that modulates intracellular Ca^{2+} release. Therefore, it acts as a second messenger regulating the activities of several hormones, such as insulin, follicle-stimulating hormone, and thyroid-stimulating hormone (TSH).

The aim of the present study was to evaluate effect of cholecalciferol and myo-inositol on thyroid function and autoimmunity in patients with subclinical hypothyroidism.

68 patients with subclinical hypothyroidism (TSH between 4.5 and 8.0 mcIU/ml) were involved in this observational and retrospective study. They were meeting the inclusion criteria as follows: age range 20–65, elevated serum thyroid peroxidase antibodies (TPO Ab) and/or thyroglobulin antibodies (Tg Ab), and normal free thyroxine (fT_4) and free triiodothyronine (fT_3) levels. A complete thyroid assessment was evaluated in patients at baseline and after 3 months of treatment. Patients were divided into three groups: untreated (n=20), treated with cholecalciferol 4000 IU/day (n=25) and treated with myo-inositol 2000 mg/day (n=23) during 3 months. Ultrasound of the thyroid gland was performed to evaluate changes in thyroid echoic pattern during the study.

Compared to baseline, levels of TSH significantly declined (5.14±0.83, vs. 3.91±1.17, mcIU/ml, respectively; p=0.003), in patients treated with myo-inositol and in 39.1% of cases it reached the normal range. After the treatment, antithyroid autoantibodies levels decreased by 31% and 39%, respectively, in those treated with cholecalciferol and myo-inositol. There were significant decrements in both autoantibodies Tg Ab and TPO Ab serum levels after administration of mio-inositol: Tg Ab levels decreased from 438.9 ± 21.8 IU/ml to 261.4 ± 22.3 IU/ml after treatment ($p \leq 0.01$) and TPO Ab from 769.6 ± 41.9 IU/ml to 472.3 ± 37.8 IU/ml, pre- and post- mio-inositol treatment, respectively ($p \leq 0.002$). The serum fT_3 and fT_4 levels of patients were slightly but significantly higher at the end of 3-month period when compared with the values at baseline: fT_3 values were 2.63 ± 0.03 pg/ml at baseline and 2.71 ± 0.02 pg/ml posttreatment ($p \leq 0.05$) and fT_4 levels were 0.93 ± 0.02 ng/ml and 1.06 ± 0.02 ng/ml ($p \leq 0.05$) pre- and posttreatment, respectively. Analysis of thyroid ultrasonography showed an echoic pattern improvement in both treated groups compared to untreated patients, although this difference was not statistically significant.

Myo-inositol and cholecalciferol treatment are effective in patients with subclinical hypothyroidism. The results of the present study show an improvement of thyroid function in patients with subclinical hypothyroidism. Thus, myo-inositol treatment is effective in patients with subclinical hypothyroidism and its effect may be improved in combination with cholecalciferol through earlier achievement of TSH levels closer to physiological concentrations.

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THE ROLE OF PERFORIN/GRANZYME-INDUCED APOPTOSIS IN THE DEVELOPMENT OF COGNITIVE IMPAIRMENT IN DIABETES MELLITUS

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Diabetes mellitus is recognized as an independent factor of cognitive impairment. The risk of dementia in patients with type 2 diabetes increases almost twice. The results of epidemiological, visualization and autopsy studies showed the presence of both cerebrovascular and neurodegenerative mechanisms of brain lesions. Cell death of key substrates – neurons and endothelial cells lays in the basis of cerebral disorders. Granzyme B is a serine protease, which exerts both intracellular apoptotic and extracellular functions, leading to tissue injury and inflammation.

The purpose of the study was to find out role of the granzyme-induced mechanisms of programmed cell death in the development of cognitive impairment in patients with type 2 diabetes.

There were examined 70 type 2 diabetes patients and cognitive impairment and 26 sex, age and body mass index comparable non-diabetic subjects as control group. Patients were classified using neuropsychological assessment tests. The Mini-mental State Examination (MMSE) test, Montreal Cognitive Assessment (MoCA) test and the determination of cognitive-induced potentials

were used to evaluate cognitive functions. Serum Granzyme B was measured by Human Granzyme B Elisa kit.

As the results of our study showed, mild cognitive impairment was diagnosed in 47 patients with diabetes, dementia – in 23 subjects accordantly. Type 2 diabetes patients had serum levels of Granzyme B by 56% higher than the control group. The changes were statistically insignificant in the group of patients with mild cognitive impairment, while in subjects with dementia the level of Granzyme B was almost twice higher than in the control. *Positive* correlations were established between the MMSE and MoCA tests results and levels of Granzyme B, whereas direct correlation – between the latent period P300 and levels of Granzyme B.

Thus, serine protease Granzyme B can play a role in the mechanisms of brain damage in type 2 diabetes by converting inactive procaspase 3 to active caspase 3. Activation of cytotoxic T-cells leads to the release of perforine and granzymes from their granules. Perforine forms in the plasma membrane of target cells the pores through which granzymes penetrate. Also, recent studies have shown that Granzyme B plays an important role in the processes of destabilization of atherosclerotic plaques, that are especially significant in the aspect of vascular dementia in diabetes.

Cognitive impairment in patients with type 2 diabetes is accompanied by an increase in granzyme-induced apoptotic processes, which can play an important role in the mechanisms of both cerebrovascular and neurodegenerative disorders.

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CORRECTION OF VITAMIN D INSUFFICIENCY IN PERSONS OVER 45 YEARS OLD WITH IMPAIRED GLUCOSE TOLERANCE

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The objective of the study was to evaluate the effect of vitamin D deficiency correction on weight dynamics, fasting hyperglycemia in persons over 45 years of age with impaired glucose tolerance.

48 patients were examined (32 women 66 7% and 16 men 33.3%) aged 45-60 years (median (Me) – 52.5 years), BMI 29.5±0.7, The duration of impaired glucose tolerance was more than 1 year, vitamin D deficiency (concentration 25 (OH) D 21-30 ng / ml) was diagnosed within the last 6 months. The experimental group included 28 patients with impaired glucose tolerance who received metformin therapy at a dose of 850 mg at night; an aqueous solution of vitamin D at a daily dose of 4000 IU/day. The control group consisted of patients (20 people) with impaired glucose tolerance who were on therapy with metformin 850 mg at night and diet therapy enriched with vitamin D. The level of vitamin D and its effect on glycemic parameters and body mass index (BMI) was evaluated during the day at the beginning and after 10 weeks of observation. Statistical processing was carried out using the Statistic 7.0 software.

After 10 weeks of therapy, in patients with impaired glucose tolerance, in addition to a subjective improvement in the general condition, clinical and metabolic indicators significantly improved: the level of vitamin D increased by 56% and the level of vitamin D reached target values ($p<0.001$), BMI decreased by 13.8% ($p<0.05$), fasting glycemia decreased to normal in 23%, drug withdrawal was noted in 12.9%. In the control group, fasting glycemia, prescribed therapy, vitamin D level did not change statistically significantly, the weight of patients decreased by 2.5%.

The appointment of an aqueous solution of vitamin D contributes to the elimination of vitamin D deficiency, a more effective correction of therapy with a hypoglycemic drug, weight in patients with impaired glucose tolerance, vitamin D deficiency.