არეობისათვის დამახასიათებელი კლინიკური და ბიოქიმიური სინდრომების ინტენსივობის სიხშირე, მეორადი არტერიული ჰიპერტენზიის თანდართვის პირობებში (პორტალური ჰიპერტენზიის სინდრომი, ხოლესტაზი, მეზენხიმური ანთება). თირკმელების I-III სტადიის ქრონიკულ დაავადებასთან ერთად მიმდინარე არაალკოჰოლური სტეატოჰეპატიტისათვის დამახასიათებელია ღვიძლის სტეატოზის უფრო მაღალი ხარისხი, ვიდრე ავადმყოფებში მხოლოდ არაალკოჰოლური სტეატოჰეპატიტით ($p<0,05$), ასევე, უფრო მაღალია ჰეპატორენალური ინდექსის მაჩვენებლის დიაგნოსტიკური ზღვარი, რომელიც მჭიდრო კავშირშია Steato-test-ის მაჩვენებელთან ($p<0,001$).

CEREBROSPINAL FLUID LEVELS OF NEUROSPECIFIC MARKERS IN ADULT PATIENTS WITH BACTERIAL MENINGITIS

Sokhan A., Zots Y., Gavrylov A., Iurko K., Solomennik A., Kuznietsova A.

Kharkiv National Medical University, Department of infectious diseases, Ukraine

Bacterial meningitis is a severe infection of the meninges (the membranes surrounding the brain and spinal cord) that is associated with high mortality and morbidity rates despite optimal antibiotic therapy and advances in critical care [8].

Bacterial meningitis is fatal in 5% to 40% of patients and causes neurologic sequelae such as focal neurologic deficits - hearing impairment, aphasia, quadriplegia, spasticity, mental retardation and other [8,12]. Up to 30% of survivors have chronic disorders of the central nervous system function [3,8]. The mechanism of brain damage during bacterial neuroinfections not entirely clear, but we know that once bacteria have gained access to the central nervous system, their multiplication triggers a complex host response consisting of humoral and cellular immune mediators, reactive oxygen intermediates, matrix-metalloproteinases, and other host-derived factors. Alterations of the cerebral vasculature, with disruption of the blood brain barrier and global and focal ischemia, ultimately lead to functional and structural brain damage. Neuronal damage is caused by the dual effects of an overwhelming inflammatory reaction and direct effects of bacterial toxins [3].

For the diagnosis of brain lesions in clinical practice we use imaging techniques such as MRI and the determination of focal neurological symptoms, behavioral or mental disorders, loss of consciousness. At the same time, patients with acute meningitis often come to the hospital with convulsions, septic shock, delirium, which exclude the possibility of brain MRI or CT scan. Currently, we have an opportunity to improve our knowledge of the pathogenesis and diagnosis of brain lesions by determining the levels of neurospecific markers in patient's cerebrospinal fluid and blood. Thus, proven diagnostic and prognostic value of increased levels of neuron specific enolase (NSE), myelin basic protein (MBP), glial fibrillary acidic protein (GFAP), and S-100 protein in patients with stroke, traumatic brain injuries, lesions of the central nervous system in newborns, multiple sclerosis [1,2,4,5,7,9,10].

We chose markers which are specific for different cells in the brain. NSE – intracellular neuronal cytoplasmic enzyme, S-100 – a protein specific for brain glial cell [1,4,10]. GFAP levels rise during the destruction of glial cells and breach the blood-brain barrier function [2,6,7], MBPs the major structural component of myelin that spirally wrap their plasma membrane around axons [7,11]. It may help to understand which specific brain cells are damaged in the process of acute bacterial meningitis, identify the diagnostic value of determining these neurospecific markers in the CSF.

The aim of study was to evaluate the diagnostic and prognostic value of cerebrospinal fluid levels of NSE, MBP, GFAP and S-100 in patients with acute bacterial meningitis.

Material and methods. Potential study participants were admitted in Kharkiv Regional Clinical Infectious Diseases Hospital (Kharkiv, Ukraine). The inclusion of patients in the research program conducted with the selection criteria. Inclusion criteria: clinical symptoms typical for acute meningitis, etiological confirmation of pneumococcal or meningococcal etiology of disease by bacteriological methods or CSF PCR, age of patients- 18 to 65 years, voluntary consent of the patient to participate in the study. Patients were excluded in the following cases: the presence of comorbidities, which can influence the level of neurospecific proteins - HIV, Alzheimer's disease, multiple sclerosis, hematological diseases, malignant neoplasms.

At hospital admission, demographic data were obtained from patients, investigation along with a number of clinical indices. Briefly, anamnesis of the disease, complains and neurological status were recorded. Past medical history was obtained along with routine laboratory exams. All significant events up to hospital discharge or death were recorded.

Patients were divided into groups depending on the etiology and severity of the disease. Were analyzed 60 cases of acute bacterial meningitis. As a comparison group

Table. CSF concentrations of neuroinjury biomarkers (S-100 protein, NSE, GFAP, MBP) in patients with acute bacterial meningitis within the first 24 h of hospital admission and on 10-12 day of treatment

Group of patients	CSF protein S-100 level, ng/l, mean ± SE		CSF NSE level, mcg/l, mean ± SE		CSF GFAP level, ng/ml, mean ± SE		CSF MBP level, ng/ml, mean ± SE	
	first 24 h of hospital admission	10-12 day of treatment	first 24 h of hospital admission	10-12 day of treatment	first 24 h of hospital admission	10-12 day of treatment	first 24 h of hospital admission	10-12 day of treatment
moderate meningococcal meningitis (n=9)	496,14± 38,53[1]*	431,35± 54,21	18,20± 1,97[1]*	17,15± 1,68	4,02± 0,28[1]*	2,58± 0,32	6,12± 0,31	6,95± 0,54
severe meningococcal meningitis (n=19)	1389,41± 105,73[1]*	1094,65± 95,21[1]*	25,57± 2,55[1]*	18,38± 3,37[1]*	8,21± 1,12[1]*	4,89± 0,65[1]*	11,56± 0,64[1]*	10,48± 0,92[1]*
moderate pneumococcal meningitis (n=10)	550,80± 19,51[1]*	480,21± 61,73[1]*	20,28± 1,91[1]*	16,89± 1,34	3,51± 0,33[1]*	2,81± 0,23	6,70± 0,41[1]*	5,33± 0,61
severe pneumococcal meningitis (n=19)	1431,53± 112,56[1]*	922,31± 197,82 [1]*	24,52± 3,11[1]*	18,41± 3,12[1]*	8,94± 1,35[1]*	4,60± 0,78[1]*	12,32± 0,57[1]*	11,63± 0,74[1]*
non-survivors (n=10)	1817± 162,56[1]*[2]*		28,31± 4,56[1]*[2]*		14,88± 1,29[1]*[2]*		13,89± 1,02	
Control group (n=12)	355,63± 29,17		15,71± 0,47		2,27± 0,12		5,43± 0,45	

[1]* - *differences between results with regard to the control group P≤0,05;*
[2]* - *differences between results of survivors and non-survivors P≤0,05*

CSF of 12 patients with acute respiratory infection (ARI) and meningism was analyzed.

CSF was aspirated by lumbar puncture. Performing of lumbar puncture was in a line with the usual protocols of diagnostics and treatment of patients with signs of meningitis. Patients involved in the study were not subjected to additional invasive procedures. Collecting CSF in patients with ARI and meningism performed only at the beginning of treatment to exclude neuroinfection. The CSF samples were immediately frozen at −70°C until subsequent analysis. CSF NSE, MBP, GFAP and S-100 protein level were identified on admission and after 10-12 days of treatment. Analysis of NSE, MBP, GFAP and S-100 protein CSF concentrations was performed using an enzyme immunoassay based on the sandwich technique in Central scientific research laboratory of Kharkiv National Medical University. Work conducted in accordance with the Declaration of Helsinki. The study was approved by the ethics committee of Kharkiv National Medical University, Kharkiv, Ukraine. All data were analyzed using «BioStat» and «Microsoft Excel» programs. P value of<0.05 was used for significance.

Results and their discussion. Of the 67 patients 36 with pneumococcal and 31 – meningococcal etiology of the disease (n=27 males; mean age 46,83 years), 12 with meningism as comparison group. All patients in comparison group were of moderate severity. In the group of patients with pneumococcal meningitis in 10 (27,78%) were moderate, 26 (72,22%) – severe, among them 7 (19,44%) patients died. In the group of patients with meningococcal meningitis – 9 (29,03%) were moderate, 22 (71,97%) – severe, 3 (9,68%) patients died. All severe patients were admitted to hospital with symptoms of cerebral edema and neurological symptoms. The mortality rate was 14,93%. The lethal outcome occurred within 1 to 8 days of hospital treatment.

The obtained data show a significant increase of the CSF level of all neurospecific markers on the first day of admission to the hospital. CSF levels of neurospecific markers dependent on severity of the disease – the highest levels were observed in non-survivors (table 1). Reliable difference in levels of all neurospecific markers in the CSF of patients according to the etiology of meningitis was not found.

In severe cases the level of neurospecific markers was significantly higher than that in moderate patients. Thus, in patients with moderate severity of meningococcal meningitis level of protein S-100 in admission was 496,14±38,53 ng/l, with pneumococcal meningitis – 550,80±19,51 ng/l (Table). In patients with severe course level of protein S-100 was significantly higher – 1389,41±105,73 ng/l in

meningococcal and 1431,53±112,56 ng/l in pneumococcal meningitis (P<0,001). In patients with ARI and meningism level S-100 was significantly lower than in all patients with bacterial meningitis – 355,63±29,17 ng/l (P <0,05). After 10-12 days of treatment levels of protein S-100 decreased, but was still significantly elevated than in the control group (P<0,05 and P<0,001). In severe course levels of protein S-100 significantly elevated than in moderate severity (P<0,001) (Table).

Significant increase CSF NSE level was noted in patients within the first 24 h of hospital admission (Table). In all patients with bacterial meningitis CSF NSE level was significantly higher compared with the control group (P <0,05). Thus, in patients with moderate severity meningococcal and pneumococcal meningitis level of NSE in CSF was 18,20±1,97 and 20,28±1,91 mcg/l. The level of NSE also depends on the severity and period of illness. Within the first 24 h of hospital admission CSF NSE level in severe meningococcal meningitis was 25,57±2,55 mcg/l, severe pneumococcal meningitis – 24,52±3,11 mcg/l, which significantly higher than in patients with moderate severity and in the control group (P <0,01). After 10-12 days of treatment, NSE level decreased, but in patients with severe disease, anyway, was higher than in the control group (P <0,05) (Table).

The highest CSF level of GFAP was observed at admission in CSF of non-survivors – 14,88±1,29 ng/ml (P<0,001). In CSF of patients with moderate pneumococcal meningitis CSF level of GFAP was 3,51±0,33 ng/ml, meningococcal – 4,02±0,28 ng/ml, and in severe pneumococcal meningitis – 8,94±1,35 ng/ml, in severe meningococcal meningitis – 8,21±1,12 ng/ml (P<0,01) (Table). After 10-12 days of treatment, patients CSF GFAP level was significantly reduced almost to control group levels, in severe patient it was significantly higher (P<0,05) (Table).

In the first 24 h of hospital admission CSF level of MBP in moderate patients with pneumococcal meningitis was 6,70±0,41 ng/ml, meningococcal – 6,12±0,31 ng/ml, in control group – 5,43±0,45 ng/ml. In severe cases of pneumococcal meningitis MBP concentration was – 12,32±0,57 ng/ml, meningococcal meningitis – 11,56±0,64 ng/ml (P<0,05). Although the level of MBP was significantly higher in patients with severe bacterial meningitis (P<0,05), it did not differ in patients with moderate and control group. We found no significant differences between CSF levels of MBP in severe survivors and non-survivors.

The present findings indicate that severe survivors and non-survivors had higher CSF neurospecific markers S-100, NSE, GFAP and MBP levels than patients from the other groups. The severe survivors and non-survivors with acute bacterial meningitis were characterized by heterogeneous neurological disorders and symptoms of brain edema. The lack of an increase of CSF NSE, S-100 protein and GFAP in moderate patients with meningitis, was particularly surprising, since in those patients the inflammatory involvement of brain parenchyma is probably negligible. This indicates the presence of damages of neurons, glial cells, even in patients who have no clinical symptoms of brain damage. Differences in the CSF levels of GFAP, NSE, S-100 protein and MBP in groups of patients with varying degrees of severity can assume that in the development of brain damage tissue during acute bacterial neuroinfections the first stage there is damage of glial cells responsible for the blood-brain barrier function, then start neuron damages and then myelin fiber.

These results indicate that CSF levels of NSE, S-100 protein, GFAP and MBP provides a good indicator for evaluation of brain cell damage and prognosis for patients with acute bacterial meningitis. Thus, the determination of neurospecific markers' levels in cerebrospinal fluid is informative for evaluating the brain cells damages not only in patients with stroke, brain injury, subarachnoid hemorrhage, as shown by other studies [1,2,4,5,7,9,10], but also in patients with acute bacterial meningitis.

REFERENCES

1. Brunkhorst R, Pfeilschifter W, Foerch C., et al. Astroglial Proteins as Diagnostic Markers of Acute Intracerebral Hemorrhage-Pathophysiological Background and Clinical Findings. Translational Stroke Research. 2010;1(4): 246–51.
2. Fünfschilling U., Supplie L.M., Mahad D., Boretius S., Saab A.S., Edgar J., Brinkmann B.G., Kassmann C.M., Tzvetanova I.D., Möbius W. Glycolytic oligodendrocytes maintain myelin and long-term axonal integrity. Nature. 2012;485:517–521.
3. Gerber J., Nau R. 2010. Mechanisms of injury in bacterial meningitis. Curr. Opin. Neurol. 23:312–318
4. Gmitterová K, Heinemann U, Krasnianski A, Gawinecka J, Zerr I. Cerebrospinal fluid markers in the differentiation of molecular subtypes of sporadic Creutzfeldt-Jakob disease. Eur J Neurol. 2016 Jun;23(6):1126-33. doi: 10.1111/ene.12991. Epub 2016 Mar 31.
5. Hajduková L, Sobek O, Prchalová D, et al. Biomarkers of Brain Damage: S100B and NSE Concentrations in Cerebrospinal Fluid—A Normative Study. BioMed Research International. 2015;2015:379071. doi:10.1155/2015/379071.
6. Hoyer C., Eisele P., Ebert A.D., Schneider S., Gass A., Fatar M., Szabo K., Alonso A. Blood-CSF-barrier dysfunction is a marker for encephalitic involvement in patients with aseptic meningitis/meningoencephalitis. Journal of clinical virology. 2016 Nov; 84:82–86. http://dx.doi.org/10.1016/j.jcv.2016.10.006
7. Kulbe JR, Geddes JW. Current status of fluid biomarkers in mild traumatic brain injury. Experimental neurology. 2016;275(0 3):334-352.
8. Lingani, C., Bergeron-Caron, C., Stuart, J.M., Fernandez, K., Djingarey, M.H., Ronveaux, O. et al. Meningococcal meningitis surveillance in the African meningitis belt, 2004-2013. Clin Infect Dis. 2015; 61: S410–S415; DOI: http://dx.doi.org/10.1093/cid/civ597
9. Papa L, Robertson CS, Wang KKW, Brophy GM, Hannay HJ, Heaton S, et al. Biomarkers improve clinical

outcome predictors of mortality following non-penetrating severe traumatic brain injury. Neurocrit Care (2015) 22:52–64.10.1007/s12028-014-0028-2
10. Rahati M, Nozari M, Eslami H, Shabani M, Basiri M., et al. Effects of enriched environment on alterations in the prefrontal cortex GFAP- and S 100 B-immunopositive astrocytes and behavioral deficits in MK-801-treated rats. Neuroscience. 2016;Apr 5. pii: S0306-4522(16)30052-5
11. Snaidero N., Möbius W., Czopka T., Hekking L.H., Mathisen C., Verkleij D., Goebbels S., Edgar J., Merkler D., Lyons D.A. Myelin membrane wrapping of CNS axons by PI(3,4,5)P3-dependent polarized growth at the inner tongue. Cell. 2014;156:277–290.
12. Zhang Y, Wei D, Guo X, Han M, Yuan L, Kyaw MH. Burden of Neisseria meningitidis infections in China: a systematic review and meta–analysis. Journal of Global Health. 2016;6(2):020409. doi:10.7189/jogh.06.020409.

SUMMARY

CEREBROSPINAL FLUID LEVELS OF NEUROSPECIFIC MARKERS IN ADULT PATIENTS WITH BACTERIAL MENINGITIS

Sokhan A., Zots Y., Gavrylov A., Iurko K., Solomennik A., Kuznietsova A.

Kharkiv National Medical University, Department of Infectious Diseases, Ukraine

At present, the great attention is given to the neurospecific markers as their elevated level in the cerebrospinal fluid corresponds to the degree of destruction of relevant CNS cells. Therefore, actual direction of the studies of the pathogenesis and diagnosis of CNS diseases is to determine levels of neurospecific markers in the cerebrospinal fluid (CSF). The purpose of the study was to evaluate the diagnostic and prognostic role of NSE, S-100 protein, GFAP and MBP levels in CSF of patients with acute bacterial meningitis. S-100 protein, NSE, GFAP and MBP levels in CSF of patients with acute pneumococcal and meningococcal meningitis were determined during admission and after 10-12 days of treatment. Patients were divided into groups depending on the etiology and severity of the disease. 60 cases of acute bacterial meningitis, as a study group, and 12 cases with acute respiratory infection and meningism, as a control group, were analyzed. It is shown that CSF levels of NSE, S-100 protein, GFAP and MBP on the first day of admission were significantly increased (P<0,05), depending on the severity of the disease. The highest levels of neurospecific markers have been identified in non-survivors (P<0,001). The concentration changes of CSF neurospecific markers are found to be helpful as a diagnostic and prognostic marker in acute bacterial meningitis.

Keywords: meningitis, neurospecific markers, CSF, diagnostic marker.

РЕЗЮМЕ

УРОВНИ НЕЙРОСПЕФИЧЕСКИХ МАРКЕРОВ В ЦЕРЕБРОСПИНАЛЬНОЙ ЖИДКОСТИ ВЗРОСЛЫХ БОЛЬНЫХ БАКТЕРИАЛЬНЫМ МЕНИНГИТОМ

Сохань А.В., Зоц Я.В., Гаврилов А.В., Юрко К.В., Соломенник А.О., Кузнецова А.А.

Харьковский национальный медицинский университет, кафедра инфекционных болезней, Украина

На сегодняшний день большое внимание уделяется изучению нейроспецифических маркеров, специфичных для тканей нервной системы. Повышенный уровень нейроспецифических маркеров в цереброспинальной жидкости (ЦСЖ) соответствует степени разрушения клеток центральной нервной системы (ЦНС). Поэтому актуальным направлением исследований патогенеза и диагностики заболеваний ЦНС является определение уровней нейроспецифических маркеров в ЦСЖ. Целью исследования явилась оценка диагностической и прогностической роли уровней нейронной специфической энолазы, основного белка миелина, глиального фибриллярного кислого белка в цереброспинальной жидкости у пациентов с острым бактериальным менингитом в динамике заболевания. В ЦСЖ пациентов с острым пневмококковым и менингококковым менингитом определен уровень белка S-100, нейронной специфической энолазы (NSE), основного белка миелина (MBP), глиального фибриллярного кислого белка (GFAP) при поступлении в стационар и спустя 10-12 дней после лечения. Проанализировано 60 случаев острого бактериального менингита и 12 случаев острой респираторной инфекции и менингизма в качестве сравнительной группы. Пациенты, в зависимости от этиологии и тяжести заболевания, разделены на группы. Показано, что уровни NSE, белка S-100, GFAP и MBP в ЦСЖ больных при поступлении были достоверно повышены (p<0,05) и находились в прямой зависимости от тяжести заболевания. Наивысшие уровни нейроспецифических маркеров идентифицированы у умерших (p<0,001). Эти показатели могут быть использованы как диагностический и прогностический маркер при остром бактериальном менингите.

რეზიუმე

ცერებროსპინალურ სითხეში ნეიროსპეციფიური მარკერების დონე ბაქტერიული მენინგიტით ზრდასრულ ავადმყოფებში

ა. სოხანი, ი. ზოცი, ა. გავრილოვი, კ. იურკო, ა. სოლომენიკი, ა. კუზნეცოვა

ხარკოვის ეროვნული სამედიცინო უნივერსიტეტი, ინფექციურ დაავადებათა კათედრა, უკრაინა

სადღეისოდ დიდი ყურადღება ეთმობა იმ ნეიროსპეციფიურ მარკერებს,რომლებიც სპეციფი-

ურია ნერვული სისტემის ქსოვილებისათვის. ცერებროსპინალურ სითხეში (ცსს) ნეიროსპეციფიური მარკერების დონე პირდაპირ პროპორციულია ცენტრალური ნერვული სისტემის შესაბამის უჯრედბის რღვევის ხარისხის; აქედან გამომდინრე, პათოგენეზის გამოკვლევათა და ნერვული სისტემის დაავადებათა აქტუალურ მიმართულებას წარმოადგენს ცერებროსპინალურ სითხეში ნეიროსპეციფიური მარკერების დონის განსაზღვრა.

კვლევის მიზანი იყო ცერებროსპინალურ სითხეში NSE-ის, S-100 ცილის, GFAP და MBP დონეების დიაგნოსტიკური და პროგნოსტიკური როლის შეფასება ავადმყოფებში მწვავე ბაქტერიული მენინგიტით დაავადების დინამიკაში. მწვავე პნევმოკოკური და მენონგოკოკური მენინგიტით პაციენტების ცსს-ში გინისაზღვრა S-100 ცილის, NSE, GFAP და MBP დონე სტაციონარში მიღებისას და მკურნალობის 10-12 დღის შემდეგ. გაანალიზებულია მწვავე ბაქტერიული მენინგიტის 60 შემთხვევა და შედარებითი ჯგუფის სახით 12 პაციენტი მწვავე რესპირატორული ინფექციით და მენინგიზმით. პაციენტები ეთიოლოგიისა და დაავადების სიმძიმის გათვალისწინებით გაყოფილი იყო ჯგუფებად.

გამოვლინდა,რომ ავადმყოფების კლინიკაში მიღების მომენტში NSE-ის,S-100 ცილის,GFAP და MBP დონე ცსს-ში იყო სარწმუნოდ მაღალი ($p<0,05$) და პირდაპირ დამოკიდებულებაში იყო დაავადების სიმძიმესთან. ნეიროსპეციფიური მარკერების უმაღლესი დონეები იდენტიფიცირებული იყო გარდაცვლილებში ($p<0,001$). აღნიშნული მონაცემები შეიძლება გამოყენებული იქნას პროგნოსტიკურ მარკერებად ბაქტერიული მენინგიტის დროს.

EFFECT OF THE CARDIOMETABOLIC RISK FACTORS ON VASCULAR AGING IN PATIENTS WITH NON-ALCOHOLIC FATTY LIVER DISEASE CONCOMITANT WITH SUBCLINICAL HYPOTHYROIDISM

Kolesnikova E., Potapenko A.

SI «National Institute of Therapy named after L.T. Mala of NAMS of Ukraine», Kharkiv, Ukraine

Despite the progress in medicine over the past decades, cardiovascular diseases (CVD) remain the most pressing issues of healthcare in many countries and represent a serious socioeconomic problem, being the leading cause of death throughout the world at 31% (in 2014) [12]. Mortality from CVD in Ukraine is 222 patients per 100 000 population. The prevalence of CVD is associated with traditional risk factors: smoking, nutrition, obesity, hypodynamia, increased blood pressure (BP), dyslipidemia, dysglycemia, as well as aging of vessels [6,18]. The main signs of vascular aging are the gain in the diameter of the aorta and in the intima-media complex thickness (IMT), and the increase of the rigidity of the vascular wall. Published results of the recent research indicate that additional risk factors such as endothelial dysfunction (ED), IMT, increased level of C-reactive protein (CRP), and risk factors combined with the Framingham Scale (sex, age, AH, dyslipidemia, smoking) are met among patients with non-alcoholic fatty liver disease (NAFLD) [15,19]. Patients with NAFLD have a high incidence of endocrinopathy. Dysfunction of the thyroid gland, in particular subclinical hypothyroidism (SH) presents special interest in recent years in this category of patients due to an increase in the frequency of its occurrence in the population - 73% in women and 30% in men [10,16]. The search for early predictors is continuing: the level of adipocytokines in the blood serum, the vascular endothelial factors, incl. vascular endothelial growth factor (VEGF-A), inflammation markers (CRP), vascular aging markers (length of telomere). The most significant causes of cell aging are the shortening of telomeres and decrease of telomerase activity. Telomeres are the terminal regions of chromosomes that were proposed as markers of the biological aging process. The relative length of telomeres is reduced with each division of cells, and the rate of shortening of telomere length is associated with the effect of oxidative stress and inflammation [4,13]. The factors associated with the risk of CVD, that can impact the shortening of length of telomeres are being actively studied in recent years [13]. The connection between leucocyte telomeres shortening and the development and progression of atherosclerosis has been shown. It is well known that the process of increasing arterial stiffness (atherosclerosis) due to a decrease in the amount of elastin and an increase in the amount of collagen, as well as qualitative changes in the structure of the arterial wall, which is associated with a disruption of vasodilation due to endothelial properties is observed with normal vascular aging. When comparing telomeres of endothelial cells obtained from atherosclerotic plaques with those from sites without atherosclerotic changes of the same human body, it was found that the former were shorter [14].

The work has been carried out within the framework of the research «To develop comprehensive programs for the prevention of cardiovascular diseases in patients with non-infectious diseases» 0116U003039; «The effect