

Introduction.

For the first time a negative effect on the course of hyperthyroidism of diabetes mellitus (DM) was described by scientists Coller and Huggins in 1927. A team of scientists found that the improvement of carbohydrate metabolism has been observed in patients with hyperthyroidism and concomitant diabetes after thyroidectomy. The influence of thyroid hormones on glucose regulation is associated with changes in insulin secretion and hormone antagonists of insulin, glucose absorption in the intestine and its utilization by adipose and muscle tissues, stimulation of gluconeogenesis in the liver [4]. There are evidences that triiodothyronine is able to enhance glucose metabolism in the liver by the action on the hypothalamic and pituitary system. This effect is realized through sympathetic fibers involved in innervation of hepatocytes and does not depend on the level of thyroid hormones, insulin and corticosteroid content in the blood. Metformin (biguanide group) belongs to drugs that reduce insulin resistance. Metformin has a wide range of pharmacodynamic effects, the main of which is to lower hepatic glucose production and to increase its absorption by peripheral tissues, to reduce the concentration of free fatty acids in blood plasma, and to slow glucose absorption in the intestine. There are also known studies of the influence of metformin on thyroid status in patients with diabetes mellitus. It was noted that the level of thyroid-stimulating hormone remains unchanged under the influence of treatment with metformin in patients with type 2 diabetes without impaired thyroid function.

The aim of this investigation was to study the influence of metformin on the indices of thyroid hormones, carbohydrate and lipid metabolism in patients with diffuse toxic goiter and type 2 diabetes mellitus and insulin resistance.

Methods. The article presents the results of the study of 21 patients with diffuse toxic goiter and type 2 DM. Treatment was conducted in two phases and each phase lasted for 3 months. During the first phase all patients received thyrostatic therapy with thiamazol, metformin was additionally prescribed in order to correct insulin resistance at the second phase.

The levels of thyroid stimulating hormone, free thyroxine, free triiodothyronine, glucose concentration, insulin, glycated hemoglobin content have been defined in the blood serum. The indices of lipid spectrum of the blood: total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides have been investigated. Calculated insulin resistance index HOMA-IR.

Results. The raise in TSH levels concentration from 0.02 ± 0.00 mMO/l to 1.75 ± 0.12 mMO/l ($p < 0.001$) has significantly been revealed as a result of thiamazol treatment in patients with

Graves' disease and type 2 DM and further increased to 2.20 ± 0.03 mMO/l ($p < 0.05$) after additional administration of metformin.

The decrease in serum of T_4 levels from 4.46 ± 0.35 ng/dl to 1.65 ± 0.06 ng/dl after thiamazol therapy ($p < 0.001$) and to the indices 1.57 ± 0.05 ng/dl on the background of combined treatment with metformin and thiamazol ($p < 0.001$) compared with initial data has been marked. Significant decreased in serum T_3 levels from 16.18 ± 1.07 pg/ml to 3.48 ± 0.11 pg/ml during thiamazol treatment ($p < 0.001$) and to 3.28 ± 0.10 pg/ml ($p < 0.001$) on the background of combined treatment with metformin and thiamazol compared with initial data has been found.

The analysis of obtained data revealed the presence of possible changes comparing final indices and results based on thyrostatic therapy. So, glucose level reduced from 7.56 ± 0.15 mmol/l to 5.20 ± 0.10 mmol/l ($p < 0.05$) and insulin reached its indices 18.53 ± 0.43 mMO/l compared with 13.09 ± 0.54 mMO/l ($p < 0.05$), HOMA-IR index decreased from 3.30 ± 0.20 units to 2.70 ± 0.14 ($p < 0.05$) units. The tendency to positive changes according to HbA1c data decreased from $7.11 \pm 0.09\%$ to $5.90 \pm 0.07\%$ ($0.05 < p < 0.1$) has been marked.

Obtained data of lipid metabolism indicate significant increase of total cholesterol level to 4.28 ± 0.12 mmol/l after all stages of treatment compared with indices prior to treatment 3.89 ± 0.12 mmol/l, ($p < 0.05$). Positive changes ($p < 0.05$) were registered in the analysis of LDL data comparing initial data (2.37 ± 0.07 mmol/l) with indices received after combined therapy (2.59 ± 0.07 mmol/l).

Conclusions

1. Euthyroidism has been achieved by the level of thyroid stimulating hormone, free thyroxine and free triiodothyronine due to thyrozol treatment of patients with Graves' disease and IR.
2. Additional administration of metformin to thyrostatic therapy with thiamazol during three months of study of patients with Graves' disease with type 2 diabetes mellitus contributed to raising the level of thyroid stimulating hormone and free thyroxine reduction within the reference standards.
3. Moderate increase in lipid metabolism such as total cholesterol and low density lipoprotein cholesterol, which did not exceed the reference standards and were at their optimal indices, has been noticed due to the investigation of patients with Graves' disease and type 2 DM.
4. Normalization of insulin resistance of HOMA-IR index due to reducing of glucose and fasting insulin has been revealed on the background of combined treatment with thyrozol and metformin in patients with Graves' disease and type 2 DM and IR.