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Determining factors of the effectiveness of medical rehabilitation of patients with autoimmune thyroiditis

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Abstract

Background: One of the most important issues in the treatment of autoimmune thyroid diseases is the choice of tactics of the physician in relation to high levels of antithyroid antibodies. Do they actively eliminate them from the body or not? We belong to the group of researchers who believe that the antithyroid antibody titer has a significant effect on the activity of the autoimmune process and accelerates the progression of the disease. Therefore, the inclusion of methods that allow the removal of antibodies from the body is an important component of treatment. In addition, these methods must be effective and safe.

Methods: 124 patients with the diagnosis of autoimmune thyroiditis with the formation of functional insufficiency were examined and treated. The observation group proposed a method of stimulating lymphatic drainage in the form of complex comprising components of plant origin. In the comparison group, the treatment complex included plasmapheresis.

Results: It was found that the high activity of the autoimmune process influences both the preservation of the secretory mechanisms and the preservation of the organ structure. Exceeding this level triggers a cascade of mechanisms, the external control of which is practically impossible. Inclusion in the therapeutic complex of stimulating lymphatic drainage of plant origin according to the developed scheme allows reducing the activity of the autoimmune process and improving the prognosis.

Conclusions: Rehabilitation methods based on stimulation of lymphatic drainage are highly effective against autoimmune diseases of the thyroid gland.

Background

Development of scientific and practical direction of rehabilitation of patients with endocrine diseases includes the treatment, which uses factors, simultaneously affecting the mechanisms of the pathogenesis of various diseases and, when properly administered, activating mechanisms sanogenesis stimulating the adaptability of the organism. The use of non-pharmacological methods can activate adaptive mechanisms that enable the functional reserves of the organism. Our studies, previously devoted to the study of the mechanisms of adaptation of patients with endocrine diseases such as diabetes mellitus, suggest that this mechanism must be taken into account both in the pathogenic aspect and in predicting the course and outcome of the disease [1]. Rehabilitation of patients with thyroid diseases is carried out on general grounds, the activity of the autoimmune process and the effect of this indicator on the effectiveness of rehabilitation are not taken into account at all. Methods for medical rehabilitation aimed at eliminating antithyroid antibodies have not been developed. All these unresolved problems served as the basis for the present study.

Purpose of study

To improve the quality of medical rehabilitation of patients with autoimmune organ-specific diseases on the model of autoimmune thyroiditis by assessing the state of the adaptive capabilities of the organism and the degree of severity of the autoimmune process and including methods of stimulating lymphatic drainage into the rehabilitation complex.

Methods

Design

Patients hospitalized in a specialized department of the endocrinology of the hospital with a diagnosis of autoimmune thyroiditis, were underwent dynamic observation for 6-12 months. The study was conducted from 2010 to 2015.

Sampling and setting

The study was conducted based on the Endocrinology Department of City Clinical Hospital name Eramishantsev (Moscow) and endocrinology department of the Regional Clinical Hospital (Izhevsk).

To solve the tasks, 124 patients have been examined and diagnosed with autoimmune thyroiditis (AIT), complicated by functional thyroid gland failure. Persons of both sexes, aged 18 to 60 years, agreed to participate in the study through the signing of informed consent (Fundamentals of Legislation of the Russian Federation, 2011).

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Inclusion in the study was carried out by random and typological sampling. All patients at the beginning of the study were in a state of de compensation (hypothyroidism) and were examined. Mild thyroid failure was observed in 36.2% of patients, the average - in 63.8% of patients. The severe degree was a criterion for exclusion from the study, because In 100% of cases was accompanied by failure of adaptation. After attaining medical compensation, the observation was carried out at the outpatient and sanatorium-resort stages of rehabilitation. The inclusion criteria – Patients of both sexes with autoimmune thyroiditis aged from 20 to 65 years. Exclusion criteria – myocardial dystrophy, hypothyroid coma and other urgent conditions. The basis for including patients in the study was also the informed consent of the patient.

Instruments and data collection procedure

All patients were examined in accordance with the developed international standards. Particular attention was paid to the hormone indices - free thyroxine (FT_4) and triiodothyronine (FT_3), thyroid-stimulating hormone (TSH), titers of antithyroid antibodies (Abs – TPO). An ultrasound examination of the thyroid gland was performed to determine the size and structure (Volume of.T.G.).

Criterion for the distribution of patients in groups was the preservation of the functional reserves of the body according to the level of the indicator of adaptive compliance (IAC). IAC was developed a formula for calculating indicator of adaptive compliance (IAC) using the method of computer simulation method of segmentation of images with a given confidence level (OR) 99,8% (patent RU 2342900 C1).

IAC = 0.011 (P-P *) + 0.014 (S-S *) + 0.008 (D-D *) + 0.009 (W-W *), where:

P - actual heart rate (beats/min);

P * - the pulse rate is ideal within the limits of the age norm (beats/min.), which is determined from the table; S - systolic blood pressure actual on average per day (mm Hg);

S * - systolic blood pressure is ideal (mm Hg), which is determined from the table;

D - the diastolic blood pressure actual on the average for a day (mm of a mercury column);

D * - diastolic blood pressure is ideal (mm Hg), which is determined from the table;

W - actual body weight at the time of examination (kg);

W * - ideal body weight (kg), which is determined by the formula.

IAC from 0 to 0,3 - functioning of the body compensated by their functional resources or medical correction; IAC is bigger than 0,3 - functioning of the body are disrupted, own resources of the organism are exhausted, and medications are not fully compensate the existing violations. The problem of mathematical calculations was solved through the development of computer program «Software determine the level of functional state and compensatory abilities of the body» (official registration Certificate № 2007614560 from 30.10.07r.).

To study the adaptive capabilities of a healthy person are often used or extreme stress impacts and on the basis of changes of various physiological or biochemical responses and their comparison with the norm judged the adaptation possibilities of the person and his health. We applied a fundamentally different approach. Assessment of adaptation reserves was carried out without the use of stress factors or loading tests. Evaluated not direct the value of health index, while the difference (gap) between the indicators of the actual index of the health of a particular individual and estimates for him if his body was in perfect condition. IAC considers not only the individual characteristics of the organism, but also the effect of consequences of influence of the external and internal environment (the way of life, the impact of adverse external factors and external factors) [2].

The indicator can used to assess not only in healthy people, but also in people with chronic diseases.

At the first stage of the study, patients were divided into two groups: 1 - (observation group) - 96 patients with AIT and functional thyroid gland deficiency with low functional reserve (FR) of the organism; 2 - (comparison group) 28 patients with a similar diagnosis and a high level of functional reserves. Each group was divided into subgroups: "a" - patients aged 18 to 40 years (23 people); "b" - patients aged 40 to 50 years (39 people); "c" - patients aged 50 to 60 years (62 people).

The method for determining the degree of severity of the autoimmune process in patients with hypothyroidism (patent No.2471411RU of 10.01.2013) including an analysis of the body's functional parameters, the total volume of the thyroid gland and the level of antibodies to the thyroid peroxidase (TPO) in blood and calculates the severity of the autoimmune process by the formula:

CAP = (-934.6 + 162.671 × V + 136.785 × A-4.434 × 2V -3.28 × V×A-4.0462 × A)/1000,

Where: CAP - coefficient of activity of the autoimmune process (determined in points); V - the total volume of the thyroid gland (cm3); A - level of antibodies to thyroid peroxidase (mE/l).

At CAP values less than 18 points - mild severity of progression of the autoimmune process, CAP in the range of 18 to 45 points - the average severity, with CAP values greater than 45 - a severe degree of progression of the autoimmune process in the thyroid gland.

Rehabilitation methods

The study of the possibility of influencing transport processes in the "blood-tissue fluid-lymph" system becomes extremely important in therapy, although it has not yet received a proper evaluation. With increased lymph formation, active tissue washing and removal of toxic products from disturbed metabolism occurs, which is especially important for autoimmune diseases with the accumulation of a large number of autoantibodies and interleukins in the intercellular space. The method of stimulation of lymphatic drainage included a sequence of drugs taking into account the mechanism of their action and the physiology of the organism in strict dependence on the process of food intake. The mechanism of action of each component of the treatment complex has been repeatedly studied and proved both clinically and laboratory studies [3,4,5].

- Start is a remedy that has a lymphostimulating action 30-40 minutes before a meal in order to activate the excretory function of the lymphatic capillaries of the intestinal wall (catrela, a leaf of cranberries in the form of tea).
- An hour after ingestion, a drug that stimulates the secretion of bile to bind lymph components that enter the lumen of the intestine
- 30 minutes after the choleretic preparation (simultaneously with the onset of food intake from the stomach into the duodenum), sorbents were assigned to evacuate complexes bound by bile components.

For standardization, the treatment was carried out according to the scheme: lymphatic drainage stimulant - "catreel" (blackcurrant leaf +

milk thistle) for 15 days 1 capsule 2 times a day or cranberry leaves infusion (20: 200) for 30 days. As a cholagogue, allohol 2 tablets were used 3 times a day or ursosan (if the patient has a biliary sludge) for 15 days. For enterosorption - polyphepan 0.5 g/kg of body weight of the patient for 10 days. After the reception of polyphepan was administered biform 1 capsule 2 times a day for 10 days to correct the dysbacteriosis. The course was prescribed in the absence of contraindications (urolithic or cholelithiasis, labile course of diabetes, individual drug intolerance). An alternative method was a discrete centrifugal plasmapheresis according to a standard procedure using a centrifuge "RS-6" and a plasma filter "Rosa" (Moscow).

Basic therapy included the administration of drugs of levothyroxine sodium and its analogues.

Data analysis procedures

Statistical processing of the data was carried out using the STATISTICA software package (StatSoftInc. Version 10.0, USA).

Results

A weak positive correlation between ABs-TPO and hemoglobin level was found in group 1a (Table 1), which indicates the effect of the level of autoimmunization (endotoxicosis) and can be caused, either by activation of hematopoiesis processes or by blood thickening.

The obtained results call into question the position of indifferent attitude to the values of the titer ABs-TPO, which has become widespread in recent years among endocrinologists. In addition, the fact that the indicator of fT4 was in a positive correlation with the volume of the thyroid gland, suggested the importance of preserving the residual secretion. To establish the relationship between the residual secretion safety index, the thyroid volume and the activity of the autoimmune process, we performed a statistical analysis of the data using three-dimensional graphs (Figure 1).

It was found that the activity of the autoimmune process, manifested by an increase in ABs-TPO to a level of 1000 IU/l, affects both the preservation of secretory mechanisms and the preservation of the organ structure. Exceeding this level triggers a cascade of mechanisms, the external control of which is practically impossible. Therefore, we obtained the maximum effect of rehabilitation measures in patients with titers of ABs-TPO up to 1000 IU/l. In addition, all after the stage of restorative treatment required a reduction in the dose of Levothyroxine. The greatest interest in our study was the definition of the relationship between the preservation of the functional reserves of the body and the functional state of an organ that underwent autoimmune aggression - in our case, patients with AIT. There was a strong negative correlation between the level of PAS and the level of free T4 in the blood r = -0.82; P <0.05. The risk of complications develops in people with low RF and low residual thyroid secretion in the AH, neuropathy, and to a lesser degree of DAP (Table 2).

After the significance of the activity of the autoimmune process as a prognostic indicator for the evaluation of the effectiveness of rehabilitation was determined, it became necessary to develop criteria for monitoring this activity - CAP. There is a strong negative correlation between the PAS level and the CAP level r = - 0.82; P <0.05. The association of the risk of complications with the activity of the autoimmune process was evaluated in 124 patients (age 18-60 years). All the titers of ABs-TPO tested exceeded 300 IU/l (ABs-TPO = 523 ± 28 IU/L). Of these, with a CAP level <18 - 4 people (3.2%); With a level of 18> CAP <45 - 53 people (42.7%); With the level of CAP ≥65 - 67 people (54%). The risk of complications increases in patients with a severe degree of progression of the autoimmune process in the thyroid gland (Table 3).

At the stage of rehabilitative treatment, the type of therapy determined the distribution of patients in the group. The observation group - 59 patients with AIT with diffuse (26 people) or diffuse-nodal form (33 patients), at the age of 46.4 ± 3.3 years, CAP = 33.6 ± 4.9 received a course of stimulation of the lymph drainage system. Comparison group - a course of plasmapheresis - 61 patients with AIT (29 people with diffuse and 32 with diffusive-nodular form), at the age

Table 1. Correlation matrix of the main morpho-functional indices in patients in the "1a" group (n = 17 people)

	Volume of.T.G. (см^3)	TSH (mkMe /l)	FT_4 (pmol/l)	Abs – TPO (Me/l)	Hb (gm/l)
Hb (gm/l)	r = +0,03	r = - 0,26	r = + 0,36	r = + 0,07*	r = + 1,00
Me	7,70	13,10	11,70	284,00	124,00
Percentile 10	0,20	1,70	3,80	6,00	99,00
Percentile 90	0,16	62,10	16,50	1000,00	145,00

Note: p <0.05 * is the reliability of the rank correlation of Spearman.

Table 2. The risk of complications in patients with low levels of RF and a low level of residual secretion of the thyroid gland (n = 87)

RR, OR / complications		RR	CI 95%	p	OR	CI 95%	p
HTN	64/87	1,05	[0,93; 1,19]	<0,05	2,78	[0,37; 20,91]	<0,05
DE	52/87	0,99	[0,90; 1,10]	<0,05	0,96	[0,15; 6,05]	<0,05
NP	42 /87	1,04	[0,95; 1,13]	<0,05	2,74	[0,27; 27,34]	<0,05

Note: RR is the relative risk; OR - odds ratio; [CI] is the range of values within which, with a probability of 95%, the expected value of OR is found, RR; HTN - arterial hypertension; DE - dyscirculatory encephalopathy; NP - neuropathy.

Table 3. The risk of complications in the examined patients with a severe degree of progression of the autoimmune process (n = 67)

RR, OR / Complications		RR	CI 95%	p	OR	CI 95%	p
HTN	58/67	2,43	[1,3;4,35]	< 0,05	5,03	[2,09; 12,09]	< 0,05
DE	60/67	1,84	[0,98; 3,48]	< 0,05	3,06	[1,14 8,15]	< 0,05
NP	47/67	1,48	[1,01; 2,16]	< 0,05	2,2	[1,08; 4,47]	< 0,05

Note: RR is the relative risk; OR - odds ratio; [CI] is the range of values within which, with a probability of 95%, the expected value of OR is found, RR; HTN - arterial hypertension; DE - dyscirculatory encephalopathy; NP - neuropathy.

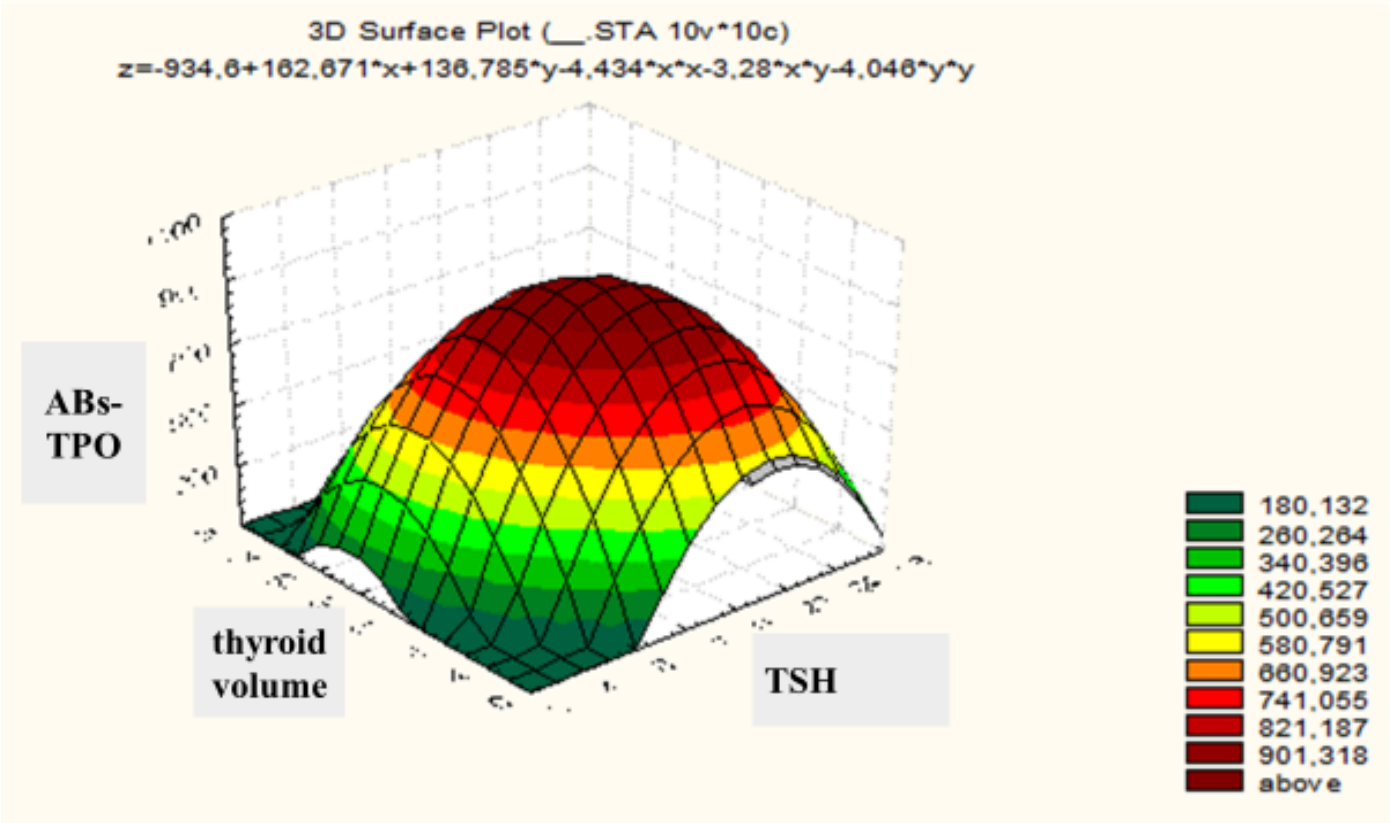

Figure 1. Interrelation of activity of autoimmune process, structure and functional insufficiency of thyroid gland. Abs-TPO - titers of antithyroid antibodies; TSH - thyroid-stimulating hormone.

of 45.3 ± 2.6 years, CAP = 37.6 ± 3.7. The determination of the level of AT-TPO and KAP was performed 1, 3 and 6 months after completion of the rehabilitation course. A month later, the observed antibody titer decreased 3-4 times in comparison with the baseline (215 ± 27 nmol/L, $p < 0.001$), the effect of the therapy persisted for 6 months. In the comparison group, there was an increase in the level of AT-TPO 1 month after the completion of the plasmapheresis course, which was associated with the redistribution of antibodies in the tissue-blood system, and decreased to the baseline level after 6 months (Figure 2).

Six months after plasmapheresis, the IAC almost matched the baseline (Figure 3). In the course of the study it was found that there is a relationship ($r = 0.48$, $p = 0.002$) between the preservation of the adaptive capabilities of the body (IAC) and the degree of severity of the autoimmune process by the CAP criterion (CAP is the activity coefficient of the process).

Adverse events

During the study, no adverse events were noted.

Conclusion

Preservation and the level of functional reserves of the organism affects the course of the autoimmune process, the formation of a functional deficiency of the thyroid gland, the effectiveness of rehabilitation of patients. In patients with a low rehabilitation potential (IAC≥0.3), a more severe course of primary hypothyroidism (28%) is observed, complications (37%) and concomitant pathology (41%) are more frequent.

Inclusion of patients with autoimmune thyroiditis with functional deficiency of the thyroid gland at the stage of rehabilitation of a complex of non-medication and plant-based agents for stimulation of lymphatic drainage and interstitial-humoral transport into the complex of restorative therapy made it possible to significantly improve the effectiveness of medical rehabilitation.

The method of predicting the course of the autoimmune process in patients with primary hypothyroidism with autoimmune thyroid disease was developed and proposed to be used. The method of quantitative evaluation of the severity of the autoimmune process (patent No. 2471411 of 10.01.13) made it possible to establish a relationship between the index of adaptive compliance (ACI) and the severity of the autoimmune process By the CAP criterion (CAP- the coefficient of activity of the process).

Authors' contributions

Irina Kurnikova was a major contributor in writing the manuscript, and analyzed and interpreted the data of patients. Tatiana Borisova participated in the examination of patients and collection of material. Ramchandra Sargar contributed to manuscript preparation. All authors read and approved the final manuscript.

Acknowledgments

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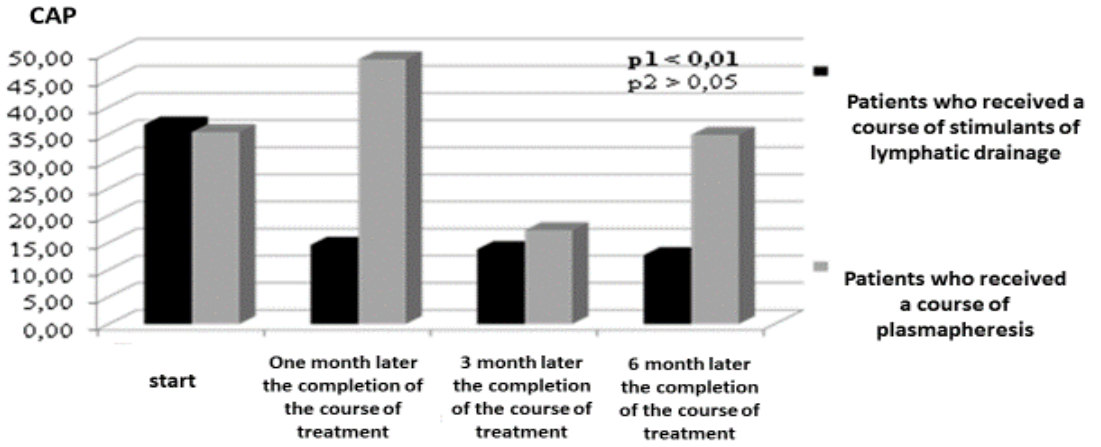

p1 - the reliability of the difference between the CAP levels before treatment and after 6 months in the observation group; p2 significant difference between the levels of CAP before treatment and after 6 months in the comparison group.

Figure 2. Dynamics of the levels of the indicator of the coefficient of activity of the process (CAP):

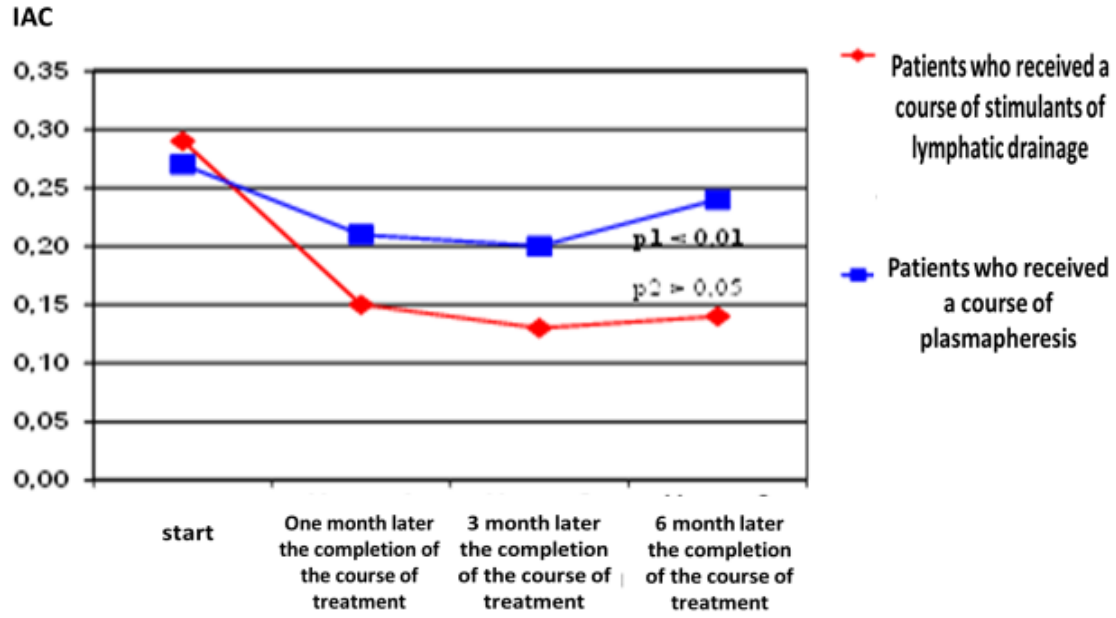

Figure 3. Dynamics of the adaptation compliance index (IAC) in the groups of patients examined: p1 - reliability of the difference between IAC before treatment and after 6 months in the observation group; P2 authenticity of the difference between IAC before treatment and after 6 months in the comparison group.

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