EFFICACY OF INTERLEUKIN 1 RECEPTOR ANTAGONIST (IL-1Ra) IN ACUTE CHEMICAL INJURY OF ORAL MUCOSA

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Introduction. Inflammatory diseases of oral mucosa (OM) are widely distributed in all age groups and permanently occupy the leading position in dental diseases. The drugs influencing on the different phases of pathological process, namely antiinflammatory, immunotropic, wound healing et al., are widely used in the treatment of the aforesaid diseases. Non-steroidal antiinflammatory drugs (NSAIDs) are widely prescribed in this case. Receptor antagonist of interleukin-1 (IL-Ra) designed developed at the Research Institute of Highly Pure Preparations corresponds to this concept. The results of the last years investigations indicate the significant changes of cytokine profile in the oral cavity in inflammatory diseases. This makes possible to suggest the efficiency of antycytokine therapy in the inflammatory diseases of OM. Still the experimenatal and a fortiriori, clinical verification of this hypothesis has not been done. The purpose of the present study was to compare the efficacy and safety of the experimental therapy of the acute chemical injury of OM with IL-Ra and traditionally used NSAIDs in systemic administration.

Objects. The research was conducted on 42 randombred female albino rats (body weight 130–200 g) using the model of acute chemical injury of OM by the application of 10% solution NaOH on the underlip. The animals were randomly divided into 4 groups: intact control, untreated animals (chemical injury), animals treated with IL-1Ra (3 mg/kg subcutaneously) during 3 days after chemical injury, and animals treated with diclofenac sodium (8 mg/kg intramuscularly) in the same regimen. The doses of the drugs equaled ED_{50} for antiinflammatory action. Body weigth and rectal temperature were determined on the 1, 3, 4, 8 days; erythrocytes and leukocytes count, haemoglobin content, ESR, total protein, AlAT AsAT, and catalase activity, concentration of TBA-reactants in blood were determined on the 3rd and 8th days. The status of OM was assessed macroscopically on the 3rd day, affected area of OM was harvested for histological study (light microscopy).

Results. Edema and hyperemia of the vestibule mucosa were observed in all animals. Apparent necrosis signs were absent in the untreated animals; the body weigth was increased by 3.5–7.9 g, the temperature was augmented in the first three days compared with intact control ($p<0.001$, $p<0.05$ respectively), the normal bowel movements were observed, there was no lethality.

Under the action of IL-1Ra clinically significant necrosis was absent in the damaged tissues. Initial body weigth was increased by 0.8–5.0 g, statistically significant hyperthermia compared with the intact control data was absent, lethality was also not registered.

Under the action of diclofenac sodium the macroscopically evident necrosis was found in 33.3% of samples; the body weigth was acutely reduced – the decrease was more than 15g in 50% of animals, and more than 25 g – in 33.3% of animals; progressive decline in body temperature compared to the untreated group and intact control data ($p<0.05$, $p<0.01$ respectively); diarrhea was observed in 50% of cases. It indicates the significant toxic effect of diclofenac sodium.

Leukocytosis and the increment in ESR ($p<0.05$) were seen in the untreated animals. Against the background of diclofenac sodium treatment anemia with the reduced haemoglobin content, as well as the increase in ESR were determined. Under the action of IL-1Ra these changes were not so significant as in diclofenac sodium group ($p<0.05$ and $p<0.01$; $p<0.001$ respectively).

Biochemical blood indicators in the untreated group did not differ significantly from the intact control data. Statistically significant differences from this group data were also absent in animals receiving IL-1Ra, except for TBA-reactants reduction ($p<0.01$). Under the influence of diclofenac sodium marked hypoproteinemia and increase in AlAT and AsAT activity, indicating augmentation in cytolysis, was observed. Activation of lipid peroxidation as evidenced by the increment in TBA-reactants in blood serum by 78% was registered as well as the reduction in antioxidant system (namely, the decrease in catalase activity).

Macroscopically extensive ulcerative necrotic lesions of all mucosa layers, submucosa, and sometimes muscular fibers were observed in the untreated animals, edge epithelization of the surface defects was not seen in these samples.

Under the action of IL-1Ra minor defects of mucosa were observed histologically. Necrotic dystrophic changes were less expressed in length and depth. Under the anticytokine therapy influence, edge epithelization was registered. After diclofenac sodium administration mucosa defects extended on submucosa and there were no evidences of the edge epithelization.

Conclusion. IL-1Ra exerts a pronounced antiinflammatory effect in acute inflammation of oral mucosa and does not demonstrate side effects inherent in traditional NSAIDs. Efficacy and safety shown in the present investigation experimentally substantiate the expediency of IL-1Ra usage in the treatment of mucosa inflammation processes.