Enzyme	Population Group	Common Phenotype	Drugs Affected	Clinical Implication
CYP3A4	African	Ultra-rapid metabolizer (~20%)	Antiepileptics, steroids	Reduced therapeutic levels

Discussion. Genetic variation in metabolic enzymes can greatly alter drug concentration and response. Routine genotyping could improve treatment safety by enabling dose individualization. However, cost and limited access to testing restrict widespread use in developing countries.

Conclusion. Pharmacogenetic diversity significantly affects clinical outcomes and drug safety. Integrating pharmacogenetic data into clinical guidelines can improve personalized therapy and reduce adverse drug reactions.

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IMMUNOMODULATING EFFECT OF AMINOGUANIDINE IN EXPERIMENTAL PERITONITIS

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Relevance. Mortality from peritonitis remains quite high, despite significant advances in modern medicine in the diagnosis and treatment of urgent surgical conditions [1, 2, 3]. Although the mandatory standard of treatment for peritonitis is surgical intervention combined with antibacterial therapy [1], adequate pathogenetic therapy is also of great importance [4]. However, insufficient knowledge of the mechanisms of inflammation in the abdominal cavity, in particular the mechanisms regulating leukocyte phagocytic activity, indicates the need for further clarification.

In turn, influencing this important link in pathogenesis may contribute to the correction of peritonitis.

Objective. To establish the immunomodulatory effect of inhibitor of the inducible isoform of NO synthase, aminoguanidine, in peritonitis in rats.

Materials and research methods. The studied animals (n=54) were divided into 3 equal series, which were administered intraperitoneally at a rate of 0.6 ml/100 g of body weight: 1st series (control) – 0.85% sodium chloride solution; 2nd and 3rd series – 15% fecal suspension (experimental peritonitis), according to the adapted method of V. A. Lazarenko et al. [5]. After this, the following were administered intramuscularly in a volume of 0.5 ml: 1-2nd series – 0.85 % sodium chloride solution; 3rd series – inhibitor of the inducible isoform of NO synthase – aminoguanidine, 15 mg/kg (Sigma, USA). In turn, in each series, 3 subgroups of rats were identified, in which the phagocytic activity of peritoneal neutrophils was determined after half a day (n = 6), one day (n = 6) and three days (n = 6). Peritoneal fluid was collected after a median laparotomy along *l. alba*, the injection of 5 ml of sterile 0.85 % sodium chloride solution into the abdominal cavity and a light massage of the abdominal wall for 20 seconds were performed. To determine the functional activity of peritoneal neutrophils, an adapted method of Yu. I. Patsula and V. S. Vlasenko (2011) [6] was used. In this case, peritoneal fluid of rats with peritonitis in a volume of 20 μl was added to the wells of a 96-well round-bottom plate for immunological studies, filled with an equal volume of 0.1% nitroblue tetrazolium solution. The sample plate was incubated in a thermostat for 30 minutes at 37°C. Then, 160 μl of 3 % acetic acid was added to each well to achieve hemolysis of the erythrocytes. Activated formazan-positive neutrophils containing dark purple formazan granules were counted in a Goryaev chamber, with 200 neutrophils counted. Statistical data processing was performed using Statistica 10.0 for Windows (StatSoft Inc., USA) using the nonparametric Kruskal-Wallis test and post hoc comparisons using Dunn's test.

Results. The research has shown a decrease in the ability of peritoneal neutrophils to phagocytosis in rats with acute peritonitis. This was evidenced by a decrease in the percentage of formazan-positive neutrophils in the peritoneal fluid after half a day of experimental peritonitis – to 44 (42; 46)%, or by 13% ($p < 0.05$), after one day – to 35 (33; 38)%, or by 22% ($p < 0.05$), after three days – to 44 (41; 45)%, or by 13% ($p < 0.05$), in comparison with the value in the «control», which may be due to the cytotoxic effect of active oxygen and nitrogen species on peritoneal phagocytes. Moreover, the number of formazan-positive neutrophils in rats with peritonitis after one day was less than after half a day by 9% ($p<0.05$), and after three days, on the contrary, it was more than after one day by 9% ($p<0.05$), which indicated the most pronounced suppression of the phagocytic activity of peritoneal neutrophils after one day of inflammation. In turn, under the administration of aminoguanidine in experimental peritonitis, the number of peritoneal formazan-positive neutrophils increased: after half a day to 59 (57; 61)%, or by 15% ($p<0.05$), after one day – up to 53 (51; 55)%, or by 18% ($p<0.05$), after three days – up to 57 (55; 60)%, or by 13% ($p<0.05$), compared with the values of the indicator in animals with peritonitis

without its administration. At the same time, no changes were noted in the content of formazan-positive neutrophils in the dynamics of the studied periods, which indicates a stable level of functional activity of peritoneal microphages. The obtained data may indicate sufficient phagocytosis activity in experimental peritonitis under the administration of aminoguanidine. Thus, administration of aminoguanidine, an inhibitor of the inducible isoform of NO synthase, to rats with peritonitis resulted in increased phagocytic activity of peritoneal fluid neutrophils, indicating a positive immunomodulatory effect on the leukocyte component of the immune defense.

Conclusions. Administration of aminoguanidine, an inhibitor of the inducible isoform of NO synthase, to rats with peritonitis resulted in an improved leukocyte response, manifested by an increase in the phagocytic activity of peritoneal neutrophils. The immunomodulatory effect of aminoguanidine in the inflammatory process in the abdominal cavity in rats may be due to the inhibition of excessive NO formation with the participation of the inducible isoform of NO synthase and the neutralization of a number of negative effects of oxidative stress, as well as an increase in the bioavailability of the NO synthase substrate, L-arginine, used to implement important metabolic pathways and maintain the activity of constitutive isoforms of this enzyme.

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