American Journal of Clinical and Experimental Medicine
2025, Vol. 13, No. 4, pp. 79-83
https://doi.org/10.11648/j.ajcem.20251304.12

Research Article

The Impact of Combined Use of Placental Extract and L-Thyroxine on Thyroid Status Parameters in Patients with Primary Hypothyroidism of Autoimmune Origin

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Abstract

The development of new approaches and the search for effective means for restoring thyroid function in primary hypothyroidism against the background of autoimmune damage is an urgent need. Currently, preparations made from placenta tissue and amniotic membrane are attracting attention. The placenta, as an organ that ensures the growth and development of the fetus, has in its composition active metabolites and immunosuppressive agents that ensure the preservation of pregnancy, and can have a positive effect when using such drugs in patients with autoimmune disorders. At present, the concept of a comprehensive approach to the treatment of autoimmune thyroiditis, which leads to hypothyroidism and subsequent complications using biologically active compounds, has not been finally formed. The solution to this problem will contribute to reducing the pharmacological burden on the patient with hypothyroidism and improving his quality of life. The aim of the work was to study the effect of the placenta extract preparation in combination with L thyroxine on the parameters of thyroid status in patients with primary hypothyroidism of autoimmune genesis. As part of the study, it was found that the combined use of placenta extract and L thyroxine led to a significant decrease in the level of ab-TPO already a month after therapy. After 6 and 12 months, the tendency to a gradual decrease in the content of ab-TPO was maintained. As for the functional state of the thyroid gland, the level of free fractions of thyroid hormones gradually reached the level of reference indicators. Thyroid-stimulating hormone after 12 months and 6 months after the repeated course was within the physiological norm. The use of monotherapy with L thyroxine restored the level of thyroid hormones and TSH, but the level of ab-TPO a year after the start of therapy was within the range of indicators before the start of therapy. The drug "placental extract" leads to a decrease in the tension of antithyroid immunity in patients with primary hypothyroidism at all studied periods and helps to slow down the progression of primary hypothyroidism in patients with autoimmune thyroiditis and normalize the parameters of thyroid status, which allows to reduce the daily dose of replacement therapy with levothyroxine.

Keywords

Autoimmune Thyroiditis, Primary Hypothyroidism, Placenta Extract, L Thyroxine, Antibodies to Thyroid Peroxidase, Thyroid Status

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Received: 25 April 2025; **Accepted:** 9 July 2025; **Published:** 23 July 2025

1. Introduction

Primary hypothyroidism (PH) is the most common endocrine pathology after type 2 diabetes mellitus worldwide [1]. Its overall prevalence ranges from 3 to 8%, and considering subclinical forms, it reaches 10 to 12% of the global population, with a consistent increase in this pathology observed in young and middle-aged individuals in recent years [2].

The development of new approaches and the search for effective means to restore thyroid gland (TG) function in PH is an urgent necessity [13, 14]. Currently, the most widely used preparations are derived from placental tissue and amniotic membranes. Researchers are particularly focused on the placenta as an organ that supports fetal growth and development and has active metabolism [3, 7, 8]. The active factor in placental preparations is classical biostimulants formed in tissues [4, 9-11]. Their mechanism of action is based on the preservation of metabolically active substances of natural origin in cryopreserved tissue that correct the human immune status and possess polypharmacological properties aimed at regulating regeneration, proliferation, and differentiation processes [5, 8, 12]. It has been established that the protein-peptide complex isolated from placental tissue exhibits pronounced antioxidant activity, immunostimulatory effects, anti-inflammatory, and reparative properties. Most of these biologically active compounds have nonspecific effects on the course of cellular and humoral immune reactions [4, 6, 10, 15].

Currently, there is still no established concept of a comprehensive approach to the treatment of PH and its complications using biologically active compounds capable of restoring the affected links in thyroid hormone metabolism. Addressing this issue will help reduce the pharmacological burden on patients with PH and improve their quality of life.

The aim of the study is to determine the possibility of using placental extract in combination with L-thyroxine for the correction of autoimmune-related primary hypothyroidism.

2. Materials and Methods

The study was conducted at the State Institution "V.Ya. Danilevsky Institute of Endocrine Pathology of the National Academy of Medical Sciences of Ukraine" in accordance with the main provisions of the Council of Europe Convention on Human Rights and Biomedicine, the Helsinki Declaration of the World Medical Association on the ethical principles of conducting scientific medical research involving humans, and the requirements of good clinical practice.

A retrospective analysis of 150 medical histories of patients with PH was performed.

Inclusion criteria for the study were: age over 18 years, presence of confirmed autoimmune thyroiditis (AIT) with PH of mild or moderate severity in a state of compensation/subcompensation.

Three study groups were formed (10 patients each), consisting of patients with PH due to AIT.

The first group consisted of patients before treatment; group 2 included patients with moderate PH in a state of compensation (n=8) and subcompensation (n=2) receiving "L-thyroxine" (LT4) therapy; group 3 included patients with mild PH in a state of subcompensation (n=4), moderate PH in a state of compensation (n=4), and subcompensation (n=2) receiving combined therapy of "L-thyroxine" (LT4) and cryopreserved placental preparation "Platex-Placental" ("placental extract").

The levels of thyroid-stimulating hormone (TSH), free thyroxine (fT4), free triiodothyronine (fT3), and antibodies to thyroid peroxidase (ab-TPO) in serum were measured using an immunoassay method.

The studied cryopreserved placental preparation "Platex-Placental" ("placental extract") produced by the State Enterprise "MNTC Cryobiology and Cryomedicine of the National Academy of Sciences, Ministry of Health, Academy of Medical Sciences of Ukraine" (certificate of registration No. 734/08-30200000) was administered intramuscularly at a dose of 2.0 ml/day; the treatment course lasted 10 days. The daily dose of "L-thyroxine" (LT4) produced by (Berlin-Chemie, Germany) was 75 mcg.

The dynamics of thyroid status parameters and ab-TPO levels were studied at one month, six months, and twelve months post-treatment, as well as upon re-administration after six months.

Statistical analysis of the research results was performed using the "Statistical 13.0" program (Stat Soft Inc., USA; serial number: ZZS999000009906307DEMO-5). Normality of variable distribution was checked using the Kolmogorov-Smirnov criteria. For comparison of several groups with non-normal distribution of variables, the Wilcoxon-Mann-Whitney test was used. Testing of null hypotheses was conducted at a significance level of $P \leq 0.05$. The obtained results are presented in tables in the form of ±S, where – mean arithmetic, S – standard deviation.

3. Results

In patients prior to therapy, elevated levels of ab-TPO and TSH were registered relative to the reference values for these indicators. The levels of free thyroid hormones in serum showed a tendency to decrease, particularly for fT4. One month after therapy for PH due to AIT, the following results were obtained. The use of LT4 led to a significant decrease in TSH and an increase in fT4 but did not affect the ab-TPO levels. When combining LT4 and the "placental extract," a significant decrease in ab-TPO was noted, while fT4 and TSH levels remained within the group receiving only LT4 (Table 1).

Table 1. Dynamics of thyroid status parameters in patients with PH one month after therapy, ($\overline{X} \pm S_{\overline{x}}$).

Group, number of patients	FT3, pmol/l	FT4, pmol/l	TSH, mIU/L	ab-TPO, IU/L
1. Before treatment, n=10	3,18±0,36	9,7±1,02	9,64±2,51	190,8±18,17
2. L-thyroxine, n=10	4,3±0,51	14,12±2,15*,#	6,12±1,18*,#	175,36±9,77#
3. L-thyroxine + placenta extract, n=10	4,58±0,95*,#	16,75±1,94*,#	5,25±1,45*,#	115,62±5,61*,#

Note: * - statistically significant differences from group 1; # - statistically significant differences between groups 2 and 3; ($p<0.05$).

Six months after treatment, the physiological levels of thyroid hormones were maintained in both the monotherapy and combination therapy groups. The TSH levels tended to normalize in both studied groups. The level of ab-TPO decreased by twofold in the group of patients receiving "placenta extract" along with LT4 (Table 2).

Table 2. Dynamics of thyroid status parameters in patients with PH six months after therapy ($\overline{X} \pm S_{\overline{x}}$).

Group, number of patients	FT3, pmol/l	FT4, pmol/l	TSH, mIU/L	ab-TPO, IU/L
1. Before treatment, n=10	3,18±0,36	9,7±1,02	9,64±2,51	190,8±18,17
2. L-thyroxine, n=10	4,95±0,64*	17,12±2,36*	3,67±0,43 *	185,45±14,84
3. L-thyroxine + placenta extract, n=10	4,68±0,46*	18,45±1,43*	2,15±0,65*,#	90,15±11,04*,#

Note: * - statistically significant differences from group 1; # - statistically significant differences between groups 2 and 3; ($p<0.05$).

The12 months after the use of combination therapy, restoration of the functional state of the thyroid gland was recorded, reactivation of the autoimmune process was maintained (the level of ab-TPO was 50 percent lower than in groups 1 and 2) (Table 3).

Table 3. Dynamics of thyroid status parameters in patients with PH 12 months after therapy ($\overline{X} \pm S_{\overline{x}}$).

Group, number of patients	FT3, pmol/l	FT4, pmol/l	TSH, mIU/L	ab-TPO, IU/L
1. Before treatment, n=10	3,18±0,36	9,7±1,02	9,64±2,51	190,8±18,17
2. L-thyroxine, n=10	3,50±0,35*	17,90±1,5*	2,54±0,23*	190,16±12,85
3. L-thyroxine + placenta extract, n=10	3,25±0,45*	16,55±2,43*	1,17±0,35*	85,72±9,36*,#

Note: * - statistically significant differences from group 1; # - statistically significant differences between groups 2 and 3; ($p<0.05$).

The 6 months after the second course of combined treatment, physiological indicators of thyroid hormone levels and ab-TPO are noted. In contrast to LT4 monotherapy. In this group of patients, the ab-TPO level returns to the values of patients before treatment (Table 4).

Table 4. Dynamics of thyroid status parameters in patients with PH 6 months after a repeated course of therapy, ($\overline{X} \pm S_{\overline{x}}$).

Group, number of patients	FT3, pmol/l	FT4, pmol/l	TSH, mIU/L	ab-TPO, IU/L
1. Before treatment, n=10	3,18±0,36	9,7±1,02	9,64±2,51	190,8±18,17
2. L-thyroxine, n=10	3,53±0,48#	16,70±0,60*	2,90±0,86*	170,6±12,8*,#
3. L-thyroxine + placenta extract, n=10	4,65±0,45*	17,24±0,45*	1,06±0,24*	40,7±8,4*

Note: * - statistically significant differences from group 1; # - statistically significant differences between groups 2 and 3; ($p<0.05$).

4. Discussion

The results obtained indicate a positive effect of the combined use of LT4 and the drug "placental extract". So, after 1 month, a significant decrease in the level of ab-TPO is noted in patients with PH due to AIT. This may indicate a positive effect on antithyroid immunity. The protein-peptide complex isolated from placental tissue and immunosuppressive agents produced by the placenta and fetus to preserve pregnancy play a significant role in the use of this drug in patients with PH due to AIT.

When observed after 6 and 12 months, as well as repeated use, a stable tendency to restore the functional activity of the thyroid gland was noted.

The obtained data and the identified trends indicate the need to expand the spectrum of studies of the effect of the drug "placental extract" on a larger number of patients, which in the case of normalization of the functional thyroid state and the absence of clinical symptoms of hypothyroidism may lead to a decrease or cancellation of LT4 hormone replacement therapy.

5. Conclusions

1) The drug "placental extract" leads to a decrease in the tension of antithyroid immunity in patients with primary hypothyroidism at all studied periods. A significantly better effect was observed after a repeated course of treatment.
2) A repeated course of treatment with the drug "placental extract" helps to slow down the progression of primary hypothyroidism in patients with autoimmune thyroiditis and normalize thyroid parameters, which allows to reduce the daily dose of LT4 replacement therapy.

Abbreviations

AIT	Autoimmune Thyroiditis
PH	Primary Hypothyroidism
TG	Thyroid Gland
"placental extract"	Cryopreserved Placental Preparation "Platex-Placental"
TSH	Thyroid-Stimulating Hormone
fT4	Free Thyroxine
fT3	Free Triiodothyronine
ab-TPO	Antibodies to Thyroid Peroxidase
LT4	"L-thyroxine"

Author Contributions

Yuriy Karachentsev: Conceptualization, Supervision
Natalia Malova: Writing – review & editing
Vadym Khaziyev: Validation, Methodology
Larysa Syrotenko: Data curation, Software
Myroslava Mykytiuk: Formal Analysis

Data Availability Statement

The data supporting the outcome of this research work has been reported in this manuscript.

Conflicts of Interest

The authors declare that there is no conflict of interest in relation to this paper, as well as the published research results, including the financial aspects of conducting the research, obtaining and using its results, as well as any non-financial personal relationships.

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