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MEANING OF INDICES OF NITRIC OXIDE SYSTEM FOR EARLY PERIOD OF PEPTIC ULCER DISEASE FORMATION IN THE PRESENCE OF PNEUMONIA

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Abstract

The diseases most often occurring in clinical picture – pneumonia and peptic ulcer disease (PUD) – have been selected for experimental investigation. **The aim of the research**: to determine the number of nitric oxide system indices in early period of peptic ulcer disease and experimental pneumonia (EP). **Methods of investigation.** The research was conducted on 35 male guinea pigs, weighing 180-210 g. Experimental pneumonia was provoked by V.N. Shlyapnikov, T.L. Solodov [et.al.] method, peptic ulcer disease was modeled by V.I. Komarov method. Activity of NO synthases was detected by V.V. Sumbaev method, L-arginine content in blood serum – by T.L. Aleinikov method, stable NO metabolites – by H.H.W. Schmidt method. Decapitation of animals was performed under ether anesthesia on the 4^{th} and 8^{th} days of inflammatory process formation in the lungs and gastric ulcer disease.

Obtained results. Investigation of the amount of stable NO metabolites in the blood of animals with PUD and EP found that this index increased by 53.9% ($P<0.05$) in relation to control animals on the 4^{th} day of experiment. Further investigation of NO level, on the 8^{th} day of these disease models, showed its significant increase as compared with intact animals – by 68,7 % ($P<0.05$). The next index taken into account was inducible NOS (iNOS), concentration of which in the blood increased by 64,0 % ($P<0.05$) on the 4^{th} day as compared

to control animals, and further this index reached its highest level – 93,4 % (P<0.05). Activity of cNOS increased on the 4th and 8th days by 21,5 % (P<0.05) and 28.9 % (P<0.05), respectively, in comparison with control. Amount of L-arginine in early period decreased by 74,9 % on the 4th day, and decreased by 86,5 % on the 8th day in relation to intact animals. **Conclusion**. Determination of certain indices of nitric oxide system showed an increase in iNOS and cNOS and stable metabolites on the background of decrease in L-arginine amount.

Key words: pneumonia, peptic ulcer disease, nitric oxide.

Introduction. Diseases of the respiratory and digestive systems are among the urgent problems of contemporary theoretical and practical medicine. Annually, according to WHO data, approximately 450 million people or 7,0 % of the earth population suffer from pneumonia. It is known to be the cause of approximately 4 million deaths worldwide. Thus, in the 19th century scientists termed pneumonia "a driver of death's echelon", but a lot of people have been recovering from the disease since the discovery of antibiotics and appearance of vaccination. Nevertheless, pneumonia is still the main cause of death in developing countries, among elderly or very young individuals and those who suffer from chronic diseases, especially elderly individuals who are at risk for development of septic complications and lethal consequences to 30,0 %, especially people over 60 and in the presence of risk factors [1].

One of the most common diseases of the gastrointestinal tract is peptic ulcer disease. Ulcer disease is a general chronic, recurrent disease with the tendency to progressing, with polycyclic course, typical peculiarities of which are seasonal exacerbations, accompanied by ulcerative defect in gastric or duodenal mucosa, and the development of complications that may result in mortality.

Hypoxia is known to play a significant role in pneumonia development. Long-lasting oxygen deprivation is accompanied by an increase in free radicals and activation of peroxide lipid oxidation. Primary targets of activity of oxygen free radicals are membranous structures of the cells, in which lipid bilayer, receptors, protein transmitters of ions and molecules (membranous canals), as well as enzymes built into the membranes, in particular ion pumps, are destroyed [2]. In our opinion, formed free radicals may also damage cell membranes of the gastric mucosa. In addition, pneumonia requires a continuous drug therapy, which may also be the cause of damage to gastric mucosa.

One of the most important mediators of intracellular and intercellular correlation in immune-neuroendocrine system is nitric oxide (NO), which is one of free radicals [3]. Nitric

oxide is one of the most important mediators of the respiratory system. Constitutive nitric oxide synthase of the endothelium of lung vessels, neurons of NANC inhibitory nervous system, epithelial cells, as well as inducible NOS (iNOS) of the airway epithelium, inflammatory and immunocompetent cells (macrophages, neutrophils, smooth cells, endothelium, myocytes) produce NO [3]. NO is regarded as an important factor of immunological reactivity, especially non-specific immunity, necessary for conduction of regulatory cytoprotective processes at the level of cell organelles and the whole body [7].

Increased NO production, having an important adaptive meaning for the body, may transform from adaptation to pathogenetic branch and become dangerous damaging factor for the body [4]. Numerous investigations dedicated to studying the role of nitric oxide system in the regulation of physiological and pathological processes. A number of scientific investigations indicate that NO plays a significant bioregulatory role in the regulation of local vessel tonus and systemic hemodynamic reactions, realization of the immune response, and neurotrophic effects [7].

Methods of investigation. The research was performed on 35 male guinea pigs weighing 180-210 g. Experimental animals were divided into three groups:

- the first group – control (intact animals), 15 animals;
- the second group – guinea pigs with PUD and EP on the 4^{th} day (10 animals);
- the third group – guinea pigs with PUD and EP on the 8^{th} day (10 animals).

Experimental pneumonia was provoked by V.N. Shlyapnikov, T.L. Solodov method [5], peptic ulcer disease was modeled by V.I. Komarov method [6]. Activity of NO synthases was detected by V.V. Sumbaev method [7], L-arginine content in blood serum – by T.L. Aleinikov method [8], stable NO metabolites – by H.H.W. Schmidt [9]. All digital results of investigation were processed statistically by Student's method.

Decapitation of animals was performed on the 4^{th} and 8^{th} days of inflammatory process formation in the lungs and peptic ulcer disease following the bioethics principles according to the decree of European convention for the protection of vertebrate animals, used for experiments and other scientific purposes (Strasbourg, 1986), Directive of European Council 86/609/EEC (1986), Law of Ukraine № 3447 – IV IV "On protection of animals against cruel treatment", general ethic principles of experiment on animals, agreed by the First national congress of Ukraine on bioethics (2001).

Results and their discussion. NO is produced in the body by a group of isoenzymes of NO-synthases (NOS), two constitutive – neuronal (nNOS) and endothelial (eNOS), as well as inducible (iNOS), each of which has its peculiarities both by the action mechanism and

biological meaning [9].

Investigation of the amount of stable NO metabolites in the blood of animals with PUD and EP found out that this index increased in the blood by 53,9% (P<0,05) on the 4th day of experiment as compared to control animals. Further investigation of these disease models on the 8th day revealed its significant increase in comparison with intact animals – by 68,7 % (P<0,05). Thus, investigation of the level of stable NO metabolites in early period of PUD and EP formation revealed its elevation (Fig. 1).

The next index, taken into account, was inducible NOS (iNOS), concentration of which in the blood increased by 64,0 % (P<0,05) on the 4th day as compared to control animals, and further this index reached its highest level – 93,4% (P<0,05) (Fig.1).

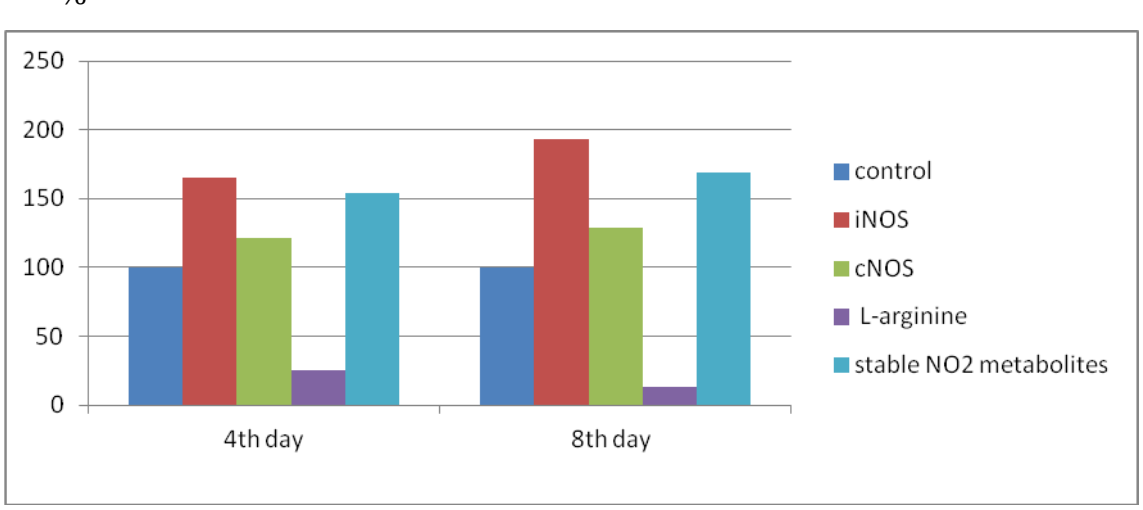

Fig.1. Amount of indices of nitric oxide system in the blood in early period of EP and PUD (% from control)

Activity of cNOS increased on the 4th and 8th days by 21,5 % (P<0,05) and 28,9 % (P<0,05), respectively, in comparison with control (Fig.1). Amount of L-arginine in early period decreased by 74,9 % on the 4th day, and decreased by 86,5 % on the 8th day in relation to intact animals. L-arginine amino acid participates in many physiological processes, particularly maintenance of nitrogen balance, regulation of immune response, antihypertensive, apoptopic and antiproliferative actions; it is also a substrate for enzymatic activity of NO-synthases, which cause the synthesis of a potent vasodilator NO [10].

Thus, determination of certain indices of nitric oxide system showed an increase in iNOS and cNOS and stable metabolites on the background of decrease in L-arginine amount, indicating impairment of metabolic processes in the presence of EP and PUD.

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