**DOI** 10.29254/2077-4214-2021-2-160-81-85
**UDC** 616.441-002-097-055.2:615.357; 618.179-084

***Hajizade A. E.***

# RESULTS OF TREATMENT WITH COMBINED HORMONAL AND PROGESTOGENIC HORMONAL CONTRACEPTIVES IN WOMEN WITH AUTOIMMUNE THYROIDITIS AT THE FERTILE AGE

**Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev (Baku, Azerbaijan)**
**Statya2021@mail.ru**

**The connection of the publication with planned research works.** This work is a fragment of the dissertation "Assessment of the state and principles of correction of the reproductive system of infertile women of fertile age against the background of thyroid dysfunction".

**Introduction**. Diseases of the thyroid gland are one of the most common endocrine pathologies. In recent years, the connection between the function of the thyroid gland and the reproductive system is of great interest [1, 2].

The prevalence rate of hypothyroidism among women of reproductive age is about 24% [3, 4]. In most cases, initial hypothyroidism, which occurs as a result of self-destruction of the thyroid gland at the final stage of autoimmune thyroiditis, is of greater clinical importance [2].

Autoimmune thyroiditis is an organ-specific autoimmune disease of the thyroid gland which is the main cause of hypothyroidism in women of reproductive age. There is no published information about the prevalence of autoimmune thyroiditis among populations, there is only data on the incidence of autoimmune thyropathy markers, antithyroid antibody carriers (9% in men, 26% in women) [1, 5].

However, we can find continuous discussions in the literature of recent years about the possible pathological effects of anti-thyroid antibody transport on reproductive function [6]. A number of studies have shown that anti-thyroid antibodies make an increased risk of developing and progressing hypothyroidism not only during pregnancy and postpartum thyropathy, but also an important factor in the development of infertility and pregnancy disorders [3, 6].

In many cases, hypothyroidism and infertility of unknown etiology as a result of autoimmune thyroiditis occur together [2, 7].

What is the mutual relationship between infertility and autoimmune disease of the thyroid gland, or is there such relationship at all? It should be noticed that the pathogenetic mechanisms describing the assosiation of autoimmune disease of the thyroid gland with infertility are quite dubious [5, 7]. Taking into consideration that the prevalence of autoimmune disease of the thyroid gland and its potential effect on infertility is contradictory, conducting of studies in this sphere should be considered as important. Currentlythere is no single idea the role of autoimmune disease of the thyroid gland in the pathogenesis of infertility and pregnancy disorders [3, 4, 7].

**The purpose of the study** is to study the effect of 12-month combined hormonal and progestogenic hormonal treatments among women with autoimmune thyroiditis of reproductive age on the thyroid and reproductive system, the level of specific anti-TPO and antithyroglobulin autoantibodies.

**Object and methods of the research.** The research materials consists of medical records of 48 patients who received complex treatment for autoimmune thyroiditis and infertility in the Department of Obstetrics and Gynecology of the Republican Clinical Hospital named after M. Mirgasimov during 2015-2021 years.

In infertile women with autoimmune thyroiditis involved to the study size and function of the thyroid gland was assessed before and in 12 months after taking hormonal drugs. Patients were divided into four subgroups for this purpose. 12 patients receiving combined oral contraceptives (COCs) and thyroxine were in the I subgroup, 12 patients receiving only combined oral contraceptives (COCs) were in II, 12 patients receiving desogestrel and thyroxine were in III subgroup, and 12 patients receiving only desogestrel were in IV subgroup.

The complex examination includes general-clinical, instrumental, laboratory methods and special examination methods. Selected examination methods were adequate for intended purposes and objectives.The level of anti-thyroglobulin antibodies (anti-TG antibodies) and anti-thyroid peroxidase antibodies (anti-TPO antibodies) was studied by the enzyme-linked immunosorbent method.

Statistical analysis of all figures obtained during the study was carried out taking into account modern recommendations. In the first stage, the parametric criteria were used, and in the next stage, a non-parametric method – Wilcoxon (Mann-Whitney) criterion was used to determine the difference between the indicators, taking into account the number of indicators in groups. All calculations were performed by the computer software Statistica 6.0, and the results were presented in tables and diagrams. When $P < 0.05$, the statistical difference was considered valid.

**The results of the study and their discussion.** During 12 months taking of combined oral contraceptives (COCs) and desogestrel as a progestogenthe formation of nodules have not been reveal in ultrasound examination of the thyroid gland. In 12 women with autoimmune thyroiditis, hypothyroidism was compensated with thyroxine before using hormonal contraception. These patients were prescribed thyroxine 50 to 100 mcg per day at a dose of 25 mcg. The dose of thyroxine was not changed during the 12-month use of combined oral contraceptives. Data on thyroid volume before and after treatment with COCs and desogestrel

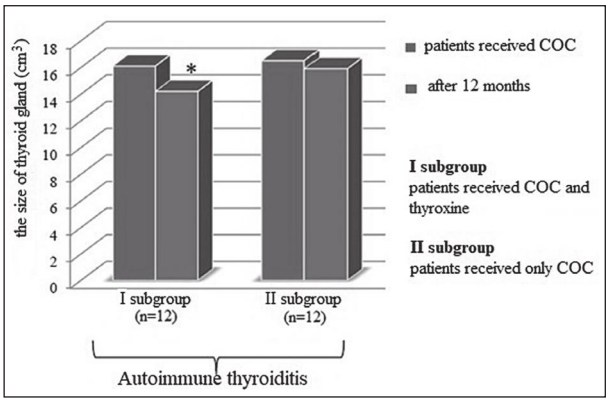


**Figure 1 – Dynamics of the size of the thyroid gland in women with autoimmune thyroiditis against the background of the use of combined oral contraceptives (COCs).**

**Note:** *- p<0,05 in comparison with initial level.

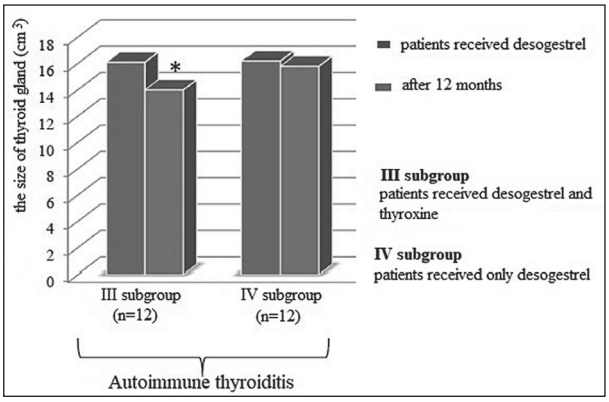


**Figure 2 – Dynamics of thyroid size against the background of the use of progestogen desogestrel in women with autoimmune thyroiditis.**

**Note:** * – p<0,05 in comparison with initial level.

in patients with autoimmune thyroiditis are presented in **Figures 1 and 2**.

In patients with subtype II thyroxine not prescribed treatment 12 months later after taking COC the volume of the thyroid gland has not changed significantly, but in subgroup I patients receiving COC against the background of thyroxine use after 12 months, the size of the thyroid gland accurately was decreased from 16,1±0,3 $cm^3$ till 14,2±0,4 $cm^3$ (p<0,05) **(Figure 1)**.

Thyroxine has a dose-dependent effect on the thyroid gland. There was no change in thyroid size at an administered dose of thyroxine of 25 mcg, and at doses of 50 mcg and higher, the thyroid gland was significantly reduced. Most reductions were respectively recorded in doses of 75 mcg and 100 mcg per day.

Thyroid volume did not change significantly after 12 months of desogestrel taking in patients of subgroup IV with thyroxine who had not been prescribed thyroxine, but thyroid size reduced from 16.1±0.3 $cm^3$ to 15.2±0.2 $cm^3$ after 12 months in patients using thyroxine (p<0.05) **(Figure 2)**.

In patients of the first subgroup with autoimmune thyroiditis taking COCs against the background of thyroxine use, after 12 months there was a significant decrease in blood TSH from 1.9 ± 0.1 mIU/L to 1.4 ± 0.2 mIU/L (p < 0.05). The change in TSH levels 12 months after taking COC among patients in subgroup II who were not prescribed thyroxine treatment was inaccurate **(Figure 3)**.

In patients, from subgroup III with autoimmune thyroiditis, taking hestagen desogestrel against the background of the use of a dose of 50-75 mcg of thyroxine after 12 months, there was a significant decrease in blood TSH levels from 2.0±0.1 mIU/L to 1.5±0.2 mIU /L (p<0,05).

In patients from subgroup IV who was not prescribed thyroxine treatment no significant difference in TSH levels was found in the blood 12 months after desogestrel taking **(Figure 4).**

In patients with autoimmune thyroiditis, TSH levels depended on the dose of thyroxine, which in turn varied depending on the initial level of TSH in the blood. This effect is not due to use of hormonal contraceptives, but as a result of compensation of hypothyroidism with thyroxine.

In women with autoimmune thyroiditis, the levels of free $T_3$ and $T_4$ in the blood before and 12 months after treatment with COCs or progestogen desogestrel are shown in **Table**.

No significant changes levels of free tri-iodothyronine in blood (T3) and free thyroxine (T4) were observed in subgroups of women with autoimmune thyroiditis who took only combined oral contraceptives (COCs) and thyroxine in addition to COCs (p>0,05).

No significant changes in free triiodothyronine and free thyroxine levels were observed after 12 months of treatment in subgroups of women with autoimmune

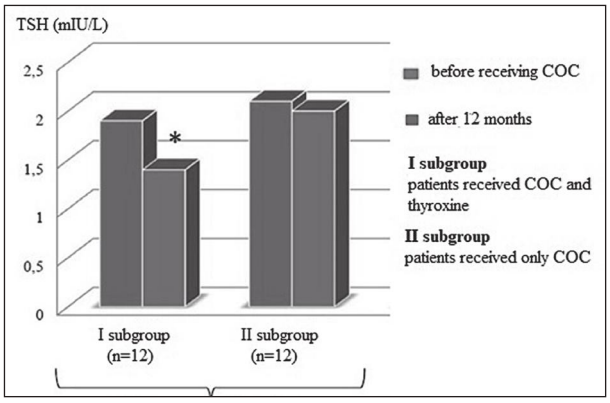


**Figure 3 – TSH levels in the blood against the background of the use of combined oral contraceptives in patients with autoimmune thyroiditis.**

**Note:** * – p<0,05 in comparison with initial level.

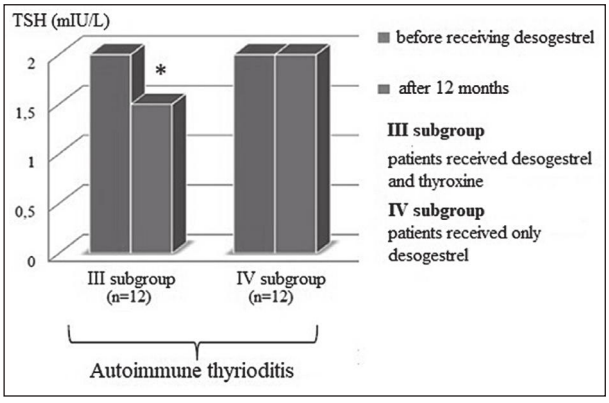


**Figure 4 – TSH level in the blood against the background of the use of desogestrel in patients with autoimmune thyroiditis.**

**Note:** * – p<0,05 in comparison with initial level.

**Table – The levels of free $T_3$ and $T_4$ in the blood before and 12 months after treatment with COCs or progestogen desogestrel in women with autoimmune thyroiditis**

| Patients subgroups | | Free $T_4$ (pmol/l) | | Free $T_3$ (pmol/l) | |
|---|---|---|---|---|---|
| | | Before treatment | 12 months after treatment | Before treatment | 12 months after treatment |
| Taking COC | Subgroup I (n=12) | 14,8±0,3 | 14,1±0,4 | 3,3±0,2 | 3,4±0,3 |
| | Subgroup II (n=12) | 14,6±0,8 | 14,9±0,4 | 3,3±0,2 | 4,0±0,6 |
| Taking desogestrel | Subgroup III (n=12) | 15,8±0,3 | 15,1±0,4 | 3,2±0,2 | 3,3±0,3 |
| | Subgroup IV (n=12) | 14,7±0,6 | 14,8±0,8 | 3,2±0,4 | 3,3±0,4 |

thyroiditis taking thyroxine in addition to progestogen desogestrel as well as progestogen desogestrel (p>0,05).

In sub-group of patients with autoimmune thyroiditis taking COC, also in subgroups of patients taking he-stagen desogestrel the results of determination of anti-thyroid peroxidase and anti-thyroglobulin antibodies in the blood before and 12 months later after are given in **Figure 5 and 6.**

In women of the II subgroup taking COC, also in women of the I subgroup taking thyroxine together with COC there was observed a significant decrease in the level of both anti-thyroid peroxidase antibodies and anti-thyroglobulin antibodies in the blood before and 12 later after the treatment (p<0,05) **(Figure 6)**. During the 12 months treatment with micro- and low dosage COC within the frames of the study no dose-dependent effects of estrogens, as well as progestogen desogestrel on thyroid volume, have been identified.

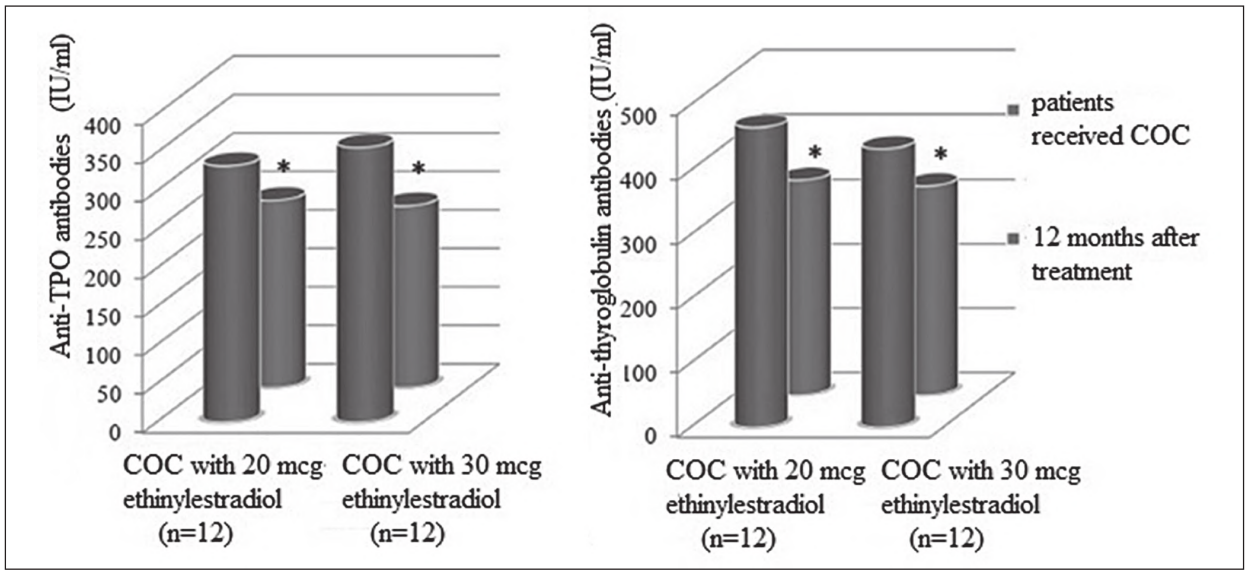


**Figure 5 – Dynamics of anti-TPO and levels of anti-thyroglobulin antibodies on women with autoimmune thyroiditis in the background of micro- and low dosage of COC.**

**Note:** * – p<0,05 in comparison with initial level.

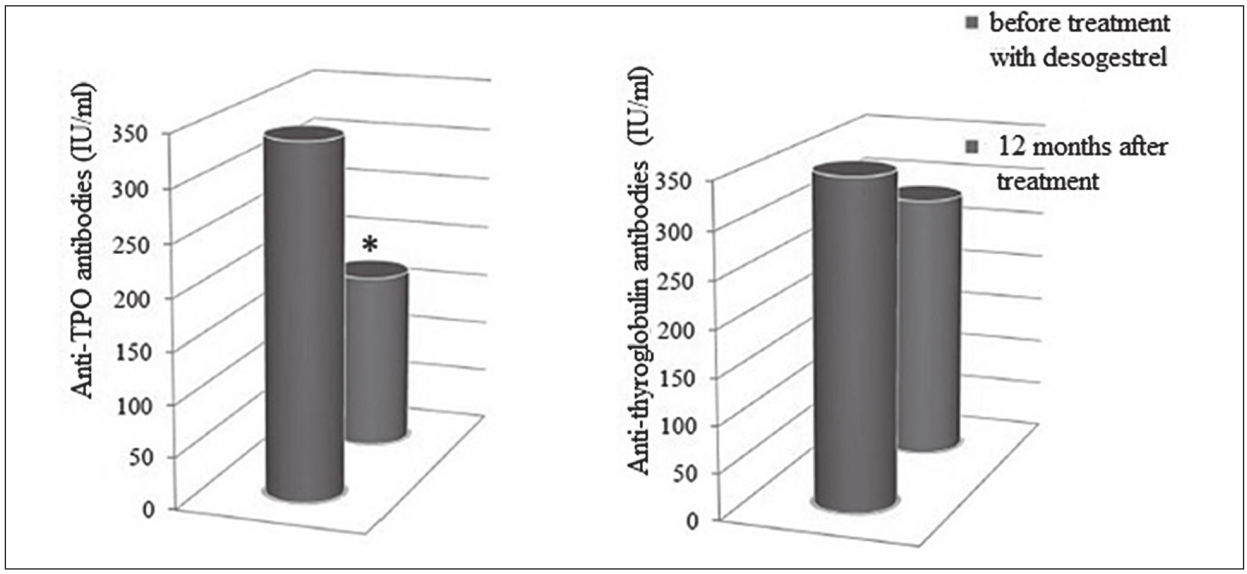


**Figure 6 – Dynamics of anti-TPO and levels of anti-thyroglobulin antibodies in women with autoimmune thyroiditis on the background of using of desogestrel in the background of micro- and low dosage of COC.**

**Note:** * – p<0,05 in comparison with initial level.

Thus, 12 months of treatment with micro- and low-dosage combined oral contraceptives (COC) in women with autoimmune thyroiditis in fertile age resulted in a significant decrease in plasma levels of anti-thyroid peroxidase and anti-thyroglobulin antibodies ($p<0.05$). Hestagen desogestrel's use for 12 months resulted in a significant reduction of only antibodies against thyroid peroxidase in plasma.

**Conclusions**.

On the background of taking the thyroxine in patients with thyroiditis taking COCs the level of TSH in blood decreases with accuracy (from 1.9±0.1 mIU/L to 1.4±0.2 ml /L) after 12 months ($p<0,05$).

In women on fertile age with autoimmune thyroiditis taking of COCs with micro- and low dosage during 12 months causes a significant decrease in the level of anti-thyroid peroxidase and anti-thyroglobulin antibodies.

Using of hestagen desogestrel during 12 months caused only accurately reduction of antibodies against thyroid peroxidise in blood.

**Prospects for further research**. Study of therapy methods in women with autoimmune thyroiditis of reproductive age.

## References


1. Perminova SG. Patologija shhitovidnoj zhelezy u zhenshhin s besplodiem. Klin. i jeksper. tireoidol. 2011;7(4):44-50. [in Russian].
2. Nikonova LV, Tishkovskij SV. Zabolevanija shhitovidnoj zhelezy i beremennost'. Autoimmunnyj tireoidit, gipotireoz, tireotoksikoz pri beremennosti: sovremennye principy diagnostiki i lechenija. Zhurnal Grodnenskogo gosudarstvennogo medicinskogo universiteta. 2016;1:82-87. [in Russian].
3. Junusov AA, Zaharov GA. Ocenka lechenija pri patologii shhitovidnoj zhelezy i reproduktivnoj sistemy u zhenshhin. Vestnik KRSU. 2014;14(4):171-174. [in Russian].
4. Perminova SG, Ibragimova MH, Nazarenko TA. Besplodie i gipotireoz Problemy zhenskogo zdorov'ja. 2008;2(3):65-75. [in Russian].
5. Mihajlova SV, Zykova TA. Autoimmunnye bolezni shhitovidnoj zhelezy i reproduktivnye narushenija u zhenshhin. Sibirskij medicinskij zhurnal. 2013;8:26-31. [in Russian].
6. Karaca N, Akpak YK. Thyroid disorders and fertility. International Journal of Research in Medical Sciences. 2015;3(6):1299-1304.
7. Kachuei M, Jafari F, Kachuei A, Keshteli AH. Prevalence of autoimmune thyroiditis in patients with polycystic ovary syndrome. Arch Gynecol Obstet. 2012;285:853-6


**РЕЗУЛЬТАТИ ЛІКУВАННЯ КОМБІНОВАНИМИ ГОРМОНАЛЬНИМИ ТА ПРОГЕСТАГЕННИМИ ГОРМОНАЛЬНИМИ КОНТРАЦЕПТИВАМИ У ЖІНОК З АУТОІМУННИМ ТИРЕОЇДИТОМ У ФЕРТИЛЬНОМУ ВІЦІ**

**Гаджизаде А. Е.**

**Резюме.** *Актуальність проблеми.* У літературі існують суперечливі погляди про поширеність аутоімунних захворювань щитоподібної залози, включаючи аутоімунний тиреоїдит та їх потенційний вплив на безпліддя, тому досить важливо продовжувати дослідження в даній галузі.

*Мета дослідження.* Дослідити вплив комбінованої гормональної та прогестагенної гормональної терапії у жінок з аутоімунним тиреоїдитом репродуктивного віку протягом 12 місяців на щитоподібну залозу та репродуктивну систему, рівень специфічних анти-ТРО та антитіл проти тиреоглобуліну.

*Об'єкт і методи дослідження.* 48 пацієнтів, що отримували комплексне лікування аутоімунного тиреоїдиту та безпліддя були об'єктами нашого дослідження. Пацієнти були розділені на чотири підгрупи по 12 жінок в кожній. Підгрупа I – реципієнти комбінованих пероральних контрацептивів (КОК) та тироксину, підгрупа II – реципієнти лише КОК, III – реципієнти дезогестрелу та тироксину, IV підгрупа – реципієнти дезогестрелу. Комплексне обстеження включає в себе загальноклінічні, інструментальні, лабораторні методи та орієнтоване на специфічні методи обстеження. Обрані методи дослідження відповідали поставленій меті та завданням.

*Результати дослідження та їх обговорення.* У пацієнтів I підгрупи з аутоімунним тиреоїдитом, що приймали КОК на фоні застосування тироксину, через 12 місяців рівень ТТГ в крові достовірно знижувався. У пацієнтів у II підгрупі, яким не було призначене лікування тироксином, зміни рівня ТТГ через 12 місяців після прийому КОК було неточним. У пацієнтів III підгрупи з аутоімунним тиреоїдитом, що отримували гестаген дезогестрел в дозу 50-75 мкг тироксину, через 12 місяців спостерігалося достовірне зниження рівня ТТГ крові ($p<0,05$). Застосування прогестаген-дезогестрела протягом 12 місяців призвело до значного зниження в плазмі крові лише вутоантитіл проти тиреоїдної пероксидази.

**Ключові слова:** аутоімунний тиреоїдит, безпліддя, гіпотиреоз, лікування безпліддя, лікування гіпотиреозу.

**RESULTS OF TREATMENT WITH COMBINED HORMONAL AND PROGESTOGENIC HORMONAL CONTRACEPTIVES IN WOMEN WITH AUTOIMMUNE THYROIDITIS AT THE FERTILE AGE**

**Hajizadeh A. E.**

**Abstract. The urgency of the problem**. Conclusions in literature about the prevalence of autoimmune diseases of the thyroid gland, including autoimmune thyroiditis and its potential impact on infertility is very contradictory and continuing of studies in this sphere is considered as important.

**The purpose of the study** is to study the effect of 12-month combined hormonal and progestogenic hormonal treatments among women with autoimmune thyroiditis of reproductive age on the thyroid and reproductive system, the level of specific anti-TPO and anti-thyroglobulin antibodies.

**Object and methods of the research.** The research materials consists of medical records of 48 patients who received complex treatment for autoimmune thyroiditis and infertility. Patients were divided into four subgroups for this purpose. 12 patients receiving combined oral contraceptives (COCs) and thyroxine were in the I subgroup, 12 patients receiving only combined oral contraceptives (COCs) were in II, 12 patients receiving desogestrel and thyroxine were in III subgroup, and 12 patients receiving only desogestrel were in IV subgroup. The complex

examination includes general-clinical, instrumental, laboratory methods and special examination methods. Selected examination methods were adequate for intended purposes and objectives.The level of anti-thyroglobulin autoantibodies (anti-TG antibodies) and anti-thyroid peroxidase antibodies (anti-TPO antibodies) was studied by the enzyme-linked immunosorbent method.

**The results of the study and their discussion.** In patients of the first subgroup with autoimmune thyroiditis taking COCs against the background of thyroxine use, after 12 months there was a significant decrease in blood TSH from 1.9±0.1 mIU/L to 1.4±0.2 mIU/L ($p<0.05$). The change in TSH levels 12 months after taking COC among patients in subgroup II who were not prescribed thyroxine treatment was inaccurate. Patients with autoimmune thyroiditis of subgroup III receiving progestogen desogestrel with a dose of 50-75 mcg of thyroxine showed a significant decrease in TSH in blood levels after 12 months ($p<0.05$). In fertile older women with autoimmune thyroiditis, 12-month use of micro- and low-dose combined oral contraceptives resulted in a significant decrease in plasma levels of anti-thyroid peroxidase and anti-thyroglobulin antibodies ($p<0.05$). Hestagen desogestrel's use for 12 months resulted in a significant reduction in plasma-only antibodies to thyroid peroxidase.

**Key words**: autoimmune thyroiditis, infertility, hypothyroidism, treatment of infertility, treatment of hypothyroidism.

***Рецензент – проф. Бобирьова Л. Є.***
**Стаття надійшла 24.12.2020 року**

**DOI** 10.29254/2077-4214-2021-2-160-85-88
**UDC** 612.014

***Hasanova S. Yu.***

# RESEARCH OF THE POSSIBILITIES OF TREATING PANCREATITIS WITH THE INTRODUCTION OF STEM CELLS

**Azerbaijan State Advanced Training Institute for Doctors named after A. Aliyev (Baku, Azerbaijan)**
**s.v.zachepylo@gmail.com**

**The connection of the publication with planned research works.** This work is a fragment of a doctoral dissertation: "The effect of cell therapy on the results of treatment of acute pancreatitis».

**Introduction.** When analyzing the possibilities of using stem cells in the treatment of pancreatitis, two main areas of research can be identified: deepening the understanding of the pathogenesis of the disease and studying the mechanisms of regeneration in various methods of therapy at the level of preclinical studies. At the same time, it was found that the causes of acute and chronic pancreatitis include lysis of pancreatic tissues due to premature activation of pro-enzymes in acinar cells and long-standing inflammation of the organ, leading to the development of fibrosis, which can affect entire regions of the gland. In pathology, the destruction of the secretory parenchyma is observed as a consequence of necrosis, apoptosis, inflammatory processes, and duct obstruction [1].

Some studies have found that autoimmune mechanisms are actively involved in the development of pancreatitis, in particular, there is an imbalance between pro – and anti-inflammatory cytokines [2].

The ability of the pancreas to self-regenerate is known, the presence of which is presumably achieved: through the presence of its own multipotent mesenchymal stem cells (MMSCs), but in fairly small quantities (1/5000 cells) [3], stem cells from the bone marrow [4] and/or the use of the bile tree as a reservoir of undifferentiated cells [5,6]. Various types of cells (associated with the ductal epithelium, mesenchymal-like, nestin-expressing, and pre-existing acinar cells) are considered as possible precursors of organ tissues [7]. However, the insufficiency of native components requires the intensification of repair by means of exogenous MMSC injections [8].

Stem cell therapy is considered as a promising therapy for autoimmune diseases, including pancreatitis [6].

In comparison with conservative therapy, the treatment of pathologies of internal organs by means of stem cells is insufficiently studied. [7]

Clinical studies of the use of MMSCs in cirrhosis of the liver have shown their effectiveness and safety [9, 10]. However, the number of patients was mostly small (up to 10). Clinical studies of the use of MMSCs for the treatment of pancreatitis are not yet available in the literature. The use of laparoscopy in the treatment of patients with acute pancreatitis has reduced the mortality rate after surgery to 13.4% [11].

**The aim of this study** is to study the possibilities of reducing the postoperative mortality rate in severe forms of acute pancreatitis using MMSCs.

**Object and methods of the research.** The research was carried out on the basis of materials from two clinics-the surgical clinic of the Institute of Advanced Training of Doctors named after A. Aliyev and the city Clinical Hospital № 3. Cord blood stem cells were obtained from the International Center for Stem Cell Cultivation "Biostem"-Donetsk, Ukraine, on the basis of a joint research project agreement. The selection of patients included informed consent, the age was 20-60 years, the diagnosis was a severe form of acute pancreatitis with normalization of the condition after symptomatic and supportive treatment, including antispasmodics, deactivators of pancreatic enzymes, correction of homeostasis by infusion of salt and protein solutions, detoxification therapy, antibiotics to prevent infectious complications. 20 people were selected. They were divided into two groups: a control group and a study group of 10 people each.

The studies did not involve patients younger than 20 and older than 60 years, with various oncological diseases, severe renal insufficiency (serum creatinine