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Study of the role of erythrocyte and leukocyte intoxication indexes in the pathogenesis of experimental peritonitis

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Abstract

The article presents the results of studying the role of erythrocyte and leukocyte indices of intoxication in the pathogenesis of experimental peritonitis. When studying the role of erythrocyte and leukocyte indices, a unidirectional trend of their change was revealed. An increase in the erythrocyte index of intoxication in the pathogenesis of experimental fecal peritonitis was established, most pronounced on the 10th day of the experiment (the level of EII increased by 107% compared to intact animals). The results of the study of the leukocyte intoxication index indicate a unidirectional trend, as in the case of the erythrocyte intoxication index. On the first day, the leukocyte index of intoxication increased on 225% ($p<0.05$), on the 4th day – on 256.7% ($p<0.05$), and on the 10th day – on 260% ($p <0.05$) compared to intact animals. It has been proven that the leukocyte index of intoxication is a more sensitive marker compared to the erythrocyte index.

Keywords: peritonitis; leukocyte index of intoxication; erythrocyte index of intoxication; pathogenesis.

Introduction. Peritonitis is a serious pathology that requires immediate treatment, which will minimize the development of complications [**Error! Reference source not found.**]. The local inflammatory process triggers a cascade of numerous pathophysiological processes that lead to damage to various organs and systems – the systemic inflammatory response syndrome [6, 9, 15]. The main pathogenetic component of peritonitis is endogenous intoxication as a result of bacterial translocation, action of neurotransmitters and tissue proteases, hypovolemia and neurohumoral intestinal paresis. The progression of peritonitis is also accompanied by the increasing aggregation activity of platelets, increased permeability of the wall of microvessels, their vasodilatation, the development of hypoxia and dissemination vascular syndrome [12, 16]. The noted violations lead to multiple organ failure, which is the main cause of death from peritonitis [8, 9].

An integral and threatening link in the pathogenesis of peritonitis is endogenous intoxication, which develops due to intestinal insufficiency, changes in the quantity and quality of intraluminal microflora, the concentration of toxins and microorganisms in the vascular bed, as well as in the lumen of the peritoneum. After an intra-abdominal infection, the patient has persistent systemic endotoxinemia, which disrupts the functional state of the liver, causes severe metabolic disorders and ED [1]. Endogenous intoxication is a polyetiopathological and polypathogenic syndrome, which is characterized by self-poisoning of the body with endogenous toxic substances (an excess of metabolic products or cellular reactions in pathological conditions) and their accumulation in tissues and biological fluids.

The aim of work – study of erythrocyte (EII) and leukocyte intoxication indices (LII) in rats against the background of experimental peritonitis.

Materials and methods. The study was conducted on 24 white nonlinear rats, which were divided into 2 groups: 1st group – intact animals (rats that were on a standard water diet and food); 2nd – rats with control pathology modelling.

According to the "Methodological recommendations for preclinical study of medicinal products", experimental peritonitis was studied on the model proposed by V. A. Lazarenko et al. (2008) [6]. This simulated pathology is close in terms of etiological factors, clinical manifestations and phasic course of the course to the similar process in humans and is acceptable for conducting a dynamic study within 10 days. Experimental rats were injected with 0.5 ml of 10% filtered fecal suspension in the abdominal cavity. The suspension was obtained by mixing isotonic solution and feces from the cecum of 2–3 intact animals, then it was filtered twice through a double layer of gauze. The resulting suspension was administered to the experimental group of animals no later than 20 minutes after preparation. In order to

avoid damage to internal organs during the introduction of fecal suspension into the abdominal cavity, the rats were kept vertically, with the caudal end up. Using the method of puncturing the ventral wall in the center of the midline of the abdomen, directing the end of the needle alternately into the right and left hypochondrium, right and left iliac regions, the same amount of fecal suspension was injected [6].

During the working with animals, the International Code of Medical Ethics (Venice, 1983), the "European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes" (Strasbourg, 1986), and the Law of Ukraine "On the Protection of Animals from Cruelty" No. 440 (dated 14.01.2020) were used [5].

EII was determined by studying the sorption capacity of erythrocytes during their interaction with methylene blue, which practically does not penetrate through their membrane under physiological conditions [2]. LII was calculated according to the method of Y. Y. Kal-Kalif (1941), which is based on the data of a general blood analysis [2].

Statistical processing of the obtained results was carried out with the help of the "Statistica 10.0" program. The probability of differences between the indicators of the control and experimental groups was determined by Student's and Fisher's tests. The level of reliability was accepted at $p<0.05$ [3].

Results of study and their discussion. On the first day of the experiment, animals of the control pathology group showed a probable increase in EII on 86.9% ($p<0.05$) compared to intact rats (Fig. 1).

On the 4th day of the study were established the progression of endogenous intoxication and an increase in EII on 90 % ($p<0.05$). On the 10th day, the level of EII increased on 107 % ($p<0.05$) compared to intact animals.

Figure 2 presents the results of the LII study – a unidirectional trend is noted, as in the case of EII. On the first day, the level of LII probably increased on 225 % ($p<0.05$) compared to intact animals (5.04±1.1 against 1.55±0.8). On the 4th day of observation, the level of LII also reliably increased on 256.7 % ($p<0.05$), and on the 10th day – on 260% ($p<0.05$) relative to the intact group of animals. Considering the obtained data, it can be stated that the leukocyte index is a more sensitive indicator than the erythrocyte index.

The obtained data can be explained as follows: it is known that endogenous intoxication is caused by the accumulation of toxic metabolites, which lead to the destruction of membranes and provoke the development of toxemia [1].

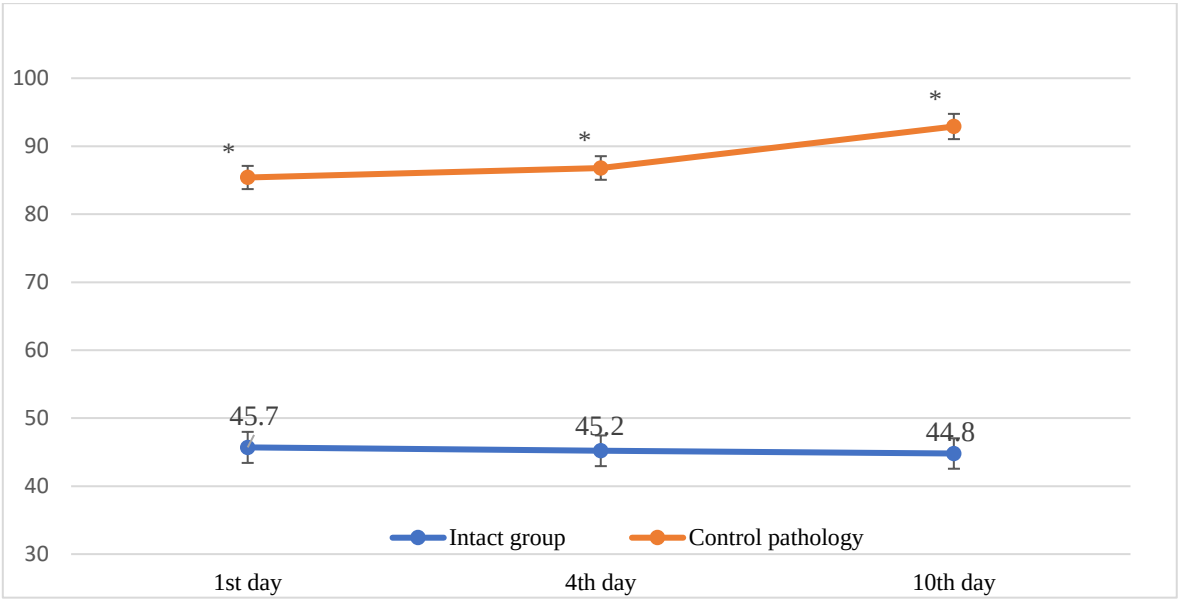

Fig. 1. Dynamics of the erythrocyte intoxication index in animals with simulated fecal peritonitis

Notes:

1. * - p<0,05 compared to the group of intact animals;

2. n – the number of animals in the group.

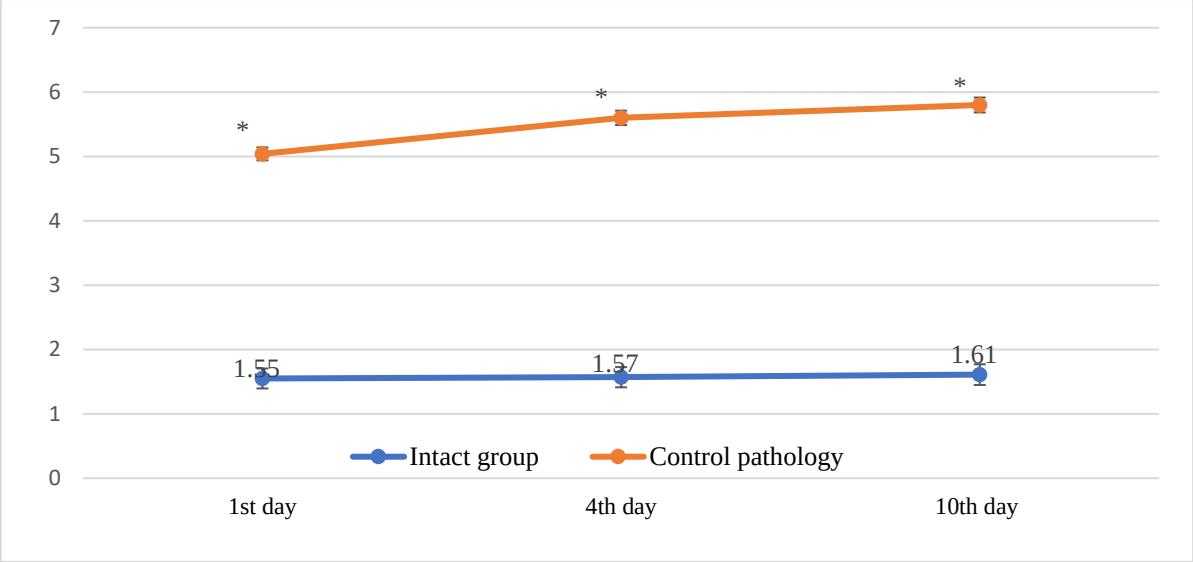

Fig. 2. Dynamics of the leukocyte intoxication index in animals with simulated fecal peritonitis

Notes:

1. * - p<0,05 compared to the group of intact animals;

2. n – the number of animals in the group.

Erythrocyte membranes are sensitive to the action of any toxins; therefore, it is appropriate to conduct an EII study in experimental peritonitis in rats. Considering our research results, EII changes indicate not only the sensitivity of erythrocyte membranes to the occurrence of peritonitis, but also the possibility of studying this pathological process in dynamics. In turn, LII is the most common index for the study of various pathological processes, which is characterized by the ratio of the level of cells that increase during inflammatory pathological processes to those that can decrease. According to literary sources, this indicator correlates with the severity of the pathological process of infectious genesis: in the range of 4-9 LII indicates a high degree of endogenous intoxication, 2-3 - indicates the presence of a necrobiotic focus or the development of a limited inflammatory process [1, 10, 11, 13].

Therefore, these markers allow a more detailed study of the course of pathological changes during the development of simulated fecal peritonitis, taking into account the fact that at the initial stage of the infectious process, toxic products accumulate in the tissues of the primary focus, and the specific targets for endotoxins are macrophages, leukocytes (mostly neutrophils) , connective tissue cells and platelets [13, 14].

Conclusions:

1. During the studying of erythrocyte and leukocyte indices role, a unidirectional trend of their change was revealed. An increase in the erythrocyte index of intoxication in the pathogenesis of experimental fecal peritonitis was established, most pronounced on the 10th day of the experiment (the level of EII increased on 107 % compared to intact animals).

2. The results of the study of LII indicate a unidirectional trend, as in the case of EII. On the first day, the level of LII increased on 225 % ($p<0.05$), on the 4th day – on 256.7 % ($p<0.05$), and on the 10th day – on 260 % ($p<0.05$) compared to intact animals. It has been proven that the leukocyte index of intoxication is a more sensitive marker compared to EII.

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