INFLUENCE OF GLYCORAZMULIN ON THE PARAMETERS OF CARBOHYDRATE METABOLISM IN ALLOXANE DIABETES

There was studied effect of glycorazmulin on the morphological structure of the liver and pancreatic gland under the conditions of alloxane diabetes. The study found that glycorazmulin eliminates pathomorphological changes that occur in alloxane diabetes in the liver and pancreatic gland, and stimulates reparative processes in these organs. The effect of this preparation is mainly directed to stimulation of the regeneration of β-cells. The elimination of histostructural changes resulted in compensation of the damaged metabolic processes in diabetes mellitus. Besides, marked increase in C-peptide in the blood is the confirmation of the insulin secretion stimulation under the effect of this preparation.

Key words: Glycorazmulin, alloxane diabetes, liver, pancreatic gland, islets of Langerhans

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Introduction

Diabetes mellitus is a chronic endocrine-metabolic disease, heterogeneous by nature. Nowadays, in relation to medico-social importance this disease is in the same range as the cardio-vascular and oncological diseases. The investigations have shown considerable growth of the number of patients with diabetes mellitus not only in economically developed but also in developing countries. The WHO data show that more than 30 mln of patients with diabetes mellitus are registered and approximately in the same number of people has the latent form of this disease development (Atkinson, 2000).

The application of the large arsenal of synthetic hypoglycemic agents is limited because of the numerous undesirable phenomena and formation of insulin resistance (Charles et al., 1998). Therefore, creation of effective and safe medicinal means on the basis of natural raw materials remains a very significant challenge (Charles et al., 1998).

Rhodiolae roseae is considered one of such plants. The pharmacological studies have shown that alcoholic extract from Rhodiolae roseae roots has biological properties similar to preparations of ginseng and Eleutherococcus (Kurkin et al., 1995). Besides, the extract of Rhodiolae roseae has cardio-protective and anti-arrhythmic properties (Maslov et al., 2007). We have found that the glycorazmulin medication consisting of Semenov’s Rhodiolae and mumiyo has intensive hypoglycemic effect in different experimental models of diabetes (Faizieva et al., 2003).

In the mechanism of carbohydrate and lipid metabolisms during the development of diabetes mellitus the functional interaction of the liver and β-cells of the pancreatic gland is of great importance, the state of which has effect on the degree of intensity of specific pathological changes. Taking it into account we suggested that it should be very useful to study the effect of glycorazmulin on the morphological structure of the liver and pancreatic gland in alloxane diabetes.

Materials and methods of research

The investigations were carried out on mature rat males prepared under the standard conditions of vivarium. Experimental diabetes was induced by single subcutaneous
alloxane administration in dose of 150 mg/kg (Baranov, 1983). In dynamics there was investigated the blood glucose level by means of enzymatic method, and C-peptide contents with radioimmune method. Two weeks later the experimental animals were administered glycorazmulin orally in dose of 100 mg/kg during three months, and the control group of animals received a physiological solution in the appropriate volume. In the end of the experiment the internal organs of animals were studied by histological investigations.

**Results and discussion**

The histological studies of internal organs of the animals from the control group demonstrated the following results.

**Liver**

The capsule is not swelling, the structure is broken in some places, sinusoids are partially extended. The vessels in triads are sclerosed. Hepatocytes are with poorly defined borders, with muddy cytoplasm. The nucleuses of a part of cells are displaced to periphery (big drop dystrophy). The part of cells loses borders, their nucleuses break up (karyorrhexis). The homogeneous mass - detritus - is formed, i.e. the hepatic tissue necrosis is developing. Insignificant leucocyte infiltration is noted around the triads. The dystrophic changes are more expressively marked on periphery lobules.

The **pancreatic gland**

The capsule is not swelling, thickening of the layers of connective tissue is noted, growth of a fatty tissue (lipomatosis). The borders between exocrine and endocrine part of the gland are well outlined. Exocrine part is formed by acinuses, which consist of the conic form cells. The nucleus is in the basal part of a cell; there the cytoplasm is darker than in the apical part. The endocrine part is formed by islets of the round form. The islet cells have lighter color, than acinus cells. The islets were of different sizes. The main part of the islets has decreased size. The small light cells with irregular nuclei of granular cytoplasm (α-cells) are distributed along the periphery of the islet. The round cells with large nucleus and dark granular cytoplasm (β-cells) are in smaller quantity. In some islets the borders of cells are poorly defined, the nuclei are broken up, i.e. it is marked necrosis. The lymphocytes are in small quantity. The specific area of the islet tissue has become sharply reduced due to these necrotic processes.

Hence, experimental diabetes is accompanied by dystrophic changes in the liver and pancreatic gland. Analysis shows that alloxane, first of all, has selective effect on the β-cells of the Langerhans islets.

The investigation of the samples from animals receiving glycorazmulin showed the following morphological changes:

**Liver**

The capsule is not swelling; walls of vessels are thickened in some sites. The hepatic arteries, veins, bilious tracts are well defined. On the periphery of the lobules found binuclear hepatocytes, which have clear boundaries and are arranged in rows; the beam structure is preserved. The cytoplasm is painted homogenously; the nucleus is of round form with well outlined borders. Necrosis and dystrophic changes are insignificant. Sinusoids are extended; lymphocyte infiltration around triads is insignificant (Figure 1).
The pancreatic gland

The capsule is not swelling, the moderate lipomatosis is noted, and the growth of connective tissue is found. Exocrine and endocrine parts are with well defined borders. The acinus cells are with clear nuclei, chromatin is finely divided. It has revealed that during long treatment the integrated acinuses are exposed to acinus-insular transformation, which is shown by the change of the nuclear apparatus and euchromatization of cells. The occurrence of acinus-insular cells may be considered as compensatory reaction, which is carried out by transformation of generically related cells. The significant part of the islets is hypertrophiastic. Due to this is increased the total mass of islet tissue of the pancreas as a whole.

Large oval nuclei with distinct nuclear membrane are found in β-cells. Their quantity is dramatically increased. If in the control animals the quantity of β-cells in the islet was approximately 53.2% of the total cellular composition of the islet, then after treatment their quantity achieved 79-80%. It allows considering, that the effect of glycorazmulin is directed mainly to stimulation of the regeneration of only β-cells. Dystrophic changes and necrosis were not observed in the pancreatic gland (Figure 2).

In parallel there was noted a reduction of blood glucose level. For example, by the end of treatment with glycorazmulin this parameter was reduced by 57.8% (6.8±0.2 mmol/l) in relation to the control one (16.1±0.3 mmol/l).

Hence, glycorazmulin eliminates pathological changes, i.e. dystrophy and necrosis in the liver and pancreatic gland occurring in alloxane diabetes, and stimulates reparative processes in studied organs.

As it has been cleared recently, the estimation of insulin secretion by definition of its level in plasma appeared unreliable. This may be explained by presence of variability of insulin concentration that is connected with its splitting in the liver by enzyme insulinase. As it is known that C-peptide and insulin are secreted by β-cells in the equimolar concentration, and that C-peptide is not secreted in the liver in the significant amount, has begun widely used the measurement of C-peptide in peripheral blood for evaluation of endogenous secretory activity of β-cells (Mari et al., 1993).

The results of the experiments showed that alloxane diabetes is characterized by significant insulin insufficiency, which is confirmed by data of the control group. Under
the conditions of experimental diabetes the introduction of glycorazmulin promoted reliable increase of C-peptide level in the blood; glycorazmulin resulted in increase of C-peptide level by 62% in 30 days in relation to control. While in the control group within one month the level of C-peptide was 0.35±0.09 pg/ml, this parameter in the studied group was 0.57±0.07 pg/ml.

The evident increase in C-peptide level is the confirmation of the stimulation of insulin secretion under the effect of this preparation.

Hence, the hypoglycemic properties of glycorazmulin are supported by stimulation of endogenous insulin secretion.

**Conclusion**

1. In elimination of disorders of carbohydrate and lipid metabolism the histostructural liver changes occurring during treatment with glycorazmulin play significant role.
2. Acceleration of hormone intracellular synthesis and the increase of general mass of the islet tissue of the pancreatic gland during treatment with glycorazmulin, result in compensation of carbohydrate metabolism.

**References**


