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Yogarathnam L., Kovaliova V.A.

RESPONSE OF NEUTROPHILS WITH COMBINED ADMINISTRATION OF L-ARGININE AND AMINOGUANIDINE IN RATS WITH EXPERIMENTALPERITONITIS

Tutors: PhD, senior lecturer Husakouskaya E.V.,
professor Maksimovich N.Y.
Department of Pathological Physiology
Grodno State Medical University, Grodno

Introduction. The morphological target in peritonitis is the peritoneum with its cavity, it is important to determine the response of peritoneal leukocytes, especially neutrophils, in the dynamics of the inflammatory process. The contribution of NO generated by different isoforms of NO synthase (NOS) - constitutive (cNOS) and inducible (iNOS), to the development of peritonitis has not been disclosed; there are no approaches to its pathogenetic therapy that involve influencing the L-arginine-NO system.

Aim: to assess the composition and phagocytic activity of peritoneal neutrophils in rats with experimental peritonitis and combined administration of L-arginine (L-Arg) and aminoguanidine (AG).

Materials and methods. Rats were administered intraperitoneally: 1st series (control) – 0.9% sodium chloride, 2nd series (experimental peritonitis, EP) – 15% fecal suspension in a volume of 0.6 ml/100 g of body weight, 3rd series (EP + L-arg + AG) . Fecal suspension was standardized by its two-stage filtration and by performing spectrophotometric and densitometric analysis. The neutrophils were determined in blood smears and peritoneal fluid was stained according to Romanovsky-Giemsa. Determination of the phagocytic activity was carried out after half a day, 1 day and 3 days of EP. For this, peritoneal exudate (20 µl) was incubated with an equivolumed 0.1% solution of nitrosine tetrazolium, followed by the addition of 160 µl of 3 % acetic acid after thermostating at 37 °C for 30 minutes. Phagocytic activity was assessed based on the number of formazan-positive neutrophils (FPN) based on their percentage. Statistical data processing was performed using the stastica 10.0 - nonparametric Kruskal-Wallis test and post hoc comparisons.

Results and their discussion. When studying the relative leukocyte formula in rats with the combined administration of L-arg and AG, a significant decrease in the severity of the nuclear shift of the leukocyte formula to the left, which is characterized as regenerative was indicated, While comparing with the hyperregenerative shift of peritoneal fluid in peritonitis. The obtained data reflects the anti-inflammatory effect of the combined use of L-arg and AG, which is due to the correction of microcirculation and metabolic disorders under the conditions of L-arg use, as well as a decrease in the activity of oxidative stress due to the inhibition of iNOS activity by AG. This reduces the severity of secondary alteration and the exudation it initiates with the emigration of leukocytes to the site of inflammation.Along with a change in the quantitative composition of neutrophils, a decrease in their ability to phagocytosis was noted in the formazan-positive neutrophils (FPN), but with the combined administration of L-arg and AG, an increase in the phagocytic activity of neutrophils was established, as evidenced by a greater number of peritoneal FPN than in animals with EP without the administration of NOS modulators. Thus, the combined administration of L-arg and AG to rats with EP led to the most pronounced increase in the ability of peritoneal neutrophils to phagocytosis among the studied NOS modulators. This may be due to a decrease in the formation of reactive nitrogen species, which have a cytotoxic effect on peritoneal phagocytes, as well as an increase in the bioavailability of L-arg to correct metabolic disorders in immunocompetent cells.

Conclusion. The response of neutrophils in rats with acute experimental peritonitis in the form of a hyperregenerative nuclear shift of the leukocyte formula to the left, along with a decrease in their phagocytic activity indicates the inhibition of nonspecific immune defense and a significant intensity of the infectious and inflammatory process. Combined administration had the most significant corrective effect in maintaining the activity of constitutive NOS isoforms and eliminating the negative effects of excess NO concentrations.