CHANGES IN THE CONTENT OF MALONIC DIALDEHYDE IN THE BLOOD OF RATS WITH PERITONITIS AND MODULATION OF NO-SYNTHASE ACTIVITY

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Resume. Modulation of nitric oxide (NO) synthase activity significantly influence the severity of oxidative stress in a rat model of fecal peritonitis, as measured by plasma malondialdehyde (MDA) levels.The most pronounced effect was observed with the combined administration of L-arginine and aminoguanidine resulting in a substantial and sustained reduction in plasma MDA concentrations compared to the untreated peritonitis group. The decrease was significant at all time points. While MDA levels in the combination group remained elevated compared to the healthy control, the data indicate that the dual modulation of the L-arginine-NO system synergistically attenuates lipid peroxidation, with the severity of oxidative stress decreasing over the three-day course of the experiment.

Keywords: malondialdehyde, peritonitis, L-arginine, aminoguanidine, oxidative stress.

Relevance. The fact that current pathogenetic therapy for peritonitis [1-2] does not significantly lower mortality emphasises the need for more research into the mechanisms behind the pathology's development. One intriguing topic is researching the effects of altering the L-arginine-NO system because there are no interventions for this system in peritonitis treatment regimens and nothing is known about the role of nitric oxide in the pathophysiology of this illness. In particular, information about the role of NO generated by constitutive and inducible isoforms of NO synthase in the development of oxidative stress, a crucial pathogenetic aspect of peritonitis, is sparse. Because NO has both pro- and antioxidant effects, more study in this field is required. [3-5].

Aim: was to investigate how altered NO synthase activity affects the levels of malondialdehyde in the blood of rats suffering from peritonitis.

Materials and methods. The study animals were split into five equal series and given intraperitoneal injections at a rate of 0.6 ml/100 g of body weight: Following the first series (control) of 0.85% sodium chloride solution and the second through fifth series of 15% faecal suspension (peritonitis), the following were given intramuscularly in a volume of 0.5 ml: 1-2nd series: 0.85% sodium chloride solution; 3rd series: L-arginine, 300 mg/kg (Sigma, USA); 4th series: aminoguanidine, 15 mg/kg (Sigma, USA), an inhibitor of the inducible isoform of NO synthase; and 6th series: L-arginine and AG at comparable concentrations. In order to measure the amount of malondialdehyde, blood was drawn from three subgroups of rats in each of the five series after half a day (1st subgroup, n = 6), one day (2nd subgroup, n = 6), and three days (3rd subgroup, n =

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6). Rats' abdominal cavities were filled with a faecal suspension in accordance with Lazarenko V.A. et al.'s approach [6], as modified [7], in order to replicate acute peritonitis. By using spectrophotometry to measure the extinction of a solution containing the pink-colored trimethyl complex of MDA with thiobarbituric acid, the amount of MDA was ascertained [8]. In this instance, 0.2 ml of the sample was mixed with 1 ml of 15% trichloroacetic acid and 1 ml of thiobarbituric acid. The samples were then boiled for 10 minutes, cooled, and centrifuged for 10 minutes at 3000 rpm. A SOLAR PV 1251C spectrophotometer (Belarus) was used to measure the final product's concentration at $\lambda = 532$ nm. The nonparametric Kruskal-Wallis test and post hoc comparisons were used to process the statistical data using the Statistica 10.0 program for Windows (StatSoft Inc., USA); the results are shown as Me (LQ; UQ) – median (lower quartile; upper quartile).

Results and their discussion. Combined administration of L-arginine, a NO synthase substrate, and aminoguanidine, an inhibitor of the inducible isoform of the enzyme, to rats with experimental peritonitis resulted in changes in the plasma levels of malondialdehyde (MDA), a secondary product of lipid peroxidation. In particular, the plasma of rats with peritonitis and combined treatment of the investigated NO synthase modulators showed the greatest reduction in MDA concentrations when compared to the values seen in rats with peritonitis either without or with their use alone. Specifically, compared to the values in experimental peritonitis without drug administration, the MDA content in the blood plasma decreased after half a day to 1.1 (0.8; 1.3) μmol/l, or three times ($p<0.01$), after one day to 1.6 (1.4; 1.8) μmol/l, or 2.7 times ($p<0.01$), and after three days to 0.9 (0.7; 1.1) μmol/l, or 3.4 times ($p<0.01$). Furthermore, by the third day of peritonitis, the MDA content in the blood plasma was 1.5 times higher than after half a day ($p>0.05$), 1.2 times lower than after half a day ($p<0.05$), and 1.8 times lower than after one day ($p<0.05$). These findings suggest that the severity of lipid peroxidation processes has decreased. When compared to the outcomes in the "control" group, differences in the MDA content in the blood plasma of rats given L-arginine and aminoguanidine together persisted. Specifically, it rose by 1.6 times ($p<0.01$) after half a day of peritonitis, 2.3 times ($p<0.01$) after one day, and 1.3 times ($p>0.05$) after three days. The decrease in [MDA] in the blood plasma of rats with peritonitis and the introduction of a combination of the studied NO synthase modulators, compared with the values with the isolated introduction of L-arginine and aminoguanidine was: after half a day - 57 (52; 65)%, $p < 0.01$, and 42 (35; 50)%, $p < 0.01$, after one day - 54 (51; 56)%, $p < 0.01$, and 34 (33; 35)%, $p < 0.01$, after three days - 61 (56; 67)%, $p < 0.01$, and 43 (35; 47)%, $p < 0.01$, respectively.

Conclusions. Thus, a decrease in the lipid peroxidation product MDA content in the blood plasma of rats with experimental peritonitis and the administration of a combination of L-arginine and aminoguanidine indicates a decrease in oxidative stress activity, which may be due to the inhibition of the cytotoxic effect of NO and the resulting peroxynitrite on cell membranes by suppressing the activity of inducible NO synthase.

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ИЗМЕНЕНИЕ СОДЕРЖАНИЯ МАЛОНОВОГО ДИАЛЬДЕГИДА ВКРОВИ КРЫС С ПЕРИТОНИТОМ И МОДУЛЯЦИЕЙ АКТИВНОСТИ NO-СИНТАЗЫ

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Резюме. Модуляция активности синтазы оксида азота (NO) значительно влияет на тяжесть окислительного стресса в модели фекального перитонита у крыс, что измеряется по уровню малонового диальдегида (МДА) в плазме. Наиболее выраженный эффект наблюдался при комбинированном введении L-аргинина и аминогуанидина, что привело к существенному и устойчивому снижению концентрации МДА в плазме по сравнению с группой с нелеченным перитонитом. Снижение было значимым во всех временных точках. Хотя уровни МДА в группе комбинированного лечения оставались повышенными по сравнению со здоровым контролем, данные указывают на то, что двойная модуляция системы L-аргинин-NO синергетически ослабляет перекисное окисление липидов, при этом тяжесть окислительного стресса снижалась в течение трехдневного курса эксперимента.

Ключевые слова: малоновый диальдегид, перитонит, L-аргинин, аминогуанидин, окислительный стресс.

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