

Bone marrow hemopoiesis in inflammatory blood system reactions

Tachykinins are a group of protein neurotransmitters that are synthesized in almost all parts of the mammalian nervous system and play an important role in the processes of nervous excitation [1, 2]. Moreover, tachykinins and their receptors are widely represented outside the nervous system: in the respiratory, cardiovascular, endocrine and immune systems, as well as in the skin and gastrointestinal tract [3]. Substance P is one of the most studied tachykinins today. Its extract was first isolated in 1931 from the horse's brain and intestines in the form of a powder (powder), hence its name [3]. Substance P is released into the intercellular substance by exocytosis in the vesicles and has a very fast half-life, ranging from a few seconds to ten minutes, depending on physicochemical conditions [4]. The major tachykinin receptors are the neurokinin 1 receptor (NK1P), also known as the tachykinin 1 receptor, which has the highest affinity for substance P; the neurokinin 2 receptor, which has the highest affinity for neurokinin A, and the neurokinin 3 receptor, the neurokinin B receptor [1, 3, 5, 6, 7]. However, each type of receptor can interact with all types of tachykinins, depending on the concentration of the individual tachykinin and the characteristics of the environment. Thus, the unsolved problem today is to determine the role of tachykinins in inflammatory blood system reactions.

The **aim** of the study was to evaluate the bone marrow hematopoiesis in inflammatory blood system reactions.

Material and methods. The prospective controlled randomized experimental study was performed on 132 WAG rats. A carrageenan model of inflammation was selected, using 10 mg of α -carrageenan (Sigma, USA) in 1 ml of saline [8], which was injected intramuscularly into the rat thigh under thiopental anesthesia. To inhibit the synthesis and effects of substance P NK-1R inhibitor aprepitant was used, which was administered intraperitoneally at a dose of 10 mg dissolved in 1 ml of isotonic sodium chloride solution, daily throughout the experiment [9]. In the dynamics of experimental inflammation studied the reactions of the blood system (bone marrow cells reactions) in the natural course of carrageenan secondary and chronic substance P. Rats were kept in the vivarium

for 10–12 individuals in a cage under standard conditions on a normal diet with free access to water. To exclude the influence of natural circadian rhythms on the indicators, the experiment was performed in the autumn-winter period in a standardized way in the morning. Rats in the control series remained intact for inflammation during the experiment or were only administered the drug and kept under constant standard conditions. Experimental rats of intervention series in accordance with the tasks were subject to modeling of inflammation and the use of a pharmacological drug - an inhibitor of NK-1 receptors of aprepitant. Stratification of animals in separate series was carried out in the amount of 6 individuals. Non-parametric statistics was used with critical p 0.05.

Results and discussion. The features of bone marrow hematopoiesis in secondary chronic carrageenan inflammation against the background of substance P blockade, which consist in signs of a less pronounced inflammatory reaction, have been established. At the early stages - 6 hours, 2 days - a smaller ($p < 0.05$) relative number of neutrophils (involved in the implementation of predominantly nonspecific reactions), megakaryocytes (which, in addition to inflammation, is a marker of the state of the hemocoagulation system) was found. This fits well with the concept of a connection between the blockade of NK1 receptors for substance P and a decrease in its activating effect on hematopoiesis. A higher content of the cell population of a lymphocytic hematopoietic lineage, established during inflammation for periods up to 5 days inclusive, can be interpreted as a compensatory reaction of the immune system with a redistribution of subpopulations of effector cells from a nonspecific link of inflammatory reactions in favor of a specific one.

Thus, in chronic inflammatory processes, chronic stress, acute inflammation, the expression of the corresponding receptors may change, which modifies the effect of neurokinins on the inflammatory process [1]. The blockage of substance P may change an inflammatory scenario and may be therefore used in experimental and clinical applications.

Conclusions:

1. Features of bone marrow hematopoiesis in carrageenan secondary chronic inflammation on the background of its suppression by administration of the NK-1 blocker substance P is a smaller ($p < 0.05$) in the early stages of the number of cells involved in the implementation of mostly nonspecific immunoinflammatory reactions and

markers blood coagulation system.

2. A higher content of the cell population of the lymphocytic germ of hematopoiesis was detected against the background of blockade against the background of blockade of substance P.

The prospects of further research is evaluation of the cell-tissue reactions in an inflammation focus in carrageenan secondary-chronic inflammation on the background of substance P blockade.

Literature

1. Navratilova E. Substance P and Inflammatory Pain: Getting It Wrong and Right Simultaneously / E. Navratilova, F. Porreca // *Neuron*. — 2019. — Vol. 101, No. 3. — P. 353–355. — doi: 10.1016/j.neuron.2019.01.034.

2. Tachykinins and tachykinin receptors: a growing family / J. N. Pennefather, A. Lecci, M. L. Candenas [et al.] // *Life Sci*. — 2004. — Vol. 74, No. 12. — P. 1445–1663.

3. Substance P and neurotensin in the limbic system: Their roles in reinforcement and memory consolidation / L. Lénárd, K. László, E. Kertes [et al.] // *Neurosci. Biobehav. Rev.* — 2018. — Vol. 85. — P. 1–20 — doi: 10.1016/j.neubiorev.2017.09.003.

4. Cough hypersensitivity in patients with obstructive sleep apnea hypopnea syndrome / C. Shi, S. Liang, X. Xu [et al.] // *Sleep Breath*. — 2018. — doi: 10.1007/s11325-018-1641-7.

5. Suvas S. Role of substance P neuropeptide in inflammation, wound healing, and tissue homeostasis // *J. Immunol.* — 2017. — Vol. 199, No. 5. — P. 1543–1552.

6. Mantyh P. W. Neurobiology of substance P and the NK1 receptor / *J. Clin. Psychiatry* // 2002. — Vol. 63, Suppl 11. — P. 6–10.

7. Pereira M. P. Neurokinin-1 receptor antagonists: promising agents in the treatment of chronic pruritus / M. P. Pereira, S. Ständer // *Curr. Derm. Rep.* — 2017. — Vol. 6, No. 4. — P. 273–278.

8. Klymenko M. Substantiation of the model of chronic (secondary chronic) inflammation / M. Klymenko, S. Tatarko, O. Shevchenko, G. Hubina-Vakulyk // *Experimental and Clinical Medicine*. — 2007. — No. 2. — P. 24–28.

9. An FDA Approved Neurokinin-1 Receptor Antagonist is Effective in Reducing Intraabdominal Adhesions when Administered Intraperitoneally, But Not Orally / R. Lim, J. M. Morrill, S. G. Prushik [et al.] // *J. of Gastroint. Surg.* — 2008. — No. 12 (10). — P. 1754–1761.