AJPMHS GLOBAL RESEARCH NETWORK

AMERICAN Journal of Pediatric Medicine and Health Sciences
Volume 02, Issue 03, 2024 ISSN (E): 2993-2149

УДК: 616.381-002-022+616.24-005.98+616-08-039.71

ANALYSIS OF FEATURES OF THE LUNG ENDOTHELIAL SYSTEM IN ABDOMINAL SEPSIS

Khotamov Ikhtiyor Eshmurotovich
Khamdamov Bakhtiyor Zarifovich
Bukhara State Medical Institute. Bukhara, Uzbekistan

Resume. Molecular and biochemical parameters of the endothelial system of the lungs during experimental modeling of abdominal sepsis showed an ambiguous picture of the changes taking place, which were of a phase nature and depended on the timing of the development of the pathological process.

Keywords: Abdominal sepsis, lungs, endothelial system.

Relevance. Throughout the last century, abdominal sepsis has been and remains a dangerous disease in which dysfunction of vital organs develops as a result of the aggression of introduced microorganisms. The high incidence of abdominal sepsis is accompanied by high mortality, which can range from 7.6% to 36.0% (1,3,5,25,26,27,28,29,30,31). Intra-abdominal contamination and secondary peritonitis are a constant source of pathogen-associated molecular patterns (through spillage of intestinal contents) and through direct damage to internal organs and abdominal organs. This "motor of multisystem organ failure" provides continuous cytokine fuel for a raging systemic response (2,4,6,8,19,38,39,40,41). For example, TNF-α and IL-1 are important pro-inflammatory cytokines. Each of them has been shown to induce vascular permeability, which leads to pulmonary edema and bleeding (9,11,13,15,17). IL-6 is a key molecule in initiating a febrile reaction, activating lymphocytes, and also plays a role in hematopoiesis. It has also been shown to cause myocardial depression (10,12,14,16,18,32,33,34,35,36,37). Over the past 20 years, the recognition of the endothelium as a full-fledged system has led to a large number of experimental and clinical studies, including in the study of the mechanisms of sepsis development.

During bacterial, fungal or viral infection, exogenous molecular patterns associated with pathogens and molecular patterns associated with endogenous damage cause activation of the endothelium and can disrupt its structure and function, that is, provoke the development of endothelial dysfunction (19,21,23,25,27).

Endothelial changes associated with sepsis should be considered appropriate to limit the spread of bacteria, as well as to control leukocyte recruitment and bacterial elimination. However, severe and persistent phenotypic changes in the endothelium can contribute to impaired microcirculatory blood flow, tissue hypoperfusion and the development of life-threatening multiple organ failure (18,20,22,24,26)

Thus, it is very difficult to distinguish between appropriate activation and endothelial dysfunction, especially considering that the response of endothelial cells may vary in different organs.

The purpose of the study: study of the endothelial lung system in abdominal sepsis.

Material and methods. The studies were conducted on laboratory purebred rats in a model of abdominal sepsis developed by us. The experiments were carried out on 106 white beardless laboratory rats weighing 200-250 grams, of both sexes, who were on a regular laboratory diet. The planned experimental studies, which included sampling, biopsies and autopsy, were based on the principle of the conditions specified in the 1986 Council of Europe Convention on the Protection of Animals.

The animals were divided into the following series of experiments: Control – 10 intact animals, not subjected to any influences and manipulations, which were on a standard grain diet. The main group consisted of 50 animals in which an experimental model of abdominal sepsis was reproduced using our improved technique.

Reproduction of the experimental model of abdominal sepsis was carried out in stages, by changing the reactivity of animals and creating a purulent necrotic focus in the abdominal cavity.

Blood sampling in experimental studies was carried out separately at the entrance and exit from the lungs. In this case, the blood at the entrance to the lungs is mixed venous blood, which came from the inferior and superior vena cava. At the exit from the lungs, we received arterial blood, which was universal for the whole body as a whole. This technique was developed and tested by a group of researchers at the Tashkent Medical Academy.

Each value obtained in different blood samples was also subjected to calculation of the venous-arterial difference, that is, the value reflecting the "delay" or "production" of the substrate in the endothelial system of the lungs.

The whole complex of studies of patients with abdominal sepsis was reduced to continuous monitoring of the state of homeostasis and functional activity of vital organs. For this purpose, functional, instrumental and laboratory research methods were carried out. Integral rating diagnostic methods such as APACHE II, SAPS, SOFA, and the Kalf-Kalifa Leukocyte Intoxication Index were also actively used.

The level of C-reactive protein (mg/l), thrombomodulin (ng/ml), Willebrand factor (IU/dL), intercellular and cellular adhesion molecules (ng/ml) were studied using an enzyme immunoassay; nitrites and nitrates (%), peroxynitrite (mmol/l), the activity of nitric oxide synthase (mmol/min/l) according to the Griss method modified by A.P. Solodko et al. on the SF-46 spectrophotometer at a wavelength of 520 nm.

The entire range of studies met the criteria of translational medicine, which used the entire range of studies, which allowed extrapolating the results of experimental studies into clinical practice.

Results and their discussion. The study of the total NO value is considered a generally accepted indicator of the nitroxyergic system of vascular tone regulation, as one of the functional criteria of the endothelial system. The average level of its content in the mixed venous blood sample at the entrance to the lungs was 26.39±3.91 mmol/l, whereas at the exit from the lungs in the arterial blood sample its level was higher and reached an average value of up to 33.41±4.64 mmol/L. The venous-arterial difference, averaging "+" 7.02±1.13 mmol/l, was positive and indicated the production of this element in the alveolar capillary network with release into the systemic circulation. It should be noted that this type of venous-arterial

difference was typical in all the series of experiments we studied. At the same time, the peak values occurred in animals of the control and comparative groups ("+" 8.44±2.17 mmol/l and "+" 8.63±2.35 mmol/l, respectively). In other cases, in the dynamics of the development of the experimental model of abdominal sepsis, the production of this substrate of the nitroxyergic vascular tone regulation system decreased from "+" 8.11±2.47 mmol/l ($p<0.05$) for a 6-hour period of reproduction of the experimental model of abdominal sepsis and to "+" 4.69±1.62 mmol/l ($p<0.05$) for a 24-hour period of disease development. In the subsequent 48, 72 and 96-hour periods of development of the experimental model of abdominal sepsis, the venous-arterial difference in NO increased again. However, the venous-arterial difference did not reach the initial value. Moreover, most of the indicators were not reliable in nature, reflecting the remoteness from the ongoing real processes associated with the development of an experimental model of abdominal sepsis.

In this regard, we conducted a dispersion analysis of the constituent elements of NO (NO2- and NO3-) as a percentage in the dynamics of the development of an experimental model of abdominal sepsis. The predominant role in the percentage value of NO2-, already for the 24-hour modeling period of abdominal sepsis, is leveled, yielding a fractional value of NO3-. In other words, there is an increased production of NO3 by the endothelial system- in conditions of ongoing disorders. This once again confirms the importance of the assessment of the component of the decay of NO, rather than its integral value. Against the background of the above-described changes, we revealed changes in the concentration of the metabolic product of the conversion of NO components, in particular NO3- to OONO- . The average content of peroxynitrite in the mixed venous blood sample at the entrance to the lungs throughout the study exceeded its level in the arterial blood sample at the exit from the lungs (2.5±0.09 mmol/l and 2.37±0.03 mmol/l; $p>0.05$).

The venous arterial difference, which was negative ("-") in nature, indicated the active utilization of this oxidant product in the endothelial system of the lungs and a decrease in its production into the systemic arterial bloodstream. In other words, the lungs, and in this case its endothelial system, performed a barrier filtration function, creating conditions for the formation of a universal blood composition for all organs of the body. The minimum values with an unreliable level of differentiation between the content of peroxynitrite in a mixed venous blood sample at the entrance to the lungs and in an arterial blood sample at the exit from the lungs were identified by us among animals of the control and comparative series of experiments. The venous-arterial difference ("-" 0.03± 0.01 mmol / l), equated to 10%, can be safely taken as such as absent.

However, in the group of animals with an experimental model of abdominal sepsis, starting from the 6-hour period of development of the pathological process, we registered an increase in peroxynitrite in a mixed venous blood sample at the entrance to the lungs, which reached its maximum value at 72-96 hours of disease progression. The level of its increase by 3.2 and 2.3 times was significantly different in relation to the early stages of modeling abdominal sepsis (6-12-hour periods). As for the change in the level of peroxynitrite in the arterial blood sample at the exit from the lungs, we can note the relative stability in the productivity of this substrate for a 6-12-hour period of development of an experimental model of abdominal sepsis. It is

during these periods that the venous-arterial difference, repeating its character as in the control series of experiments, becomes maximally significant, reaching a peak at the 12-hour period of development of abdominal sepsis ("-"1.46±0.12 mmol/l). Such a nature of changes in the endothelial system of the lungs in the dynamics of the development of an experimental model of abdominal sepsis led to an increase in the differentiated value between venous and arterial blood samples by 3 times ($p<0.001$).

Meanwhile, starting from the 24-hour period of development of the experimental model of abdominal sepsis, there is a decrease in the venous-arterial difference to "-" 0.74±0.12 mmol/l ($p<0.05$), which in subsequent periods led to an inversion of values, due to a change in the nature of the formation of peroxynitrite, which began to be actively synthesized ("+") in the endothelial system of the lungs. Its increase in the arterial blood sample at the exit from the lungs, starting from this period of development of the experimental model of abdominal sepsis, was significantly pronounced, especially at 48-hour (7.4 times compared to 6-hour and 7.1 times compared to 12-hour periods) and at 72-hour (8.9 three times in relation to the 6-hour period and 8.5 times in relation to the 12-hour period) terms.

Thus, it is possible to state an increase in peroxynitrite in various blood samples, depending on the timing of the development of an experimental model of abdominal sepsis, which was characterized by a transition from a state of transient phenomena to steadily progressive ones, indicating the depletion of compensatory capabilities of the endothelial lung system itself. As evidence for the above conclusion, we consider the dynamics of changes in the activity of the iNOS enzyme in the studied blood samples at the entrance and exit from the lungs.

In particular, in intact animals, the activity of this enzyme is inhibited as it passes through the endothelial system of the lungs. The same character of the endotheliocyte ratio can be seen in relation to a group of animals of the comparative series.

The continuation of the increase in venous-arterial difference among animals with an experimental model of abdominal sepsis is interesting. However, as in the case of peroxynitritis, this character completely changes starting from the 24-hour period of development of the experimental model of abdominal sepsis.

The activity of this enzyme in the arterial blood sample increases at the exit from the lungs. And although such an increase was within ± 10% of the level, nevertheless, we no longer received the effect of iNOS inhibition. This, in turn, may indicate a decrease in the activity of the physiological enzyme systems of endothelial and neuronal NO synthase and the progression of oxidative processes leading to the destruction of endotheliocytes in the capillary network of the lungs.

In the dynamics of the development of the experimental model of abdominal sepsis, identical changes occurred in the concentration of intercellular and cellular adhesion molecules. In intact animals, a decrease in the concentration of these molecules was noted as blood passed through the endothelial system of the lungs. The venous-arterial ICAM-1 content decreased by 29.8 times ($p<0.001$ is a reliable value in the arterial blood sample at the exit from the lungs in relation to the mixed venous blood sample at the entrance to the lungs).

According to the content of VCAM-1, the decrease occurred slightly less – by 22.9 times, although it was also stable and reliable ($p<0.001$ is a reliable value in an arterial blood sample at the exit from the lungs in relation to a mixed venous blood sample at the entrance to the lungs). Such changes correspond to physiological parameters, which are confirmed by the presence of high tone in the arterial circulatory system. Also interesting is the identical level of change in the venous-arterial difference (24.4 times, respectively) for both indicators. This was due to a decrease in the specific gravity of intercellular adhesion molecules and an increase in cell adhesion molecules in a mixed venous blood sample at the entrance to the lungs. When modeling abdominal sepsis, starting from the 6-hour study period, we noted a progressive decrease in the level of venous-arterial difference. At the same time, the minimum value in relation to the venous-arterial difference ICAM-1 was noted for the 24-hour period of development of the experimental model of abdominal sepsis, whereas in relation to VCAM-1 – for the 48-hour period of development of the experimental model of abdominal sepsis. This, apparently, was due to the phasing of changes in the endothelial system of the lungs, where at the first stage intercellular adhesion prevailed, and subsequently cellular adhesion, which indicates the presence of endotheliocyte apoptosis.

The leveling of the values of the venous-arterial difference in this period of experiments was also noted by us in relation to vWF. The maximum level of vWF formation in the endothelial lung system occurred during the 12-hour period of development of the experimental model of abdominal sepsis (1.2 times). In subsequent periods, as the pathological process progressed, an increase in the venous-arterial difference for a 24-48-hour study period indicated a cumulative characteristic between vWF in a venous blood sample at the entrance to the lungs and in an arterial blood sample at the exit from the lungs.

This nature of the changes was also reflected in the subsequent development of the experimental model of abdominal sepsis, in which the productivity of vWF in the endothelial blood system at the exit from the lungs indicated active structural and functional disorders already in the vessels of the small circle.

Analysis of the venous-arterial difference showed that the endothelial system of the lungs reacted sensitively to changes in the focus of destruction. At the same time, the main character of the endothelial system of the lungs at the first stage was reduced to blocking the flow of pathological substrates into the systemic arterial bloodstream, and at the second stage of the development of an experimental model of abdominal sepsis, the lungs cease to create a barrier to the generalization of the inflammatory process, opening the way for the development of multiple organ dysfunction.

Conclusions.

1. An increase in peroxynitrite in various blood samples, depending on the timing of the development of an experimental model of abdominal sepsis, which was characterized by a transition from a state of transient phenomena to steadily progressive ones, indicating the depletion of compensatory capabilities of the endothelial lung system itself.

2. The productivity of vWF in the endothelial blood system at the exit from the lungs indicated active structural and functional disorders already in the vessels of the small circle.

3. The main character of the endothelial system of the lungs at the first stage was reduced to blocking the flow of pathological substrates into the systemic arterial bloodstream, and at the second stage of the development of an experimental model of abdominal sepsis – the lungs cease to create a barrier to the generalization of the inflammatory process, opening the way for the development of multiple organ dysfunction

Literature:

1. Azizov Y.H., Okhunov A.O., Azizova, P.H. Metabolic activity of lungs in the development of an experimental model of surgical sepsis. // European Science Review, 2018, V.11, #12, P.66-69.
2. Afanasyeva T.M. Endothelial dysfunction. Availability of early diagnosis. Health and education in the 21st century. 2016;18(11):101–104.
3. Babadzhanov B.D., Okhunov A.O., Atakov S.S. Methodology for the study of metabolic lung function in small laboratory animals // Methodical recommendation. – 1992.-Tashkent,34 c.
4. Barkhatova N. A. Peritonitis and abdominal sepsis: etiology, systemic response, choice of antibacterial therapy // Indelible tablets: sepsis et cetera: Collection of materials of the conference of the Association of General Surgeons dedicated to the anniversary of the Department of General Surgery of YAGMU, Yaroslavl, May 18-19, 2020. – Yaroslavl: Digital printing House, 2020. – C. 41-45.
5. 5. Clinical and nosological characteristics of peritonitis and abdominal sepsis in an urban multidisciplinary hospital in the context of the COVID-19 pandemic / A. A. Naydenov, A.V. Gostimsky, I. V. Karpatsky, M. V. Gavshchuk // Journal of Emergency Surgery named after I.I. Dzhanelidze. – 2021. – № S2. – C. 53-54.
6. Determination of optimal fluid balance in patients with abdominal sepsis in the postoperative period / S. A. Tochilo, A.V. Marochkov, T. I. Klepcha [et al.] // Surgery of Belarus - state and development : collection of materials of a scientific and practical conference with international participation and the XVII Congress of Surgeons of the Republic of Belarus, Mogilev, October 12-13, 2023 of the year. – Minsk: Belarusian State Medical University, 2023. – pp. 546-547.
7. Ostroumova Yu. S. Comparative assessment of criteria for predicting the course of secondary peritonitis and abdominal sepsis: specialty 14.01.17 "Surgery": dissertation for the degree of candidate of medical Sciences / Ostroumova Julia Sergeevna, 2021. – 110 c.
8. Safarov S.S., Khamdamov B.Z. Differentiated immunotherapy in purulent-septic complications of acute pancreatitis. Publishing house "Kamolot". Bukhara – 2022. 115 b.
9. Teshaev O.R., Muradov A.H., Sadykov R.R., Khamdamov B.Z. Improved results of treatment of purulent wounds with complex use photodynamic trerapy and CO2 lazer in the experiment. European Science Review. Austria, Vienna 2016 March-April №3-4. – P. 185-189.
10. Khamdamov B.Z.. Comparative evaluation of methods of amputation related to tidiotarus witn severe forms of diadetic foot syndrome. European Science Review. Austria, Vienna 2014 Septemba-October №9-10. - C. 58-60.
11. Khamdamov B.Z. After high amputations in diabetic foot syndrome, changes in the quality of life patients. Samarkand. Problems of biology and medicine. №1, 2019., (107) - S. 115-117.

12. Khamdamov B.Z. Complex treatment of diabetic foot syndrome with critical ischemia of the lower extremities. Journal of Biomedicine and Practice. Tashkent 2020, Special issue. Part 5. – With. 801-814.
13. Khamdamov B.Z. Method of laser photodynamic therapy in the treatment of wound infection in diabetic foot syndrome. Biology of wa tibbiet muammolari . Problems of biology and medicine №1 (116) 2020. – C. 142-148
14. Khamdamov B.Z. Morphological changes in the application of photodynamic therapy in the treatment of wound infection in an experiment. Journal of Morphology. St. Petersburg. 2020. Volume 157 (2-3). –C. 223-224.
15. Khamdamov B.Z. Optimization of methods of local treatment of purulent-necrotic foot lesions in diabetes mellitus. Journal. A new day in medicine. 2018, №4 (24) - C. 112-115.
16. Eshbekov M.A., Khamdamov B.Z. Indicators of the thyroid profile in various clinical forms of glomerulonephritis and correlations with the cytokine system // Journal of Theoretical and clinical Medicine. Tashkent, 2023- №6.- C.175-185.
17. Khamdamov B.Z., Nabieva U.P., Eshbekov M.A., Agzamova T.A. Cytokine profile in patients with glomerulonephritis depending on the clinical course// Journal of theoretical and clinical medicine. Tashkent, 2023- No.4.- C.112-116.
18. Khamdamov B.Z., Nabieva U.P., Eshbekov M.A. The level of immunocomposite reactions in chronic glomerulonephritis // Materials of the international scientific and practical conference "EDUCATION, SCIENCE, MEDICINE" dedicated to the 80th anniversary of the Academy of Sciences of the Republic of Uzbekistan, Tashkent, June 22, 2023. Journal of Theoretical and Clinical Medicine. Tashkent, 2023- No. 3.-C.184 https://www.elibrary.ru/item.asp?id=54206955
19. School systems for predicting the course and outcome of peritonitis and abdominal sepsis / Y. S. Ostroumova, I. M. Batyrshin, N. R. Nasser [et al.] // Bulletin of the Dagestan State Medical Academy. – 2019. – № 4(33). – C. 64-71.
20. Chalupova M., Horak J., Kramna L. Gut microbiome diversity of porcine peritonitis model of sepsis. Sci Rep. 2022 Oct 19;12(1):17430.
21. Characteristic features of morphological, structural and histochemical liver disorders at different stages of experimental abdominal sepsis / S. A. Alekseyev, D. D. Myadeletz, V. Y. Khryshchanovich [et al.] // Medical Journal. – 2019. – No. 2(68). – P. 47-51.
22. Kaur H, Chandran VP, Rashid M, Kunhikatta V, Poojari PG, Bakkannavar SM, Balakrishnan JM, Thunga G. The significance of APACHE II as a predictor of mortality in paraquat poisoning: A systematic review and meta-analysis. J Forensic Leg Med. 2023 Jul;97:102548.
23. Khamdamov B. Z., Akhmedov R. M., Khamdamov A. B. The use of laser photodynamic therapy in the prevention of purulent-necrotic complications after high amputations of the lower limbs at the level of the lower leg in patients with diabetes mellitus. Scopus Preview. International journal of Pharmaceutical Research. Volume 11, Issue 3, July-Sept, 2019
24. Khamdamov B. Z., Nuraliev N.A. Pathogenetic approach in complex treatment of diabetic foot syndrome with critical lower limb ischemia. American Journal of Medicine and Medical Sciences, 2020 10 (1) 17-24 DOI: 10.5923/j.20201001.05.
25. Khamdamov B.Z. Indicators of immunocitocine status in purulent-necrotic lesions of the lover extremities in patients with diabetes mellitus. American Journal of Medicine and Medical Sciences, 2020 10 (7): 473-478 DOI: 10.5923/j.20201001.08

26. Khamdamov, B., & Dekhkonov, A. (2022). Clinical and laboratory parameters of the wound process complicated by the systemic inflammatory response syndrome in patients with diabetes mellitus. Journal of education and scientific medicine, 2(3), 25-29. Retrieved from https://journals.tma.uz/index.php/jesm/article/view/349

27. Khamroev, U., & Khamdamov, B. (2022). Features of changes in endothelial system parameters in patients with diffuse toxic goiter. Journal of education and scientific medicine, 2(3), 62-67. Retrieved from https://journals.tma.uz/index.php/jesm/article/view/358

28.Khamdamova M.T. Ultrasound features of three-dimensional echography in assessing the condition of the endometrium and uterine cavity in women of the first period of middle age using intrauterine contraceptives // Biology va tibbyot muammolari. - Samarkand, 2020. - No. 2 (118). - P.127-131.

29.Khamdamova M. T. Ultrasound assessment of changes in the endometrium of the uterus in women of the first and second period of middle age when using intrauterine and oral contraceptives // Biomedicine va amaliyot journals. – Tashkent, 2020. - No. 2. - Part 8.- P.79-85.

30. Khamdamova M.T. Features of ultrasound parameters of the uterus in women of the first and second period of middle age using injection contraceptives // New day in medicine. Bukhara, 2020. - No. 2/1 (29/1). - P.154-156.

31. Khamdamova M.T. Features of ultrasound images of the uterus and ovaries in women of the second period of middle age using combined oral contraceptives // New day in medicine. Bukhara, 2020. - No. 2 (30). - P. 258-261.

32. Khamdamova M.T. Individual variability of the uterus and ovaries in women who use and do not use various types of contraceptives // New day in medicine. Bukhara, 2020. - No. 3 (31). - pp. 519-526.

33.Khamdamova M. T. Echographic features variability in the size and shape of the uterus and ovaries in women of the second period of adulthood using various contraceptives // Asian Journal of Multidimensional Research - 2020. – N9 (5). - P.259-263.

34. Khamdamova M. T. Somatometric characteristics of women of the first and second period of adulthood using different contraceptives with different body types // The american journal of medical sciences and pharmaceutical research - 2020. – N8 (2). - P.69-76.

35. Khamdamova M.T., Zhaloldinova M.M., Khamdamov I.B. The state of nitric oxide in blood serum in patients with cutaneous leishmaniasis // New day in medicine. Bukhara, 2023. - No. 5 (55). - P. 638-643.

36. Khamdamova M.T., Zhaloldinova M.M., Khamdamov I.B. The value of ceruloplasmin and copper in blood serum in women wearing copper-containing intrauterine device // New day in medicine. Bukhara, 2023. - No. 6 (56). - pp. 2-7. 37.Khamdamova M. T. Bleeding when wearing intrauterine contraceptives and their relationship with the nitric oxide system // American journal of pediatric medicine and health sciences Volume 01, Issue 07, 2023 ISSN (E): 2993-2149. P.58-62

38. Khamdamova M. T. The state of local immunity in background diseases of the cervix // Eurasian journal of medical and natural sciences Innovative Academy Research Support Center.Volume 3 Issue 1, January 2023 ISSN 2181-287X P.171-175.

39.Khamdamova M.T., Khasanova M.T. Various mechanisms of pathogenesis of endometrial hyperplasia in postmenopausal women (literature review) // New day in medicine. Bukhara. 2023. - No. 8 (58). - P. 103-107.

40. Khamdamova M.T. Reproductive Health of Women Using Copper-Containing Intrauterine Contraception // Eurasian Medical Research Periodical Volume 28 January 2024, ISSN: 2795-7624 .www.geniusjournals.org P. 39-45.

41. Khamdamov I.B. Advantages Of Laparoscopic Hernioplasty in Obesity Women of Fertile Age // Eurasian Medical Research Periodical Volume 28 January 2024, ISSN: 2795-7624 .www.geniusjournals.org P. 33-38.