EXPERIMENTAL STUDY OF ANTIDIABETIC PROPERTIES OF RECOMBINANT INTERLEUKIN-1 RECEPTOR ANTAGONIST

Maaroufi Omar, Shchokina C. G., Ulanova V. A., Bukhtiyarova I. P.
National University of Pharmacy, Kharkiv, Ukraine
acya@ukr.net

Introduction. Diabetes mellitus (DM) has an important place in the structure of mortality and among the causes of disability violations and the deterioration of the quality of life. According to the International Diabetes Federation today the number of diabetes patients has reached 366 million in the world, and in 2030 will reach up to 552 million. Therefore, optimizing diabetes care is one of the most actual health problems.

According to modern concepts of the pathogenesis of diabetes, one of the leading roles in the deaths of beta-cells is played by the pro-inflammatory cytokines, one of which - the interleukin-1 (IL-1). IL-1 inhibits the production of insulin by β-cells and stimulates their apoptosis. Due to activation of IL-1 nitric oxide increases in β-cells, which induces NO-synthetase activity and eventually leads to β-cell destruction.

Aim. The aim of this work was the experimental study of the IL-1 raleukin original recombinant antagonist receptors effect, got by St. Peterburg Research Institute of Pure Biochemicals, on the development of alloxan diabetes in rats.

Materials and methods. The absolute insulin deficiency of the direct β-cytotoxic genesis was induced with help of the single subcutaneous injection of alloxan in a dose of 150 mg / kg of white mongrel rats weighing 160-220 g, which were kept at a pre-day starvation diet.

As a comparison, formulations synthetic hypoglycemic drug metformin, which is included in the CD standards of both types of treatment, and anakinra, IL-1 recombinant antagonist receptors with proven hypoglycemic activity, which is a structural analog of the test drug. Drugs were administered in a treatment regime four times - after 40-50 min. after administration of alloxan, and 24, 48 and 72 hours: raleykin in dose of 7 mg / kg anakinra and 8 mg / kg - subcutaneously, metformin 100 mg / kg - intraperitoneally. After 40-60 min. after the last administration of study drugs the animals were anesthetized with sodium thiopental, and taken out of the experiment. When decapitation, blood was collected and liver isolated for biochemical studies.

Insulin levels of hemoglobin (Hb), glycated hemoglobin (HbA1c) and C-reactive protein (CRP); in liver homogenates - the level of diene conjugates (DC), TBA-reactants (TBA-P) and reduced glutathione (WG) were detected in the blood serum.

Results and discussion. Raleukin and anakinra unlike metformin significantly increased insulin levels in the blood serum of animals in 2,2-2,4 times. Under the influence of raleukin Hb content in blood serum of rats was significantly increased by 1.3 times, HbA1c - decreased by 1.5 times in comparison with the indicators in the control group pathology. Against the background of metformin Hb content was significantly increased in 1,1 times, HbA1c - decreased by 1.2 times. Introduction anakinra contributed to the significant increase Hb content 1.2 times, reduction in HbA1c - 1.4 times. Under the action of interleukin the level of CRP in the serum of rats significantly decreased in 1.9 times compared with that in the control group of diseases under the action of metformin - in 1.5 times, against the backdrop of anakinra - 1.7 times.

The use of studied drugs contributed to the normalization of lipid peroxidation product levels in rat liver homogenates. Against the background of raleukin and anakinra content DK decreased by 1.6 times, under the influence of metformin - in 1,3 times. In groups of raleukin and anakinra level of TBA-P in liver homogenates of rats significantly decreased by 1.4 times, the content of SH increased by 1.6 times compared with the corresponding figures in the blood of animal disease control group. The increase of the SH shows the protective effect of the studied drugs regarding the free radicals that accumulate near the ß-cells during insulitis.

Conclusions. Thus, on the model of alloxan diabetes in rats original antagonist recombinant IL-1 receptor exhibits an antidiabetic effect on the severity of which is not inferior to anakinra and superior to metformin.

It can be assumed that the positive effect of raleukin is the result of the IL-1 receptors blockade in the pancreas and in the following protection of ß-cells from the damaging effect of alloxan as well as it is associated with the ability of the drug to increase the insulin-producing ability of ß-cells, to inhibit the reaction of non-enzymatic glycosylation, inhibit the development of inflammatory processes in the ß-cells and reduce the severity of oxidative stress in the body of experimental animals.

The results of these studies indicate the prospects of further experimental study of the anti-diabetic properties of raleukin for subsequent inclusion of the drug in the complex of type I diabetes therapy.