EFFECTS OF SOME DRUGS ON FREE RADICAL PROCESSES IN THE GASTRIC MUCOSA IN THE MODEL OF INDOMETHACIN GASTROPATHY

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Introduction. One of the urgent problems of practical medicine is gastropathies that develop when using anti-inflammatory drugs [1,2,8,19]. The reason for this is that non-steroidal anti-inflammatory drugs (NSAIDs) are widely used not only as anti-inflammatory, anti-aggregant, but also as antipyretic and pain relievers [3,4,11,20]. However, in these cases, almost all patients have gastric disorders [5,11,14]. Taking into account that the effectiveness of preventive measures and tools used in gastropathies is low, the creation of new drugs is one of the important tasks of pharmacology [5,7,16]. Free radical oxidation - the development of oxidative stress has been found to be one of the main links in the pathogenesis of many pathologies, including gastropathies [6,7,8,9,10]. The formed free radicals damage the subcellular structures and biological membranes of cells. As a result, dysfunction of organs and systems is observed [9,17,18]. Therefore, it is necessary to use substances with antioxidant properties to prevent gastropathy. In this regard, the new compound Lesboxol, which has gastroprotective properties in models of gastropathy induced by stress, ethanol, reserpine and indomethacin, was of particular interest. Lesboxol is a complex drug consisting of dry extracts of 4 types of plants - Hypericum scabrum, Ziziphora pedicellata, Elder grass (Medi asia macrophylla), common licorice (Glycyrrhiza glabra)[1,3]. Although Lesboxol reduces the development of gastropathy under the influence of pathogenic factors, its cytoprotective properties have not been fully studied.

Purpose of work. Comparative study of the effect of Lesboxol, Misoprostol and Mucogen on the process of peroxidation of fats in the gastric mucosa and the activity of enzymes of the antioxidant system in gastropathies developed under the influence of Indomethacin.

Materials and Methods.

Experimental studies were conducted on male rats with an initial weight of 165-185 g. Five groups of six animals each were formed. One day and 2 hours before the induction of the gastropathy model, the animals of the first, second and third groups were injected intragastrically with the following doses: Misoprostol - 0.2 mg/kg, Lesboxol - 50 mg/kg, Mucogen (rebamipid) - 100 mg/kg. The fourth group of rats was given the appropriate amount of water (control), and the fifth group consisted of healthy animals, which served as a control for the rest (healthy). In animals of the first, second, third and fourth groups, nonsteroidal anti-inflammatory drug (NSAQV) - indomethacin 60 mg/kg in physiological solution was administered intragastrically to create a model of gastropathy [10,13]. Rats were deprived of food for 24 hours before creating a model of indomethacin-induced gastropathy.

24 hours after the introduction of drugs, the activity of lipid peroxidation products (LPO) and antioxidant system (AOT) enzymes was determined.

For biochemical studies, animals were slaughtered under light ether anesthesia in a cold room at a temperature of 0 ± 4 ° C. After the gastric mucosa was separated, the weight was determined and washed with cold physiological solution. A homogenate was prepared in a 3-4 times volume of 15 TB/ml contrical and 3 TB/ml heparin solution in a glass container with a Teflon pestle. Homogenates were centrifuged at 9,000 g for 30 min to pellet nuclei, mitochondria, and cellular debris. It is known that the increase in LPO processes in the cell membrane and subcellular structures leads to the degradation of membrane phospholipids, which, in turn, disrupts intracellular homeostasis and slows down complex metabolic and synthetic processes in the cell. The main powerful defense mechanism in the cell that prevents LPO activity is the antioxidant system. The vital activity of the cell directly depends on the level of activity of factors that enhance lipid peroxidation and the activity of AOT enzymes [5,19]. Considering the above, in order to evaluate the state of lipid peroxidation, we measured the amount of lipid peroxidation products [acyl hydroperoxide (AtsGP), malondialdehyde (MDA)] and AOT [catalase (KT), superoxide dismutase (SOD)] enzymes in the supernatant fraction of the gastric mucosa homogenate. activity was determined. AtsGP was determined by the method of V.B. Gavrilov and others [9]. The method is based on separation of lipid hydroperoxide with a heptane-isopropanol mixture in an acidic environment, and then measuring the optical density with a spectrophotometer at a wavelength of 233 nm. The amount of AtsGP was expressed in relative units relative to mg of protein. MDA was determined by the method of L.I. Andreeva [7]. Products reacting with thiobarbituric acid were calculated using a molar extinction coefficient of MDA of 1.56x105 mol cm and calculated per mg of protein. QD activity was determined by the method of M.A. Korolyuk [12]. The method is based on the ability of H2O2 to form a stable color with molybdenum salts. The staining intensity was measured in a spectrophotometer at a wavelength of 410 nm. The obtained data are expressed in mmol H2O2/min.mg of protein. SOD activity was determined by the percent reduction of nitrotetrazol blue in alkaline medium and expressed in conditional units per mg of protein [15,16]. The results of the studies were subjected to statistical processing using the Biostat 2009 software package, the significance of M ± m characteristics and the differences in the considered samples according to the Student's test were evaluated according to the statistical method. Differences between the compared groups were considered at the 95% ($P<0.05$) confidence level.

Results and its discussion.

The results of biochemical studies showed that the amount of AtsGP increased by 89.0%, MDA increased by 71.7%, CT activity decreased by 36.8%, and SOD decreased by 62.7% in the gastric mucosa of control animals compared to healthy animals. observed. Therefore, the damage of indomethacin to the gastric mucosa (MShQ) is based on the development of oxidative stress, which was manifested in an increase in the level of lipid peroxidation products and a decrease in the activity of protective enzymes of AOT.

In our experiment, it was observed that the changes in the group of animals that received gastroprotective agents for the purpose of prevention were different. AtsGP and

MDA concentrations in the gastric mucosa under the influence of misoprostol were reduced by 12.6% and 2.0% compared to the control, but it was not statistically significant. As shown in Table 1, these data were 16.4 and 12.5%, respectively, in mucogen-treated animals, and 28.2 and 27.3%, respectively, in lesbokhol-treated animals.

It can be said that the studied gastroprotectors reduce the intensity of free radical oxidation (ERO), which may be the result of an increase in the activity of the antiradical system. Indeed, CT and SOD activity increased by 6.4 and 61.7%, and mucogen by 25.8 and 68.3%, respectively, in misoprostol-treated animals. We found higher changes in studied parameters in animals treated with lesboxhol, where CT activity was 45.1% higher and SOD was 140.0% higher compared to the control group. Apparently, lesbokhol is superior not only to misoprostol, but also to mucogen in terms of pharmacological activity. In general, the presented results of biochemical studies show that the increase in ERO as a result of the reduction of AOT is the main pathogenetic factor in the development of destructive-erosive damage of the gastric mucosa in indomethacin-induced gastropathy. Drugs studied in the treatment of gastropathy prevent the development of ERO and have a beneficial effect on the components of the immune system of the gastric mucosa. In this regard, lesbokhol is relatively superior to the effectiveness of other drugs. This situation can be the basis for its use as an effective tool in stomach pathology.

The conclusion.

1. One of the important causes of gastropathies developed under the influence of indomethacin is an increase in the process of peroxidation of fats due to a sharp decrease in the activity of enzymes of the antioxidant system.

2. Synthetic analogue of prostaglandin E1 - Misoprostol shows a weak antioxidant effect in gastropathy developed under the influence of indomethacin.

3. Prostaglandin E2 production-stimulating drug Mucogen is based on the cytoprotective effect of a statistically reliable reduction of peroxide oxidation of fats in the gastric mucosa and an increase in the activity of the antioxidant system.

4. In terms of its pharmacological activity, "Lesboxol", a combination of plant extracts, is superior to Mucogen and especially Misoprostol in gastric injury caused by indomethacin.

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