

ABSTRACT

of the PhD dissertation titled: «Functioning of the lymphatic system and contractile activity of lymphatic vessels in abdominal inflammation» by Yessenova Makpal submitted for the degree of Doctor of Philosophy (PhD) on the educational program «8D05102-Biomedicine»

General characteristics of the work. The thesis is devoted to the study of microbial features in peritoneal exudate in the acute inflammatory process, as well as adrenergic innervation of the vascular system, their microstructure, and the observed changes in blood flow velocity in vessels in the acute inflammatory process.

The relevance of the work. Inflammation of the abdominal cavity is one of the processes that can cause pathologies of various body functions, local changes and intoxication. Inflammation of abdominal cavity organs remains one of the urgent problems of modern medicine. This is due to the constant increase in the number of patients suffering from severe forms of the disease. In addition, the mortality rate as a result of widespread inflammatory processes is high - up to 20-70%. It is shown that the relevance of this problem is determined by the reaction of blood and lymphatic vessels to the impact of external and internal environmental factors that ensure adaptation of local haemodynamics to the needs of the organism. The main causes of abdominal cavity inflammation are exacerbation of endogenous intoxication syndrome and foci of infection leading to decompensation of vital organs and systems. The main cause is marked endogenous intoxication, and its main source is the release into the abdominal cavity of a large amount of exudate with microbes and their exo- and endotoxins. Massive endogenous toxemia leads to the development of systemic inflammation or systemic inflammatory response syndrome with active participation of the immune system. Inflammation of the abdominal cavity is accompanied by excessive release of microbial toxins from the purulent and destructive focus of the abdominal cavity, peritoneal exudate and damaged intestine into the biological environment of the body. It is known that the lymphatic system is not indifferent in disorders of internal organs and body systems, and in changes of regional lymphatic capillaries, blood vessels and lymph nodes as a natural way of clearing inflammation, as well as in maintaining the balance of the internal environment. Restoration of circulating blood composition and volume often depends on the functional state of the lymphatic capillaries of the inflamed area, their resorptive capacity and transport function. One of the main causes of inflammatory process development is gastrointestinal (GI) autoinfection, where the type of microorganisms and their virulence are a factor determining the features of disease development, clinical manifestations and outcome. Therefore, based on experimental studies, it is important to determine the changes in microbial composition observed in the interstitial fluid isolated from the abdominal cavity during inflammatory processes. Studies in this direction, have theoretical and practical importance.

The aim of the study. Study of biochemical parameters of lymph and blood, innervation of the vascular system and their structural changes, blood flow and contractile activity of blood vessels during inflammatory processes in the abdominal cavity.

To achieve this goal, the following tasks were solved:

1. To study abdominal cavity microorganisms during the acute inflammatory process and assessment of sensitivity to antibacterial drugs in *in vitro* conditions.
2. To investigate the blood flow rate, lymph flow rate and biochemical composition of blood and lymph in inflammation of abdominal cavity organs
3. To study morphometric indices of structural and functional changes of lymphatic and vascular systems during abdominal cavity inflammation.
4. Determine the adrenergic innervation of the lymphatic system during inflammation of the abdominal cavity.
5. To study the contractile activity of lymphatic vessels in abdominal cavity inflammation.

Object of research. The study was conducted on laboratory white rats of the Sprague Dawley (SD) line. The objects of the study were lymph, lymphatic vessels, blood and blood vessels.

Research Methods. Experimental groups with abdominal inflammation were taken as a research model. The materials obtained for the study are further supported by microbiological, biochemical, morphological, morphometric and histochemical methods. The assessment of lymph and blood coagulability is carried out using the TS 4000 coagulometer (HTI, USA, 2013). The amount of total protein, cholesterol, triglycerides, total lipid, urea, creatinine, and bilirubin was determined in blood and lymph samples. The levels of enzyme activity: alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, amylase were determined in blood and lymph by the generally accepted method using the COBOS INTEGRA 400 (USA) automatic biochemical analyzer. Contractile activity of isolated lymphatic vessels and nodes was studied using the generally accepted method. Morphology of lymphatic and blood vessels was determined by creating semi-thin (1 μm) and ultra-thin sections 50-70 nm thick on a «Leica EM UC7» ultratome (Leica Microsystems, Germany). Leica DME (Germany) was used as a light microscope, Image J (Wayne Rasband, USA) was used for morphometric analysis. The methods for preparing histological preparations and morphometric analysis were used. Blood flow velocity was analysed with rheogram Sonomed «Mitsar-Reo-300» (Russia), and blood flow velocity was analysed with the help of rheogram «Winreo» (Russia). A special histochemical fluorescence-microscopic method was used to study the adrenergic nervous apparatus of lymphatic vessels.

Scientific novelty of the research work. The dynamics of adaptive changes in blood flow velocity, blood and plasma volume, as well as haematological and biochemical indices of lymph and blood in laboratory animals were assessed for the first time under conditions of simulation of inflammation of abdominal cavity organs. For the first time data on the lymphatic thoracic duct in abdominal cavity inflammation, peculiarities of morphology and functional state of the vascular

system, including lymphatic vessels, changes in morphometric indices, structures of innervation of lymphatic and blood vessels and contractile activity of lymphatic vessels were obtained. The thesis work was the first to show haemodynamic reactions in abdominal inflammation.

Scientific and practical significance of the work. The role of the lymphatic system in drainage-compensatory and adaptive reactions of the organism during inflammation of internal organs of the abdominal cavity is shown for the first time, which will allow to prevent and reduce negative effects on visceral functions of the organism. The microbiological composition of inflammatory exudate and its effect on morphofunctional and structural state and morphometric indices of the lymphatic thoracic duct increase in diameter and endothelial layer, decrease in vessel wall thickness, and in the intestinal wall increase in diameter and all layers of the vessel change in abdominal inflammation are shown. The interrelation of inflammatory exudate on lymph flow and biochemical indices and rheological properties of lymph was shown for the first time. The destructive changes of adrenergic innervation of lymphatic vessels and nodes and its connection with reduced spontaneous and induced (vasoactive substances) contractile activity of lymphatic vessels, which, in turn, led to a decrease in the transport function of the lymphatic system, were shown.

The results of the study lecture on the curriculum of the course 'human physiology' 2 course on the educational programme «6B05108-Biomedicine» of the Department of Biophysics, Biomedicine and Neuroscience of the Kazakh National University named after Al-Farabi, Faculty of Biology and Biotechnology, and on the curriculum of the training course «Human anatomy and physiology» of the 3rd year of the educational programme «Chemistry and Biology» of Zhetysay State University, introduced as a seminar class (act on the introduction of completed research work into the educational process, Appendix A, B).

Basic principles put forward during the defense:

1. The bacterial microflora of inflammatory exudate in acute inflammatory process was studied, as a result of which microorganisms *Pr.mirabilis*, *Klebsiella spp.*, *Listeria*, *Sarcina* and *E.coli* were identified. These microorganisms were found to be highly sensitive to the new generation antibiotics Lomefloxacin and Norfloxacin.

2. Changes in prothrombin time, thrombin time and activated partial thromboplastin time of lymph and blood during inflammation in rats are characterized by a decrease in their clotting time and an increase in viscosity, which in turn contributes to a decrease in the rate of lymph movement in the body.

3. During the inflammatory process in the abdominal cavity the thickness of endothelial cells of abdominal aorta, inferior vena cava and abdominal segment of lymphatic duct was studied, which increased by 3,43%, 48,52%, 4,98% in comparison with the control. There was a change in their diameters - lymphatic vessels increased by 45,82%, vein diameter decreased by 11,90%, artery diameter - by 14,32%.

4. It has been established that during abdominal inflammation in the wall of the thoracic lymphatic duct and blood vessels of the abdominal cavity adrenergic

innervation is disturbed, the level of catecholamines decreases in sympathetic nerve fibres, which leads to impaired innervation and, as a consequence, vascular regulation.

5. The contractile activity of the thoracic lymphatic duct in abdominal inflammation was studied, and a decrease in its spontaneous and induced contractile activity was shown.

The personal contribution of the dissertation author to the implementation of the results of the research work presented for defense. All results of the dissertation were obtained with the personal participation of the author. The dissertation candidate independently conducted an analysis of literary data on the research topic, experiments, processing and analysis of research results, wrote and formatted the dissertation manuscript.

Approbation of the work. The main provisions of the dissertation and the research results were presented at the following international scientific conferences and symposia:

- International scientific conference of students and young scientists “Farabi’s World” (Almaty, Kazakhstan, 2021);

- Materials of the International Scientific and Practical Conference “Current Problems of Biology and Biotechnology”, dedicated to the 70th anniversary of Professor S.T. Tulekhanov, corresponding member of the National Academy of Sciences of the Republic of Kazakhstan, Doctor of Biological Sciences (Almaty, Kazakhstan, 2021);

- International scientific conference of students and young scientists “Farabi’s World” (Almaty, Kazakhstan, 2022);

- I International Scientific and Practical Conference “Integration of Sciences: Biophysics, Biomedicine, Neuroscience” (Almaty, Kazakhstan, 2022);

- International research competition “New Science”, research work of the year (Petrozavodsk, Russia, 2023);

- IEEE Ural-Siberian Conference on Computational Technologies in Cognitive Science, Genomics and Biomedicine, CSGB 2023 – Proceedings. (Novosibirsk, Russia, 2023);

- Materials of the XV International Scientific and Practical Conference named after Academician Yu.I. Borodin “Lymphology: from fundamental research to medical research (Novosibirsk, Russia 2023);

- XXIV Congress of the Physiological Society named after I.P. Pavlov (St. Petersburg, Russia, 2023);

- *BIO Web of Conferences*, Morphometric changes in the blood and lymphatic channels during inflammation (Almaty, Kazakhstan, 2024).

The main results of the dissertation were heard annually at the Scientific and Technical Council of the Faculty of Biology and Biotechnology of Al-Farabi Kazakh National University, at meetings of the Department of Biophysics, Biomedicine and Neuroscience.

Publications of articles. The results of the study on the topic "Functioning of the lymphatic system and contractile activity of lymphatic vessels in abdominal inflammation" were published 12 scientific articles, of which 2 article was

published in a journal included in the Scopus database (Q2 percentile 59 and Q3 percentile 30), Hirsch index -1, as well as 3 articles in republican scientific journals on the list of the Committee for Control in the Sphere of Education and Science of the Republic of Kazakhstan, 6 in international and republican scientific and practical conferences of Kazakhstan, 1 monographs were published.

The structure of the doctoral dissertation. The thesis consists of normative references, notations and abbreviations, introduction, literature review, research materials and methods, as well as research results and their discussion, conclusion, used sources, tables and figures and appendices. The volume of the work is 127 pages, including 6 tables, 44 figures, 249 literature sources and 5 appendices.