечной и информационной деятельности остается актуальной. Также анализируются мнения всемирно известных специалистов в этом направлении.

Annotation. It is known that the pricing policy in marketing activities includes the base price, the contract price, the variable price, the transaction price, the current price, the discount price, etc., combines pricing methods. Libraries can use all pricing methods depending on the general information market environment.

Prices for paid library and information services, first of all, the volume and intensity of demand for the corresponding services, the quality and efficiency of services (efficiency, completeness, relevance, etc.), the cost of their development, the total amount of advertising costs, features of the service market, prices in other competitive markets. , the cost of labor incentives, wear and tear of equipment and, finally, income, profit, etc. is determined taking into account factors. It is known that the same costs arise for unpaid services.

Undoubtedly, the formation of prices depends on the technology of preparing the corresponding services in each library and library system, the professional level of the staff and the general condition of the material and technical base of the library. For these reasons, it is not yet possible to establish a single price for the same service for all libraries.

Currently, the most widely used pricing method in libraries is the average cost + profit method. The profit margin with this pricing method can be calculated from 20% to 50% of the average cost. This method dates back to Soviet times and does not meet modern requirements.

From this point of view, the need to develop a unified methodology for assessing library and information activities remains relevant. The opinions of world famous experts in this area are also analyzed.

Ключевые слова: информационный рынок, цена информации, информационное обслуживание, библиотечно-информационное обслуживание.

Key words: information market, information price, information service, library and information service.

The group of intangible resources in the production process also includes library and information activities. In the 21st century, the increased interest of information services in the production process requires a separate study of these processes.

Professionals, intellectuals, inventors, regulatory and technical documents, brands, trademarks, copyrights and many other information assets are valued in integration with library information resources. Also, new opportunities to search for information using

modern means of communication, access to paid and free databases, rating and PR technologies are associated with the process of information massaging and dissemination of information, promotion.

Some economists also refer to "relationship capital" as consumer capital. They call "relationship capital" the relationship between the enterprise and the organization's partners (suppliers and recipients). The result of this relationship is that buyers trust and prefer the company. Partnerships often provide more value than material resources.

The specificity of library and information activities, its cultural, social, political, psychological and pedagogical properties have always been a factor that hinders the development of a single formula for evaluating this activity. This issue has always attracted the attention of experts, and in this assessment several directions were taken as a basis: political (representing an attribute of the state and power) assessment and value (representing a material equivalent).

The problem of assessing library and information activities is becoming more and more urgent, since the acceleration of information processes and the growing influence of information on everyday life and the economy ensure the capitalization of information.

Experts believe that the system of economic methods for managing the economy, financial recovery, the development of market relations, balancing the national economy, changing various forms of ownership, self-financing, increasing the efficiency of social production and national income, improving economic mechanisms and its impact on the final product - all this depends on implementation of the pricing mechanism.

As the forms and methods of information services increase, trust in information structures increases in terms of the relevance of the service and the relevance of the request.

At that time, the reliability of the information that the library information service could provide was so high that it was not available in any local or integrated information retrieval system. The relevance of the request can also be high due to the library factor. The library information service is the only structure that provides dialogue between the consumer and the librarian. So far, there are no other ways to guarantee the accuracy and relevance of information outside of this dialogue.

For example, a small example. It is possible to create a library with a collection of one hundred thousand copies for a school library, which, if considered separately, may be considered a rich collection, but would be useless in terms of supporting the teaching in that school.

If this example is applied to the structures of government, we will face a great information chaos. So the success of the information service is not in the size of the fund, but in its rationality. At all times, the factor that ensures this rationality has been that of the professional librarian.

The desire to have full access to the growing mass of information in the global information space is impossible and unnecessary. If professional library

information activity is used, the criteria of supply and demand are properly studied, it is possible to correctly assess the information process, information product, and get high rates. In his book "Modern problems of librarianship" Professor A.A. Khalafov shows that the use of modern technologies, the growth of information masses, the complexity of consumer demands require new approaches to the theory of librarianship.

Today, when the requirements of consumers, forms and methods of requesting information, methods of searching for information are becoming more complicated, a new level of professionalism requires the assessment of information, information process, information product with new criteria.

But how to evaluate library and information activities? In the classical economic literature, pricing is determined by the following formula:

$$\text{Price} = \text{cost} + \text{profit} + \text{tax}$$

In many cases, marketing costs are added to the above pricing formula, which play an important role in pricing. Marketing is becoming more and more important in today's globalized society.

Building an informed society requires that the assessment of library and information activities be more differentiated and expressed in more specific formulas.

The works of American, English and Russian researchers on the problem are limited to commentaries on the problem in only one direction. The work of the British researcher B. Peter "Assessment of Library Activity" (meaning the monograph translated into Russian in 2009) attracts attention in this direction.

Given the complex functionality of library and information activities, B. Peter identifies and analyzes the categories of assessment activities. When adding the "goal" function to the Investigator Assessment Model, the following picture emerges.

Resource-goal-process-product-result-impact

This can be an approximate structure of the system for assessing library and information activities.

Evaluating the information, the experts tried to approach the issue from the following point of view.

- 1. Evaluation of information**
- 2. Evaluation of the information product**
- 3. Evaluation of the information process.**
- 4. Rate the quality of the information.**

The well-known Russian researcher Yuzvishin considers the information invaluable. This is the main tool for the development of nature and society. Other experts evaluate an information product in terms of the amount of time spent on it and the cost of the process. In the field of assessing the quality of information, researchers have put forward broader and more meaningful ideas.

American researchers recommend using the criteria of accuracy and completeness when assessing the quality of information. For example, out of 10,000 units of information, there is information that corresponds to only 50 units of a request. Real search capabilities only find 25 units, of which only 20 match the topic and 5 units do not match the query. In this case, the accuracy is expressed by the formula $20/25 = 0.8$, completeness $20/50 = 0.4$. It is also noteworthy that

these formulas can be applied to the service provided by modern means of communication, as well as to the traditional service of library information activities. These methods are also used in modern automated information retrieval systems and are used to determine the effectiveness of a service.

Methods for measuring the quality of library and information activities can only be considered important as a system. Thus, it is advisable to conduct a systematic analysis of the organizational model. For this, the structure of the assessment system proposed by B. Peter is extremely important.

When assessing the information activity of a library, it can be considered only as a conditional assessment of the processes carried out in the direction of creating an information product. Thus, the assessment of the socio-political effectiveness of library and information activities, the assessment of pedagogical and psychological effectiveness are calculated according to different criteria. Evaluation of information services in the course of library and information activities serving state and national interests should be carried out by evaluating the "result" and "impact" functions in the algorithms specified by B. Peter.

At present, the assessment of the goals of the information activity of the library is interpreted by the nature of the goal. For example, information security and national interests are heavily funded and become part of the day-to-day work of broad information structures. In a market economy, competing parties often adapt pricing policies to their goals and manipulate market prices.

In addition, since the outcome and impact categories have social and political implications, the formula $\text{Price} = \text{Target} + \text{Income} + \text{Tax}$ does not match its estimate. In this regard, the proposed formula for the overall assessment of library and information activities can be summarized as follows.

$$\text{Price} = \text{Objective} - (\text{Information Product} + \text{Result} + \text{Impact}) = 0$$

In the presented formula

- general assessment of the information activity of the library,
- financial resources allocated in accordance with the objectives,
- the cost of the information product,
- the financial equivalent of the result.

So, $\text{Price} = 0$ if the financial resources allocated in accordance with the conditional goals become a relevant information product and the corresponding result is obtained (then the average rational amount of funds allocated to each consumer) and the effectiveness of these results fully corresponds to the goals, the optimal cost of the library's information activities is zero. If the equality is above zero, we can talk about the effectiveness of the team, the use of innovative methods and best practices, if it is below zero, the lack of professionalism of the team, they do not cope with their responsibilities.

In Peter's algorithms, all components characterize and depend on each other. For example, an information product resulting from library and information

activities ultimately becomes an information resource. Information retrieval processes, as well as service processes, the implementation of goals and objectives depends on the material and technical base of the enterprise, the results depend on it and affect the quality of efficiency.

The "goal" component that we add to the algorithms is involved in both shaping and evaluating most of the other components.

Evaluation of the Objective component takes place over time and space, defines policies and funding systems, and is expressed in a specific framework. For example, the scope of government funding for educational literature, the budget allocated to various library and information institutions, the difference in the cost of librarians' work is determined by goals. Targets also contribute to the pricing of products. A number of information resources, despite their specific value, are distributed free of charge, which serves this purpose. In other cases, the information sold in the high-paying information marketplace for profit is also consistent with the purpose.

Economic theorists argue that the globalization of society has led to the transition from a commodity economy to a financial economy, and the informatization of a global society has provided a transition from a financial economy to an information economy. Consequently, in the context of the information economy, prices for information resources, information products and information processes, pricing mechanisms should be based on relevant laws, formulas and be adequate. The results and effectiveness of modern assessment methods (IF-impact factor) in many cases can be justified in the scientific literature. However, this does not apply to social literature, especially fiction. According to the statistics of the Russian State Library for 2010, Dantsova's works were circulated in the country more than Dostaevsky's works, books were sold in publishing houses, more books were made out in libraries. This increases the "impact factor" of Dansova, but does not make it more valuable than Dostaevsky's works. Also, according to M. Tunjay from Thomson Reuters, "the archaeological excavations at the mound in the province of Kazakhstan contain very important information for Kazakhstan, but according to the international rating, IF may be zero."

In the scientific literature, the IF score is based on a reference system. Suppose that a chemical laboratory has been working on an important project for 6 years and submits a scientific article at the end of the project. expressed in numbers. Since these rates are only valid for one year, new rates are calculated for the next year. In this case, the study is only mentioned in another work, and this work is nominated for a Nobel Prize or State Prize for its importance. This indicator does not affect the impact factor of the article.

By the way, it should be noted that in the current pandemic, the importance of various scientific articles and scientific papers will not be able to compete with the topic of Covid-19.

Many Russian researchers have noted in their writings that the assessment based on "reference" is conditional. However, since at present this is the only

working mechanism in the rating assessment process and is of a commercial nature, no alternative to assessing the impact factor through the analysis of "references" has yet been formed.

A number of international organizations involved in information marketing use special pricing mechanisms. These methods, widely used in practice, can be grouped as follows.

1. Assessment per unit of information
2. Assess the use of information over time.
3. Evaluation of information "by number" of users.

For example, (conditionally) the use of the Russian National Electronic Library occurs online, and a document (depending on its size) is sold to users for 0.1–12 US dollars. The watch requires \$ 8 for usability. Another company, Lexis Nexis, determines the annual subscription based on the number of people served by the libraries. \$ 5,000 for 50 thousand people, \$ 8 thousand for 100 thousand people, 10 thousand for 250 thousand people, 20 thousand for 500 thousand, 35 thousand for 1 million, 60 thousand for 2 million, for a library network with more than 2 million potential customers At a price of \$ 70,000.

When analyzing prices in information resource centers, which are especially active in the information market, there is a serious impact on the prices of marketing technologies, special PR-companies. Information is capitalized gradually and continuously.

At the present stage of the rapidly growing informatization of economic relations, the development of market relations requires the emergence of a new global market for information services, and this market is being formed. The specificity of modern market relations, involving the interaction of subjects of different composition, interests and goals, requires the formation of a new stage that allows everyone to use information resources.

Probably, the conditional "chaos" will continue on the information market for some time. In the near future, it is necessary to take many legal and organizational measures to regulate the information market throughout the world.

LIST OF REFERENCES

1. Xələfov A.A. Kitabxanaşünaslığın müasir problemləri. Bakı. BDU-nun nəşri. 2012. 56 s.
2. Kazimi P.F. İnformasiya mühəndisliyi kitabxana fəaliyyətində . B. BDU., 2011.-230 s.
3. Məmmədov M. Ə. Kitabxanaların idarə olunmasında marketinqin rolu//Kitabxanaşünaslıq və bibliografiya, elmi-nəzəri, metodiki və təcrübi jurnal.- B., 2009.-N1,- s.47-54
4. Qurbanov A., Kazimi P., Məmmədov M., Kitabxana informasiya fəaliyyətinin menecmenti və marketinqi. Bakı. Mütərcim. 2012. 280 s.
5. Сусллова И.М. Ключев В. К. Менеджмент библиотечно-информационной деятельности. М. Профессия. 2011.-610 стр.
6. Колесникова М.Н. Менеджмент библиотечно-информационной деятельности. 2009.-390 стр.
7. Казими П. Информационная инженерия. Германия. Ламберто Академия Публикейшн. 2013. 84 с.
8. Голубенко Н.Б. информационные технологии в библиотечном деле. Ростов н/д, Феникс, 2012, 282 стр.
9. Форсайт Патрик. Маркетинг в книгоиздании. - М.; Школа издательского и медиа бизнеса, 2012.-221 стр.
10. Брофи Питер. Оценка деятельности библиотек: Принципы и методы.-М.; «Омега-Л», 2009.-357 стр.

SOCIO-HEALTH CONSEQUENCES OF THE RISKS OF SENIORS

Bočáková Oľga

associate professor

University of Ss. Cyril and Methodius in Trnava

Faculty of Social Sciences

Slovak republic

Kubičková Darina

assistant professor

University of Ss. Cyril and Methodius in Trnava

Faculty of Social Sciences

Slovak republic

Abstract. Seniors need to have contact with other people because they are often not only dependent on them, but very eager to have and feel the closeness of humanity. At the same time they feel lonely, their emotional satisfaction is valuable at their age, bringing their own social price to the forefront and last but not least the priority to belong to others. The aging phase is linked to the very narrow position of seniors in society, and their social status is deplorably low. The manifestations of this dimension are correlated with attributing the negative qualities of their personality and the associated low competencies.

Keywords: Seniors. Society. Social status. Aging. Health.

People who retire change their established life regime. The change and coping with it is not easy for everyone. By retirement, society loses its wealth, valuable experience, and knowledge of the creative

paradigm. If we evaluate the current attitude in society towards seniors, we can state that in the ranking of values it is in the negative bar. Old age is understood as the next stage of a person's life path, which is classified

in terms of negative perception, such as deterioration, reduced competences, burden and often even a heavy burden. Humanity and positive acceptance cannot be considered in this dimension. The situation in the current social climate calls for society to accept the old age and the process of human aging as a reality and natural development, because it is an inseparable part of life. The vision and consequently the goal of our living and existence in society cannot be the segregation of seniors, but rather their integration into it. Man begins to age at his/her birth, that is, at this very moment of life, s/he begins the process of aging. The key issue for the aging process is the genetic base itself and the equipment of the family environment. Aging is an irreversible biological process that affects whole nature. Life expectancy is genetically determined and specific to each species. The same is true of humans where a multifactor type of inheritance is assumed. Old age is the final stage of the aging process, it is the end of the natural evolutionary process of each individual" [11].

Social aging is manifested by a decrease in interest in its environment, loss of various activities, impairment of adaptation, etc. Draganová (2006) is of the opinion that "the stage of old age as a social phenomenon is dealt with by applied sociology, which is called gerontology. The increasing share of older people in the demographic structure of the population and the changes in social relations brought by old age raise a specific social issue that is becoming the subject of the sociology of old age". The social aspect of aging is closely related to retirement, which can evoke in the elderly the loss of friends, direct contacts, colleagues, loss of status or financial loss [2].

According to Dvořáčková (2012), another manifestation of social hardship is that "elderly people show loneliness, often feel lost, without love, unnecessary, lacking support from family and loved ones. All these aspects can lead to subsequent anxiety or depression, causing aggression, accompanied by anger, which may further increase loneliness." [3] In a deeper analysis, the phenomenon of loneliness can be distinguished from the perception of different aspects. Kupka (2014) divides loneliness as follows:

- interpersonal loneliness,
- intrapersonal loneliness,
- existential loneliness,
- social isolation,
- emotional isolation [9].

According to Žiaková (2008), the causes of loneliness are:

- causes of personality variables
- situational variables [15]

The first perception of causes is the long-term survival of loneliness. Depression is closely expressed and associated to this assignment. The content of the loneliness is the fact that each person perceives and experiences his/her life situation differently and consequently the loneliness itself can manifest. The most common causes belonging to this state of causes are e.g. long-term illness, divorce, care for sick parents, etc. Hrozenková and Dvořáčková (2013) appeal to the needs of seniors and recall that "the concept of social functioning is considered important" [4].

"Since time immemorial, people have been forced to contemplate their lives and reflect on its meaning. Although they understood the meaning of life in practical terms, such considerations became a source of inspiration and potential changes for which this reasoning motivated them. They lacked the concept of quality of life as we know it at present" ([12].

"The first approach was to the quality of life in today's understanding of healthcare in connection with psychiatric patients and even chronically ill people, whose impact of the disease manifested itself not only in the physical and mental sphere, but also socially. Later, the problem of quality of life came from healthcare facilities to the general public, especially in connection with new health and social problems" [12].

"Family life is of great importance to the elderly and he usually expects some help from the family. It makes it possible to create an emotional and social background for the last phase of life, which is extremely important for aging and old age. In fact, the emotional background function is actually the only function that the present family has retained and has not given to society" [6]

The aim of social policy is to eliminate or at least alleviate the unfavorable social situation of the individual, the family. The social policy tool is social security, which consists of: social insurance, social support, social assistance, and social services have a special position [1].

Another important aspect for humans at any age is health care. As stated in the statistics people in the EU are most likely to die from circulatory diseases (ischemic heart disease, cerebrovascular disease) and cancer. Risk factors such as smoking, excessive alcohol consumption, unhealthy diets contribute significantly to the development of these diseases. "Adult people, leading a healthy lifestyle that includes physical exercise, eating fruits and vegetables, avoiding smoking and drinking alcohol can expect 12 years longer life than they would otherwise" [5]

The table shows that the chances of an individual in his/her 70's to live 90's are decreasing with an increasing number of risk factors in his/her lifestyle.

Table 1

The presence of risk factors in the 70's

None of the five risk factors	54
Sedentary lifestyle	44
High blood pressure	42
Obesity	32
Diabetes	28
Smoking	25
Three out of five risk factors	14
All five risk factors	4

Source: Yates et al., 2008, Sarafino & Smith (2011) [13]

The mission of protecting and promoting health, including the senior population, is to consolidate, protect and promote health through community-wide measures, with the emphasis on multi-sectoral cooperation. International and national community programs, including seniors as the target group, are also an important part of the support and protection of seniors' health.

Seniors, as a risk group, very often become the object of violence for various reasons and reasons. The rights of seniors are dealt within our country by the Program of Protection of the Elderly, adopted by the Government of the Slovak Republic in 1999. The seniors must feel sure that they will receive adequate assistance in case of ill-treatment.

Piscová (2007) states that "the economic and social level of aging is the most widely presented issue in media. However, very little is said about how society should reflect on old age as such, what quality of life in old age should have, what conditions for old people should be ensured by society itself" [10] It is necessary to state that the rights of the elderly unfold and

participate in the context of fundamental human rights, without age restriction. "The general rights of older people are contained in the International Aging Action Plan adopted by the United Nations General Assembly in 1992. Equally, the rights of older patients are declared in the Charter of the Rights of the Elder, proclaimed by the International Geriatric Association in Adelaide, Australia in 1997" [11].

We can say that the poor or even morbid treatment of older people by their own family and others has only recently come to the attention. Kalvach (1995) states that "risk groups in terms of abuse and abuse include:

- *ordinary women, widows, aged 70-80 with lower education than the secondary,*
- *pensioners on the poverty line, but also elderly people with sufficient wealth,*
- *elderly people living with their relatives,*
- *defenseless and vulnerable persons with physical and mental loss" [7]*

Table 2

Profile of the victim of violence

Health group	Socio - economic group
mentally ill people	disabled
people with dementia	lonely older people
somatically ill people	wealthy older people
sensory impaired people	poor elderly people
physically impaired	roommates of older parents in multi-generation families
disabled people	institutionalized older people
dying people	

Source: Koval' (2001) [8]

Table 3

Overview of forms of elder abuse

Harassment	Neglect	Exploitation	Misuse	Abuse
emotional	active	financial	property	mental
physical	passive	property	emotional	physical
sexually	self-neglect	physical	political	systematic

Source: Koval' (2001) [8]

The issue of elder abuse is often taboo in our society. However, this does not lead to the conclusion that it does not exist. Mostly they are hidden or more precisely classified cases that rarely or at all come to the surface.

Tošnerová (2000) explains that "the cultural maturity of a nation is measured by various partial sometimes comical measures of e.g. mouthwash, soap, paper, water and so on. However, it is best documented

by how it cares for geronts and what the old age of geronts of that nation is like." [14].

BIBLIOGRAPHICAL REFERENCES

- [1] BOČÁKOVÁ, O. 2015. Sociálna politika a sociálne zabezpečenie (vysokoškolská učebnica). Brno: TRIBUN EU, s r. o., 2015. s.170. ISBN 978-80-263-0938-3.

- [2] DRAGANOVÁ, H. 2006. Sociálna starostlivosť. Osveta. ISBN 978-80-8063-240-3.
- [3] DVOŘÁČKOVÁ, D. 2012. Kvalita života seniorů – v domovech pro seniory. Praha: Grada. ISBN 978-80-247-4138-3.
- [4] HROZENSKÁ, M., DVOŘÁČKOVÁ, D. 2013. Sociální péče o seniory. Praha: Grada. ISBN 978-80-247-4139-0.
- [5] KVAAVIK, E., BATTY, G. D., URSIN, G., HUXLEY, R., & GALE, C. R. 2010. Influence of individual and combined health behaviors on total and cause-specific mortality in men and women: The United Kingdom Health and Lifestyle Survey. Archives of Internal Medicine.
- [6] JANKOVÝCHOVÁ, L., BELOVIČOVÁ, M. Zdravé starnutie a kvalita života seniorov. Ošetrovateľský obzor 6, 2009, č. 3, s. 90. Dostupné na internete: <<http://www.osevratelsky.herba.sk/3-2009/zdrave-starnutie-a-kvalita-zivota-seniorov>>.
- [7] KALVACH, Z. 1997. Týrání, zneužívání a zanedbávání seniorů jako medicínský problém Praha: Česká lékařská společnost J. E. Purkyně. 1997, roč. 136, č. 6. ISSN 0008–7335.
- [8] KOVAL, Š. 2001. Týranie starších ľudí. Košice Pont. ISBN 80-967611-2-9.
- [9] KUPKA, M. 2014. Psychosociální aspekty paliativní péče. Praha Grada. ISBN 978-80-247-4650-0.
- [10] PISCOVÁ, M. 2007. Aktivna staroba: želanie alebo realita? Forum. Scientiae et Sapientiae. XIV/1: 40–41. ISBN 80-7149-865-3.
- [11] POLEDNÍKOVÁ, E. 2006. Geriatrické a gerontologické ošetrovateľstvo. Martin: Vydavateľstvo Osveta, spol. s. r. o. ISBN 80-8063-208-1.
- [12] RADKOVÁ, L., BIELOVÁ, M. 2004. Spokojnosť občanov v domovoch dôchodcov ako súčasť kvality života. Geriatria, 2004, č. 2, s. 59 -60. ISSN 1335-1850.
- [13] SERAFINO, E. P., & SMITH, T.W. 2011 Health Psychology: Biopsychosocial Interactions. New York: John Wiley & Sons, Inc. ISBN 9781118425206.
- [14] TOŠNEROVÁ T. 2000. Špatné zacházení se seniory a násilí v rodině - průvodce pro zdravotníky a profesionální pečovatele. Praha: UK Ambulance pro poruchy paměti. 2000. ISBN 80-238-5875-0.
- [15] ŽIAKOVÁ, E. 2008. Osamelosť ako sociálny a psychologický jav. Prežívanie osamelosti vo vybraných sociálne rizikových skupinách. Prešov: Grafotlač. ISBN 978-80-8068-731-1.

THE SELF-GOVERNING REGION OF TRENCIN IN THE DIMENSIONS OF SOCIAL CARE AND SOCIAL HELP

Bočáková Oľga

associate professor

University of Ss. Cyril and Methodius in Trnava

Faculty of Social Sciences

Slovak republic

Adamkovičová Beáta

assistant professor

University of Ss. Cyril and Methodius in Trnava

Faculty of Social Sciences

Slovak republic

Abstract. In this paper, we focus on the self-governing region of Trenčín. On the basis of statistical data, we offer an overview of social policy and social security. We focus also on social care, social support in dimensions of Trenčín region. As for social services, we deal with compensations for persons with disabilities.

Keywords: Self-governing region. Social care. Social policy. Social security. Social help. Social services. Statistics.

Higher territorial unit, self-governing region, is a basic unit of regional self-administration. As stated by Peková et. al. (2002), the main objective of regional self-administration, is a care for the needs of citizens of given region or territory. In this paper, we focus on the self-governing region of Trenčín in the dimensions of social care for citizens and social help [4].

The self-governing region of Trenčín is located in the northwestern part of Slovakia and its area is 4,501 km². The self-governing region of Trenčín has the population of more than 587,364 citizens.

Districts of the self-governing region of Trenčín are shown on the Map 1.

Map 1. Districts of the self-governing region of Trenčín



Source: The self-governing region of Trenčín [6]

The self-governing region of Trenčín consists of 9 districts. In following table, we are focusing on demographic indicators about the population of the self-governing region of Trenčín.

Based on obtained data from Statistical Office of SR from 2018, we introduce the demography of the population in the self-governing region of Trenčín.

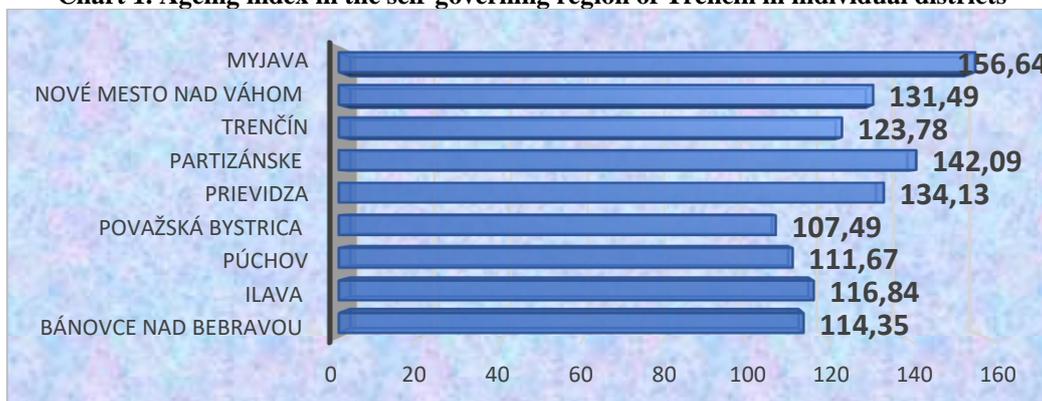
Table 1.

Demographic profile of the population in the self-governing region of Trenčín

	YEAR 2018
Population of SGRT	587 364
Share of SGRT population on total population of SR	10,79 %
Average age of SGRT population	40,22
Population 0-14 years old	79 961
Population 15-64 years old	407 024
Population 65 years old and more	100 379
Ageing index	125,53

Source: Statistical office of SR, 2018 []

Chart 1. Ageing index in the self-governing region of Trenčín in individual districts



Source: Statistical office of SR, 2018 [6]

From the chart, we can deduce that the highest ageing index is in Myjava district, and the lowest is in Povazska Bystrica district.

Bočáková (2015) states that a work belongs to the main attributes of an individual. A work represents irreplaceable place in human’s life. It is a basic condition for dignified existence. Besides the material benefits, a work provides also a feeling of self-realization and social usefulness, and it helps create social connections and relationships [1]. Magurová (2007) state following contributions of work and work-life:

- Provides an opportunity to ensure financial security
- It is a source for securing the living
- Enables social contact with other people
- Provides an opportunity for social position and personal prestige
- Enables to assert oneself and present own ideas and thoughts [2]

Nowadays, unemployment belongs to main social problems. Unemployment is accompanied by the

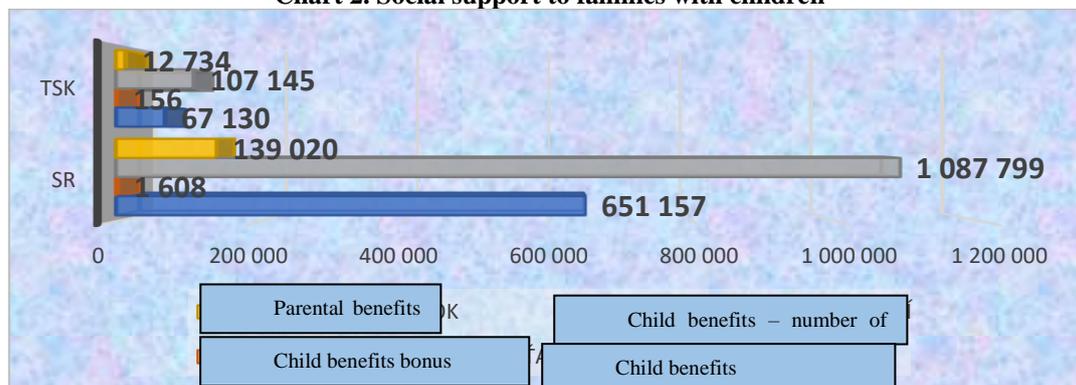
decrease of life quality, social exclusion, decrease of self-confidence and in some cases also social-pathological events.

Social insurance is a basis of social security. As stated by Bočáková (2015) it is characterized according to risks, for which insurance covering are determined, and according to population insurance groups [1]. Regarding the right for benefits, this is connected with paying the contributions. Social insurance, as written by Repková (2012), represents financial security of an individual and family members in the period of appearance of life situations [5]. These can be predicted, and against which the given person is insured.

In the area of social care for the population, the first place is taken by social support for families, which got into unpleasant social situation.

In following chart and table, we focus on providing the social support to families with children in the self-governing region of Trenčín.

Chart 2. Social support to families with children



Source: Office of labor, social affairs, and family, 2020 [3]

In December 2019, in Slovak Republic, there was provided 651,157 child benefit payments, 1,608 child benefit bonuses, and the parental benefit was drawn by 139,020 parents. In the same period, in the self-governing region of Trenčín, the child benefit was

provided in 67,130 cases, child benefit bonus in 156 cases, and the parental benefit was drawn by 12,734 parents.

In individual districts of the self-governing region of Trenčín, the data are following.

Table 2.

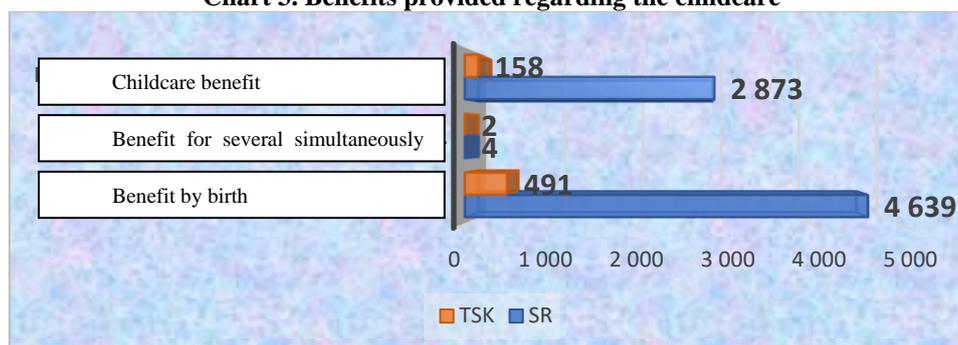
Providing of social support to families with children in the self-governing region of Trenčín in 2019

DISTRICT	CHILD BENEFIT	CHILD BENEFIT BONUS	CHILD BENEFIT – NUMBER OF CHILDREN	PARENTAL BENEFIT
Bánovce nad Bebravou	4 272	9	6 909	784
Ilava	6 770	17	10 826	1 259
Myjava	2 829	6	4 341	538
Nové Mesto nad Váhom	7 368	10	11 757	1 414
Partizánske	4 928	12	7 810	967
Považská Bystrica	7 448	9	12 065	1 472
Prievidza	14 527	60	22 585	2 762
Púchov	5 431	9	8 863	1 046
Trenčín	13 557	24	21 989	2 492

Source: Office of labor, social affairs, and family, 2020 [3]

Below, you can also see the overview of provided benefits on childcare, benefits by birth, etc.

Chart 3. Benefits provided regarding the childcare



Source: Office of labor, social affairs, and family, 2020 [3]

In December 2019, in Slovak Republic, there was provided 4,639 benefits by birth, from which in the self-governing region of Trenčín it was 491 benefits.

Based on data from the Office of labor, social affairs, and family, 2020, we have processed benefits provided for a childcare according to individual districts of the self-governing region of Trenčín.

Table 3.

Benefits provided for a childcare in individual districts of the self-governing region of Trenčín

DISTRICT	BENEFIT BY BIRTH	BENEFIT FOR SEVERAL SIMULTANEOUSLY BORN CHILDREN	CHILDCARE BENEFIT
Bánovce nad Bebravou	19	1	3
Ilava	58	0	25
Myjava	14	0	2
Nové Mesto nad Váhom	53	0	13
Partizánske	39	0	6
Považská Bystrica	59	0	18
Prievidza	106	0	27
Púchov	38	0	18
Trenčín	105	1	46

Source: Office of labor, social affairs, and family, 2020 [3]

The most benefits by birth in December 2019 was provided in the district of Prievidza and Trenčín. The task of the state and the self-governing region is also to deal with social care of a person/persons with

disabilities. In this regard, an important role plays the Act 448/2008 Coll. on social services, and the Act 447/2008 Coll. on financial contributions for the compensation of serious disabilities.

Table 4.

Provided selected compensations for persons with serious disabilities in the self-governing region of Trenčín in December 2019

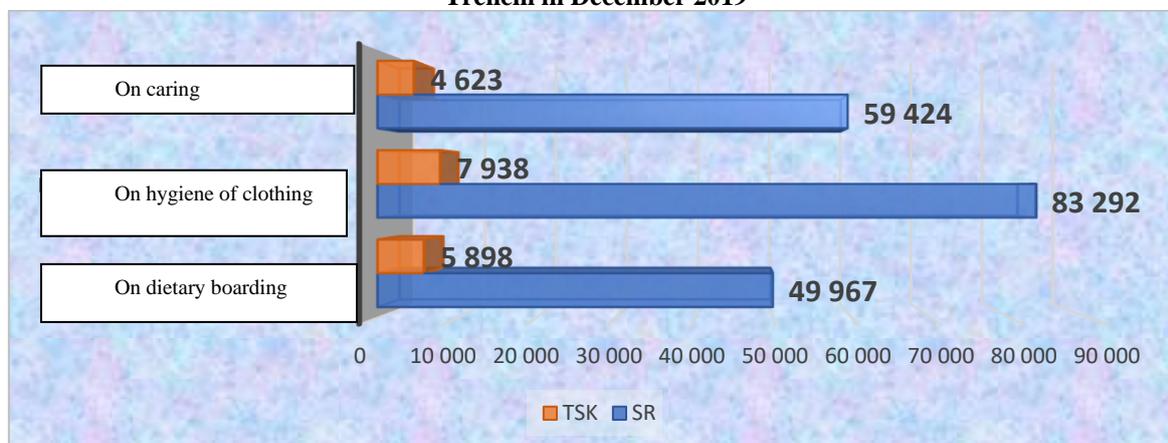
DISTRICT	PERSONAL ASSISTANCE	TRANSPORTATION	OPERATION OF PASSENGER VEHICLE
Bánovce nad Bebravou	46	15	335
Ilava	54	2	303
Myjava	20	3	162
Nové Mesto nad Váhom	64	1	533
Partizánske	67	13	377
Považská Bystrica	73	5	468
Prievidza	133	19	1 037
Púchov	36	6	326
Trenčín	150	24	551

Source: Office of labor, social affairs, and family, 2020 [3]

Relatively frequent compensation of serious disability is providing the benefit on the operation of passenger vehicle.

Chart 4.

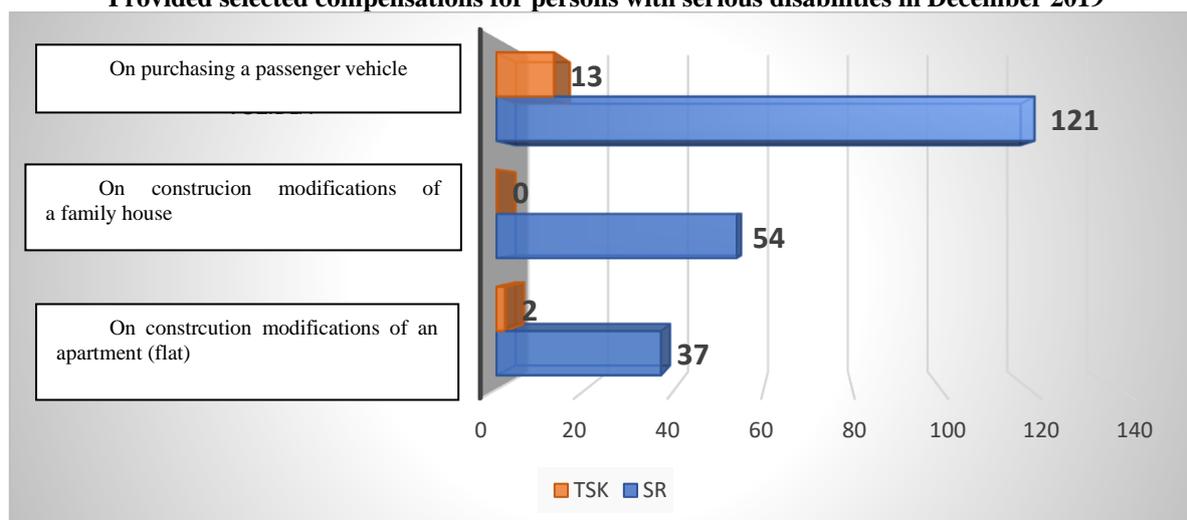
Provided selected compensations for persons with serious disabilities in the self-governing region of Trenčín in December 2019



Source: Office of labor, social affairs, and family, 2020

Chart 5.

Provided selected compensations for persons with serious disabilities in December 2019



Source: Office of labor, social affairs, and family, 2020 [3]

Table 5.

Provided selected compensations for persons with serious disabilities in the self-governing region on Trenčín in December 2019

DISTRICT	ON CONSTRUCTION MODIFICATIONS OF AN APARTMENT (FLAT)	ON CONSTRUCTION MODIFICATIONS OF A FAMILY HOUSE	ON PURCHASING A PASSENGER VEHICLE
Bánovce nad Bebravou	0	0	1
Ilava	0	0	1
Myjava	0	0	0
Nové Mesto nad Váhom	2	0	3
Partizánske	0	0	0
Považská Bystrica	0	0	3
Prievidza	0	0	2
Púchov	0	0	1

Trenčín	0	0	2
----------------	---	---	---

Source: *Office of labor, social affairs, and family, 2020* [3]

In the area of social care, social help is provided to people in unpleasant social situation in the form of a benefit in material need.

Material need is a state, when the income of household members does not reach the sum of life

minimum, and household members are not able or cannot ensure or increase the income. A life minimum is 214,83 Euro per normal person.

Table 6.

Number of receivers of benefits in material need in the self-governing region of Trenčín

DISTRICT	NUMBER OF RECEIVERS OF BENEFITS IN MATERIAL NEED	SHARE OF PERSONS IN MATERIAL NEED ON THE POPULATION IN %
Partizánske	534	1,17
Bánovce nad Bebravou	290	0,80
Považská Bystrica	380	0,61
Prievidza	811	0,60
Myjava	130	0,49
Ilava	283	0,48
Nové Mesto nad Váhom	231	0,37
Púchov	160	0,36
Trenčín	380	0,33

Source: *Office of labor, social affairs, and family, 2020* [3]

The most registered persons receiving the benefit in material need in the self-governing region of Trenčín is in Prievidza district.

Social services are usually understood as services of various social subjects aimed at social needs of people, who would get into the state of social need without these services, or at least in the risk zone for falling into this state [5].

Social services are one of forms of social help for people in unpleasant social situation. A problem of the self-governing region of Trenčín is (un)availability of social services. People criticize long waiting period for placing into the facilities of social services. Nowadays, a big focus is put on the quality, financing, and availability of social services.

Current trend in social services is their deinstitutionalizing and a transfer to community social care.

Regarding the objectives and priorities of development of social services in the self-governing region of Trenčín, we introduce following factors:

Ensuring the availability of social services in accordance with the community needs

- support of persons with disabilities
- support of families with children
- support of persons in unpleasant life situation
- support of remaining the persons in home environment

Support of the transfer of social services receivers from institutional care to community care

- building of independent family houses
- support of independent living
- activation for independency of persons with disabilities

Increasing the quality of provided social services

- area of personal conditions
- area of material conditions

We have tried to map the situation in the area of social care and social help in the self-governing region of Trenčín. In this region, institutional care predominates over home care. Home care is less costly for the state, and it is an advantage for a client / patient, since he/she stays in a home environment. A particularly important place in the system of social services belongs to day-caring.

We can state that social care and social help is on the level of all-Slovakia average.

Reference:

[1] BOČÁKOVÁ, O. 2015. Sociálna politika a sociálne zabezpečenie. Brno : Tribun, 2015. 170 p. ISBN 978-80-263-0938-3.

[2] MAGUROVÁ D. 2007. Hospic- model a filozofia starostlivosti o chorých. In: Ošetrovatelstvo a pôrodná asistancia. V, 2007, number 6, pp. 4-6.

[3] Office of labor, social affairs, and family, 2020. Available on: <https://www.upsvr.gov.sk/>

[4] PEKOVÁ, J. 2002. Veřejné finance. Praha : Aspi Publishing, 2002. 456 p. ISBN 80-86395-21-9.

[5] REPKOVÁ, K. 2012. Sociálne služby v kontexte komunálnej sociálnej politiky. Bratislava : IVPR, 2012. 176 p. ISBN: 978-80-7138-135-8.

[6] Statistical office of SR. Available on: <https://www.statistics.sk/>

[7] The self-governing region of Trenčín. Available on: <https://www.tsk.sk/>

Editor in Chief – Ivaschuk G. O., Doctor of Technical Sciences, Kiev Institute of Technology, Kiev, Ukraine

Assistant Editor – Stepanenko O.I., Doctor of Physical Sciences, Ternopol National Technical University, Ternopol, Ukraine

- Alfred Merphi - Doctor of Economics, University of Chicago, Chicago, United States
- Yen Lee - MD, wellness center «You Kang», Sanya, China
- Avital Gurvic - Doctor of Education, University of Haifa, Haifa, Israel
- George Perry - Doctor of Chemistry, Columbia College, New York, USA
- Isa Wright - Doctor of Sociology, Moraine Valley Community College, Chicago, USA
- Jessie Simmons - Doctor of Engineering Sciences, San Diego State University, San Diego, USA
- Nelson Flores - Doctor of Philology, Wheelock College, Boston, USA
- Andrey Chigrintsev - Doctor of Geographical Sciences, University of South Carolina, Columbia, United States
- Oleg Krivtsov - Doctor of History, National Museum of Natural History, Washington, USA
- Angelina Pavlovna Alushteva - Candidate of Technical Sciences, Institute of Computer Systems and Information Security (ICSiIS), Krasnodar, Russian Federation
- Elena Dmitrevna Lapenko - Candidate of Law, Institute of Law, Volgograd, Russian Federation
- Aleksandr Ole - Doctor of Biological Chemistry, University of Stavanger, Stavanger, Norway
- Emily Wells - Doctor of Psychological Sciences, Coventry University, Coventry, England
- Leon Mendes - Doctor of Pharmaceutical Sciences, Universitat de Barcelona, Spain
- Martin Lenc - Doctor of Economics, Uni Köln, Germany
- Adel Barkova - Doctor of Political Sciences, Univerzita Karlova v Praze, Prague, Czech Republic
- Vidya Bhatt - Candidate of Medical Science, University of Delhi, New Delhi, India
- Agachi Lundzhil - Doctor of Law, The North-West University, Potchefstroom, South Africa
- Musaev Odil Rakhmatovich – prof. Department of Theory and Practice of Democratic State Building of the National University of Uzbekistan

Layout man: Mark O'Donovan
Layout: Catherine Johnson

Consulting group "Education and Science"
Ukraine, Kiev, Peremogi, 56/1, office 115
Web-site: <https://american-issue.info>
E-mail: info@american-issue.com

Copies: 1000 copies.
Ukraine, Kiev, Peremogi, 56/1, office 115