

COMBINED EFFECT OF STRESS WITH NONSTEROIDAL ANTI-INFLAMMATORY DRUGS AND IRRADIATION ON NITROSO-OXIDATIVE PROCESSES IN DIGESTIVE ORGANS

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Introduction. Digestive organs may simultaneously be affected by different factors, such as stress, xenobiotics and other cytotoxic and ulcerogenic agents. Significant role among them belongs to nonsteroidal anti-inflammatory drugs and irradiation. Simultaneous combined effect of stress and ulcerogenic factors, different due to their pathogenetic mechanism, requires deeper elucidation.

The studies were conducted on white out-breed rats weighing 200-240 g. Rats were divided into 6 groups: the first – control group animals (n=10), the second – animals (n=8), which during 20 days were irradiated in daily dose 1sGy (total dose 20 sGy); the third group – animals (n=8), who were exposed to the effect of water-immobilisation stress (WIS) during 5h; the 4th group - animals (n=8), exposed to the action of WIS after the end of the effect of low intensity X-ray irradiation (total dose 20 sGy); the fifth group – animals (n=8), administered COX blocker naproxen (10 mg/kg); the 6th group – animals (n=8), administered naproxen on the background of WIS. In homogenates of the mucous membranes of stomach (MMS), small intestine (MMSI) and large intestine (MMLI) activity of NO-synthase, arginase, myeloperoxidase (MPO), superoxide dismutase (SOD), catalase, content of TBA-active products and nitrite-anion were determined, in blood plasma – content of H₂S, nitrite-anion and L-arginine. Statistical procession of the results was performed using the methods of variation statistics with the help of ANOVA "Statistica" package.

Independent effect of WIS, blocker of COX/COX-2 (naproxen) and irradiation in total dose of 20 sGy resulted in the increase of the content of TBA-active products, nitrite-anion, activity of inducible NO-synthase (iNOS) and MPO in MMS, MMSI and MMLI homogenates;

in blood plasma the content of nitrite-anion increased, whereas H₂S and L-arginine concentration decreased. At that destructive macroscopic lesions of the mucous membranes, predominantly MMS, were noted under the effect of WIS and naproxen and absent under the conditions of irradiation. The combined effect of WIS with naproxen increased the area of destructive damage in MMS, at that TBA-active products content increased in the digestive organs mucous membranes, however iNOS activity decreased. Under the conditions of WIS effect on the background of irradiation the increase of TBA-active products content, activity of catalase and cNOS and decrease of iNOS activity compared to the indices of the independent effect of WIS were noted.

The combined effect of stress and COX-1/COX-2 blocker naproxen showed the cytoprotective role of prostaglandins and interrelationship between NOS and COX. The effect of stress on the background of the low intensity irradiation showed the cytoprotective effect of radiation, the key role in which belongs to the decrease of iNOS activity. The changes of the level of lipid peroxidation processes and iNOS activity under the conditions of the combined effect of stress with different ulcerogenic factors do not change simultaneously, mediating specific morphologic changes of the mucous membranes of the digestive organs.