

## INTERRELATION OF NON-DRUG CORRECTION OF MENOPAUSAL DISORDERS AND FUNCTIONING OF THE PITUITARY-THYROID SYSTEM IN WOMEN WITH METABOLIC SYNDROME

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In perimenopausal women, the frequency of thyroid diseases and metabolic syndrome (MS) increases. In this work, the effect of non-drug correction programs for menopausal disorders on the structural and functional state of the thyroid gland in patients with MS was evaluated. For that, five groups of women (330 people total) aged 45–50 years with climacteric syndrome (CS) against the background of MS were examined. For the index group and the experimental groups the following was used: basic treatment, exercise therapy, drinking balneotherapy, additional oral intake of multivitamins and minerals, as well as physical therapy — vibrotherapy, chromotherapy, music therapy, aromatherapy, aeroionotherapy in various combinations. In the control group, only basic treatment was used. The levels of thyroid-stimulating hormone (TSH) and free thyroxine (free T4) in serum were determined, a sonographic study of the thyroid gland was performed. According to the study results, the use of correction programs using physical therapy methods improved the functioning parameters of the pituitary-thyroid system in the surveyed patients. In women with moderate-severity CS, the best results were obtained while simultaneously using all the mentioned above physiotherapy methods: during the transition period the TSH decreased by 6.5%, during the postmenopausal period — by 5.6%, the level of free T4 increased by 6.5% and 6.6% respectively ( $p < 0.05$ , applied to both parameters). It can be concluded that non-drug programs, including physical therapy, have a protective effect on the thyroid gland function. In case of moderate-severity climacteric syndrome, the program with simultaneous use of vibrotherapy, chromotherapy, music therapy, aromatherapy, aeroionotherapy has priority.

**Keywords:** climacteric syndrome, metabolic syndrome, thyroid status, physical therapy modalities

**Author contribution:** Berihanova RR — collection and processing of materials, obtained data analysis, writing of the text; Minenko IA — study concept and design.

**Compliance with ethical standards:** the study was conducted according to international ethical requirements of WHO (GCP — Good Clinical Practice standard) and to Declaration of Helsinki: Ethical Principles for Medical Research Involving Human Subjects; the study was approved by the Ethics Committee of I.M. Sechenov First Moscow State Medical University (protocol No 01-13 dated January 23, 2013).

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## ВЗАИМОСВЯЗЬ НЕМЕДИКАМЕНТОЗНОЙ КОРРЕКЦИИ КЛИМАКТЕРИЧЕСКИХ РАССТРОЙСТВ И ФУНКЦИОНИРОВАНИЯ ГИПОФИЗАРНО-ТИРЕОИДНОЙ СИСТЕМЫ У ЖЕНЩИН С МЕТАБОЛИЧЕСКИМ СИНДРОМОМ

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У женщин в перименопаузе частота тиреоидной патологии и метаболического синдрома (МС) увеличивается. В данной работе оценивали влияние нелекарственных программ коррекции климактерических расстройств на структурно-функциональное состояние щитовидной железы (ЩЖ) у пациенток с МС. Для этого обследовали пять групп женщин (всего 330 человек) 45–50 лет с климактерическим синдромом (КС) на фоне МС. У основной группы и групп сравнения применяли: базовое лечение, лечебную физкультуру, питьевую бальнеотерапию, дополнительный пероральный прием поливитаминов и минералов, а также физиотерапию — вибротерапию, хромотерапию, мелотерапию, ароматерапию, аэроионотерапию в различных сочетаниях. В группе контроля применяли только базовое лечение. Определяли уровни тиреотропного гормона (ТТГ) и свободного тироксина (Т4св) в сыворотке крови, проводили эхографическое исследование ЩЖ. Согласно результатам исследования, применение программ коррекции с использованием физиотерапевтических методов улучшило параметры функционирования гипоталамическо-тиреоидной системы у обследованных. У женщин с КС средней степени тяжести лучшие результаты получили при одновременном использовании всех перечисленных методов физиотерапии: в переходном периоде ТТГ снизился на 6,5%, в период постменопаузы — на 5,6%, уровень Т4св увеличился соответственно на 6,5% и 6,6% ( $p < 0,05$ , относится к обоим параметрам). Можно сделать вывод, что нелекарственные программы, включающие физиотерапию, обладают протективным влиянием на функцию ЩЖ. При КС средней степени тяжести преимущество имеет программа с одновременным применением вибротерапии, хромотерапии, мелотерапии, ароматерапии и аэроионотерапии.

**Ключевые слова:** климактерический синдром, метаболический синдром, тиреоидный статус, физиотерапия

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**Соблюдение этических стандартов:** исследование проводили согласно международным этическим требованиям ВОЗ (правила GCP — Good Clinical Practice) и Хельсинкской декларации Всемирной медицинской ассоциации по проведению биометрических исследований на людях; исследование одобрено комитетом по этике Первого Московского государственного медицинского университета имени И. М. Сеченова (протокол № 01–13 от 23 января 2013 г.). Все пациентки подписали информированное добровольное согласие на включение в исследование.

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At the stage of extinction of ovarian function, conditions are created for the formation of polymorbid pathology [1–3]. Often a woman enters the menopause having the background of somatic ill-being, in particular, having metabolic syndrome (MS), the prevalence of which in the overall population in developed countries is 25–40% [4]. In the period of aging estrogen deficiency, the frequency of occurrence of MS increases [5–7]. Involutional changes in the body are also associated with an increase in the frequency of thyroid diseases [8–10]. Perimenopausal thyroid dysfunction in the thyroid gland is found in 19.5% of women living in the iodine-deficient region, and hypothyroidism is most often detected — 16.7% [11]. The presence of conjugation points in the pathogenetic chains of menopause, MS and thyroid diseases determines the aggravation of metabolic-endocrine disorders by the principle of mutual complication of comorbid conditions [12, 13]. At the forefront of therapeutic measures aimed to stop age disorders, the menopausal hormone therapy of systemic and local action is worth [14]. However, the presence of contraindications to menopausal hormone therapy, the use of a large number of medicines for comorbid pathology, hormonophobia, characteristic for many women, preclude the appointment of estrogen preparations [15]. The need to search for effective non-drug technologies aimed to correct metabolic and endocrine disorders and maintain a decent quality of life in women with MS in peri- and postmenopausal period becomes obvious. The aim of the work was to assess the impact of complex non-drug correction programs for menopausal disorders in patients with MS on the structural and functional state of the thyroid gland.

## METHODS

Clinical study of 330 women was performed. The duration of the observation was six months.

Using randomization method the five groups of surveyed patients were formed (see below). Each group was divided into two subgroups depending on the total modified menopausal index level: subgroup 1 — patients with mild climacteric syndrome (CS), subgroup 2 — patients with moderate severity CS. Index group (A) — 60 women, who used the «A» treatment complex; first experimental group (B) — 59 women, who used the «B» complex; second experimental group (C) — 66 women,

who used the «C» complex; third experimental group (D) — 70 women, who used the «D» complex; control group (E) — 75 women, who used the «E» complex (Table 1). At the stage of assessment of endocrine profile in dynamics, it was expedient to divide the subgroups into subsubgroups according to the period of the woman's life: perimenopausal period (P) and postmenopause (M).

The groups had no statistically significant differences in age, social status, level of education, region of residence, genital and extragenital pathology spectrum.

Inclusion criteria: 45–50 year old women (average age  $47.2 \pm 3.2$  years) in the perimenopausal period or early natural postmenopause (up to two years); the presence of the original MS, diagnosed according to the recommendations of experts of the Russian Scientific Society of Cardiologists on diagnosis and treatment of metabolic syndrome (second revision, 2009); duration of MS from two to five years; the presence of CS of mild or moderate severity, typical complicated form (against the MS background); no menopausal hormone therapy in the personal medical history; no thyroid gland dysfunction initially.

Non-inclusion criteria: the presence of gross mental disorders, alcohol and drug addiction, acute diseases of the cardiovascular system, acute inflammatory diseases, hemorrhage and liability to it, malignant or unverified neoplasms, tumors in growth stage or in a condition requiring surgical treatment; signs of severe organ failure; presence of original thyroid dysfunction according to hormonal tests; presence of 3rd degree intestinal dysbacteriosis; diabetes mellitus presence; vaginitis presence.

Exclusion criteria: individual intolerance to physical factors; individual intolerance to the components of the vitamin and mineral preparations. There were no such patients.

Basic treatment was used in all groups. It included the normalization of lifestyle and sleep, nutritional treatment, increased physical activity. The patients controlled the components of the treatment themselves. Principles of treatment: personalized approach, consisting in the individual calculation of the basal metabolism, physical exercises in the comfort zone for each patient, temperature conditions also in the comfort zone for the patients, carrying out of antihypertensive therapy for hypertension; nutritional therapy during the entire observation time; lifestyle correction (all study participants were motivated to quit smoking). In the index

**Table 1.** The number of patients and the applied methods of treatment in groups

		Index group (A), <i>n</i> = 60		First experimental group (B), <i>n</i> = 59		Second experimental group (C), <i>n</i> = 66		Third experimental group (D), <i>n</i> = 70		Control group (E), <i>n</i> = 75	
Subgroup 1 population	P	32	17	30	17	34	18	36	19	38	20
	M		15		13		16		17		18
Subgroup 2 population	P	28	13	29	15	32	17	34	18	37	20
	M		15		14		15		16		17
Applied methods		Complex «A»		Complex «B»		Complex «C»		Complex «D»		Complex «E»	
		Basic treatment		Basic treatment		Basic treatment		Basic treatment		Basic treatment	
		Exercise therapy		Exercise therapy		Exercise therapy		Exercise therapy		–	
		Drinking balneotherapy		Drinking balneotherapy		Drinking balneotherapy		Drinking balneotherapy		–	
		Additional oral use of multivitamin and mineral preparation		Additional oral use of multivitamin and mineral preparation		Additional oral use of multivitamin and mineral preparation		Additional oral use of multivitamin and mineral preparation		–	
		vibrotherapy, full-spectrum and selective chromotherapy, music therapy, aromatherapy, aeroionotherapy		vibrotherapy, – – – music therapy, aromatherapy, aeroionotherapy		– full-spectrum and selective chromotherapy, music therapy, aromatherapy, aeroionotherapy		–		–	

group there were 12 smokers (20.0%), in the first experimental group 11 smokers (18.6%), in the second experimental group 14 smokers (21.2%), in the third experimental group 14 smokers (20.0%), in the control group 16 smokers (21.3%). Of them 6 women (10.0%) from the index group, 5 women (8.5%) from the first experimental group, 6 women (9.1%) from the second experimental group, 7 women (10.0%) from the third experimental group and 7 women (9.3%) from the control group smoked more than 10 cigarettes a day. These patients either quit smoking or reduced the number of cigarettes smoked per day to five. There were no patients among those who constantly took antihypertensive drugs before being included in the study. When a cardiologist diagnosed arterial hypertension during the study period, patients received standard antihypertensive therapy — moxonidine (Physiotens) 200 µg orally 1 time a day (Order of the Ministry of Health of the Russian Federation dated November 9, 2012, № 708H «On approval of the standard of primary health care for primary arterial hypertension (hypertensive disease)»). Antihypertensive therapy in the index group was received by 11 (34.4%) patients from A1 subgroup and 13 (46.4%) patients from A2 subgroup; in the first experimental group — 11 (36.7%) patients from B1 subgroup and 14 (48.3%) patients from B2 subgroup; in the second experimental group — 12 (35.3%) patients from C1 subgroup and 15 (46.9%) patients from C2 subgroup; in the third experimental group — 13 (36.1%) patients from D1 subgroup and 16 (47.1%) patients from D2 subgroup; in the control group — 14 (36.8%) patients from E1 subgroup and 17 (46.0%) patients from E2 subgroup. Of these, in the index group during the observation period only for one patient (3.6%) of the A2 subgroup there was a need to double the daily dose of moxonidine (from 200 to 400 µg), in the second subgroups of the first, second and third experimental groups there were 2 (6.9%), 3 (9.4%) and 3 (8.8%) such patients respectively. In the control group in E2 subgroup, it was necessary to increase the dose of moxonidine for 4 (10.8%) patients, and for one of them up to 600 µg per day.

### Basic treatment

Basic treatment was performed during the whole observation period. *Nutritional treatment.* To calculate the individual daily caloric need, the basal metabolic rate was calculated using the formula recommended by WHO:  $BM = (0,0342 \cdot M + 3,5377) \cdot 240$ , where BM was basal metabolism value (kcal), M was body mass (kg). Then determined the total energy consumption, adjusted for the coefficient of physical activity:  $E = F \cdot BM$ , where E was total energy consumption (kcal), F was correction factor (1,1 — low, 1,3 — moderate, 1,5 — high activity), BM was basal metabolism value (kcal). For a gradual decrease in body weight, a diet with a lower energy value was taken, subtracting 600 kcal from the total energy consumption value. Split meals were recommended, 5–6 times per day, taking small portions at the same time. The diet included foods containing complex carbohydrates (cereals, fruit, vegetables), rich in dietary fiber; the use of simple carbohydrates, saturated fats, salt (up to 3 g per day) was limited, coffee and alcohol were not allowed. *Physical activity* was recommended considering the state of health and tolerance. Daily walking in the fresh air for 30 minutes was offered. In addition to quitting smoking, all patients were motivated to keep up the work-rest regime.

### Exercise therapy

Was used during the entire observation time. A daily morning hygienic gymnastics (10–15 min) was conducted in the form

of a set of exercises aimed to improve the overall tone of the cardiovascular system and to remove muscle hypertonia, as well as daily training of the pelvic floor muscles (Kegel Exercises), focused on strengthening the periureteral and perivaginal muscles, the anal sphincter, the increase in the functional volume of the bladder without the participation of the abdominal, gluteal and femoral muscles [16].

### Drinking balneotherapy

A balneotherapy course was performed from the very beginning of the study, repeated after three months. The duration of each course was four weeks. The ingestion of Essentuki No. 4 mineral water in a volume of 180–300 ml (3 ml per 1 kg of body weight) at room temperature 30 minutes before main meals (3 times a day) was prescribed.

### Additional oral use of multivitamin and mineral preparation

The oral intake of vitamin and mineral preparation was prescribed: 22 balanced components, including iodine in the form of potassium iodide in the amount of 225 µg (Menopace®, registration number № П N015844/01; Vitabiotics Ltd; UK) and calcium carbonate with colecalciferol (D3 vitamin) (Calcium-D3 Nycomed, registration number № П N013478/01; Nycomed Pharma; Norway). Menopace® was taken daily in 1 capsule with or after a meal. The treatment course duration was six months. Calcium-D3 Nycomed, containing 1250 mg of calcium carbonate (equivalent to 500 mg of elemental calcium) and 5 µg (200 IU) of colecalciferol (D3 vitamin) was taken orally 1 tablet twice a day for one month, the course was repeated after three months.

### Physical therapy

For the complex health effects the multifactor physical therapy unit Spectra Color SPA System (Sybaritic Inc., USA, registration certificate of the Ministry of Health of the Russian Federation № 97/532 dated May 22, 1997) was used. When combining physical factors and procedures, their compatibility was taken into account in accordance with the Annex to «The list of necessary medical services and procedures available in specialized sanatoriums to the patient according to the profile of his disease. Methodical instructions» (approved by the Ministry of Health of the Russian Federation on December 22, 1999, № 99/229). The exact dosage of each influencing factor according to the degree of intensity and time of exposure was carried out. *General vibrotherapy* was carried out for 15 minutes: with the help of multipoint vibration transmitters mounted in the capsule bed, the effect of a manual massage was created, providing anesthetic and relaxing effect, as well as contributing to the rapid removal of fatigue and restoration of muscle performance. A vibration mode with a varying frequency from 10 to 60 Hz and an increasing amplitude up to 7 mm was used, the vibration frequency increased during 8–10 s. *Full-spectrum chromotherapy* was carried out for 30 minutes, using wavelength from 760 to 400 nm. *Selective chromotherapy* was applied (the green light was used for 30 minutes, wavelength 530 nm). Through a stereo sound system with a CD player, passive (receptive) musical therapy was carried out using relaxing melodies for 30 minutes. Aromatherapy oils were sprayed through the four-channel system inside the capsule for aromatherapy: lavender (*Lavandula officinalis*) and common fennel (*Foeniculum vulgare*). *Aeroionotherapy* (cooling the face with ionized cool air with a predominance of negative

ions) was applied for 30 minutes. Sessions in the conditions of the Spectra Color SPA System physical therapy unit were performed twice a week for 30 minutes, the course consisted of 10 sessions. The course was repeated after three months. A total of 20 procedures were performed during the observation.

### Measurement methods

Assessment of the severity of climacteric disorders was performed using the modified menopausal Kupperman index (version by Uvarova EV, 1983) [17]. Using the automated IFA processor NEXgen (Adaltis S.r.l.; Italy) and the hormone diagnostic reagents (Alkor Bio; Russia) the serum levels of thyroid stimulating hormone (TSH) (reference values: 0.23–3.4  $\mu\text{IU/ml}$ ) and free thyroxine (free T4) (reference values: 9.5–22.6  $\text{mmol/l}$ ) were determined. Ultrasound examination of the thyroid gland was performed on the expert class multifunctional system MyLab 70 (Esaote; Italy) using the 4–13 MHz linear sensor with color flow mapping. When performing the sonography of the thyroid gland the size and structure of the gland was assessed, as well as the presence, size and type of blood flow of the nodules.

### Methods of statistical data analysis

Sample size was not previously calculated. Statistical analysis of the research results was carried out using a standard software package STATISTICA® for Windows 6.0 (StatSoft Inc; USA). Quantitative indicators are presented as the number of cases ( $n$ ) and the average error of the arithmetic mean ( $m$ ). The significance of differences in the mean values was determined by Student's  $t$ -test. For comparison of relative indicators characterizing the frequency of a particular characteristic the non-parametric method according to the Pearson  $\chi^2$  criterion was used. Differences were considered statistically significant when  $p < 0.05$ .

## RESULTS

Structural changes on the part of the thyroid gland, according to sonography, were more common in women with moderately severe CS than in women with mild CS: 105 (65.7%) and 90 (52.9%) women respectively ( $p < 0.05$ ). The structure of the deviations according to the thyroid sonography data of the examined patients is reflected in Table. 2.

After six months of observation, according to the sonography data, two patients of the E2-M subgroup (control group) were first diagnosed with nodules. In the remaining groups, the number of patients with structural changes in the thyroid gland according to the sonography data remained unchanged.

In most patients initially the thyroid gland had normal size. Sonographic monitoring was performed after six months of treatment. The Table. 3 presents the average values of the

volume of the gland in the subgroups of examined patients in the dynamics, before treatment and after six months of therapy. It should be noted that in patients with moderately severe CS the volume of the thyroid gland was significantly higher than in patients with mild CS. After six months of therapy, the average volume of the thyroid gland significantly decreased in patients with mild CS in subgroups A1, B1 and C1 — by 11.3%, 7.2% and 7.6% respectively ( $p < 0.05$  compared with pre-treatment rates;  $p > 0.05$  when comparing rates between subgroups). Among patients with moderate-severity CS, a significant decrease in the average thyroid volume was found only in A2 subgroup — by 10.7 % ( $p < 0.05$ ). In subgroups 2 of all three experimental groups, a slight decrease in thyroid volume was noted, but it was not reliable. The tendency for this indicator to increase in the E1 and E2 subgroups of the control group attracted attention, but the changes were not statistically significant ( $p > 0.05$ ).

By the time of the beginning of the study, patients of all groups had no abnormal thyroid function — the mean values of free T4, TSH were within the reference intervals, however, in participants of the study with moderately severe CS the free T4 level was lower, and the TSH level was higher than the corresponding indicators of patients with mild CS. In addition, it was noted that in patients in the period of early postmenopause, the level of free T4 was lower, and the level of TSH was higher in comparison with patients in the perimenopausal period ( $p < 0.05$ ). After six months of treatment, the average values of TSH and free T4 in all subgroups corresponded to the euthyroid state. However, after six months of therapy, subclinical hypothyroidism was detected in one (6.3%) patient of the D2-M subgroup, and in the control group the greatest increase in the frequency of hypothyroidism was demonstrated — it was observed in 2 (11.1%) patients of the E1-M subgroup, in 3 (16.7%) patients of the E2-P subgroup and in 4 (23.5%) patients of the E2-M subgroup.

The dynamics of changes of the levels of TSH and free T4 in the groups of surveyed patients is presented in Table. 4. After six months of therapy in all subgroups of the index group the level of TSH decreased significantly — in A1-P by 10.0%, in A2-P — by 6.5%, in A1-M — by 7.3%, in A2-M — by 5.6% ( $p < 0.05$ ), and the level of free T4 increased by 8.1%, 6.5%, 7.7%, 6.6% respectively ( $p < 0.05$ ). Patients in the perimenopausal period with mild CS from the first and second experimental groups also demonstrated a significant decrease in TSH and the increase in free T4: in subgroup B1-P, the level of TSH decreased by 5.1%, in subgroup C1-P by 8.8%, and the level of free T4 increased by 6.5% and 7.1% respectively ( $p < 0.05$ ). It should be noted that there were no statistically significant differences between the subgroups A1-P, B1-P and C1-P. In other subgroups of the experimental groups, there was a slight decrease in the level of TSH and an increase in the level of free T4, however, changes of characteristics relative to baseline were not reliable. In all subgroups of the control group, there was a decrease in the level of free T4 and an increase in

**Table 2.** Structural changes of the thyroid gland in the groups of surveyed patients according to the results of ultrasound investigation

Nature of change	Index group, $n = 36$ , abs (%)		First experimental group, $n = 34$ , abs (%)		Second experimental group, $n = 39$ , abs (%)		Third experimental group, $n = 41$ , abs (%)		Control group, $n = 45$ , abs (%)	
	A1, $n = 17$	A2, $n = 19$	B1, $n = 16$	B2, $n = 18$	C1, $n = 18$	C2, $n = 21$	D1, $n = 18$	D2, $n = 23$	E1, $n = 21$	E2, $n = 24$
Diffuse changes	5 (29.4)	5 (26.3)	5 (31.3)	6 (33.3)	6 (33.3)	7 (33.3)	6 (33.3)	8 (34.8)	7 (33.3)	8 (33.3)
Palpable abnormalities	6 (35.3)	7 (36.8)	5 (31.3)	6 (33.3)	5 (27.8)	6 (28.6)	6 (33.3)	7 (30.4)	6 (28.6)	7 (29.2)
Overlapping changes	6 (35.3)	7 (36.8)	6 (37.5)	6 (33.3)	7 (38.9)	8 (38.1)	6 (33.3)	8 (34.8)	8 (38.1)	9 (37.5)



the level of TSH, and in the subgroups E2-P, E1-M and E2-M, the changes were statistically significant: Accordingly, the level of TSH increased by 5.5%, 5.6% and 6.3%, and the free T4 level regressed by 4.4%, 5.1% and 7.8% ( $p < 0.05$ ), which indicated a decrease in thyroid function.

## DISCUSSION

We found a high frequency of structural changes in the thyroid gland according to the results of ultrasound investigation in women with MS; in women with a moderately severe CS, sonographic abnormalities in the structure of the thyroid were more common than in women with a mild CS. According to literature data, in peri- and postmenopausal women, the thyroid diseases increase by 2–2.5 times [18]. A higher incidence of thyroid diseases in patients with MS compared with persons not suffering from MS was indicated [19, 20]. Our results

suggest a decrease in thyroid function in women with ageing, which is consistent with literature data [21].

Therapeutic programs were formed taking into account the mechanism of action of each applied factor and the pathogenesis of disorders characteristic for CS and MS. The programs were based on diet and normalization of lifestyle, which corresponds to the recommendations of experts from Russian Scientific Society of Cardiologists on diagnosis and treatment of metabolic syndrome (2009) [22], as well as recommendations of Russian Society of Obstetricians and Gynecologists for the management of women in menopause (2016) [23].

The use of drinking mineral waters is justified by their stimulating effect on metabolism by improving functional interactions in the entero insular system, increasing the sensitivity of tissues to insulin, enhancing the utilization of glucose by the liver, activating antioxidant defence enzymes.

**Table 3.** The average volume of the thyroid gland in the groups of surveyed patients ( $M \pm m$ , ml)

Control point	Index group, $n = 60$		First experimental group, $n = 59$		Second experimental group, $n = 66$		Third experimental group, $n = 70$		Control group, $n = 75$	
	A1, $n = 32$	A2, $n = 28$	B1, $n = 30$	B2, $n = 29$	C1, $n = 34$	C2, $n = 32$	D1, $n = 36$	D2, $n = 34$	E1, $n = 38$	E2, $n = 37$
Before treatment	16.69 $\pm$ 0.44	18.07 $\pm$ 0.50°	16.17 $\pm$ 0.42	18.14 $\pm$ 0.54°	16.26 $\pm$ 0.33	18.25 $\pm$ 0.54°	16.22 $\pm$ 0.29	18.21 $\pm$ 0.55°	16.29 $\pm$ 0.27	18.22 $\pm$ 0.51°
After six months of treatment	14.81 $\pm$ 0.32#	16.14 $\pm$ 0.35#	15.0 $\pm$ 0.36#	17.79 $\pm$ 0.35°*	15.03 $\pm$ 0.28#	17.63 $\pm$ 0.28°*	15.78 $\pm$ 0.27*	17.85 $\pm$ 0.24°*	16.61 $\pm$ 0.34*	18.71 $\pm$ 0.28°*

**Note:** \* —  $p < 0.05$  compared with the index group rates; # —  $p < 0.05$  compared with pre-treatment rates; ° —  $p < 0.05$  when comparing rates between subgroups 1 and 2.

**Table 4.** The results of hormonal studies in the groups of surveyed patients ( $M \pm m$ )

Subgroup	TSH, $\mu\text{IU/l}$ (0.23–3.4 $\mu\text{ME/ml}$ )		Free T4, $\text{pmol/l}$ (9.5–22.6 $\text{mmol/l}$ )	
	Before treatment	After six months of treatment	Before treatment	After six months of treatment
Index group, $n = 60$				
A1-P, $n = 17$	2.61 $\pm$ 0.06	2.35 $\pm$ 0.05#	13.81 $\pm$ 0.35	14.93 $\pm$ 0.34#
A2-P, $n = 13$	2.76 $\pm$ 0.05°	2.58 $\pm$ 0.03#°*	12.59 $\pm$ 0.36°	13.41 $\pm$ 0.30#°
A1-M, $n = 15$	2.87 $\pm$ 0.04	2.66 $\pm$ 0.03#	12.36 $\pm$ 0.18	13.31 $\pm$ 0.15#
A2-M, $n = 15$	3.04 $\pm$ 0.04°	2.87 $\pm$ 0.03#°*	11.83 $\pm$ 0.16°	12.61 $\pm$ 0.14#°
First experimental group, $n = 59$				
B1-P, $n = 17$	2.55 $\pm$ 0.05	2.42 $\pm$ 0.04#	13.83 $\pm$ 0.31	14.73 $\pm$ 0.38#
B2-P, $n = 15$	2.78 $\pm$ 0.07°	2.69 $\pm$ 0.03°*	12.61 $\pm$ 0.28°	13.03 $\pm$ 0.20°*
B1-M, $n = 13$	2.90 $\pm$ 0.04	2.75 $\pm$ 0.4#	12.28 $\pm$ 0.17	13.11 $\pm$ 0.13#
B2-M, $n = 14$	3.01 $\pm$ 0.04°	2.90 $\pm$ 0.04°*	11.87 $\pm$ 0.11°	12.2 $\pm$ 0.09°*
Second experimental group, $n = 66$				
C1-P, $n = 18$	2.61 $\pm$ 0.02	2.38 $\pm$ 0.03#	13.88 $\pm$ 0.20	14.86 $\pm$ 0.20#
C2-P, $n = 17$	2.76 $\pm$ 0.05°	2.71 $\pm$ 0.03°*	12.68 $\pm$ 0.19°	12.86 $\pm$ 0.16°*
C1-M, $n = 16$	2.85 $\pm$ 0.02	2.73 $\pm$ 0.02#	12.34 $\pm$ 0.11	13.19 $\pm$ 0.07#
C2-M, $n = 15$	3.03 $\pm$ 0.02°	2.96 $\pm$ 0.03°*	11.88 $\pm$ 0.11°	12.13 $\pm$ 0.09°*
Third experimental group, $n = 70$				
D1-P, $n = 19$	2.64 $\pm$ 0.02	2.51 $\pm$ 0.03°*	13.75 $\pm$ 0.18	14.01 $\pm$ 0.16*
D2-P, $n = 18$	2.77 $\pm$ 0.06°	2.75 $\pm$ 0.03°*	12.69 $\pm$ 0.16°	12.8 $\pm$ 0.15°*
D1-M, $n = 17$	2.86 $\pm$ 0.02	2.77 $\pm$ 0.02°*	12.36 $\pm$ 0.10	12.48 $\pm$ 0.08*
D2-M, $n = 16$	3.01 $\pm$ 0.02°	2.99 $\pm$ 0.05°*	11.99 $\pm$ 0.10°	12.11 $\pm$ 0.17°*
Control group, $n = 75$				
E1-P, $n = 20$	2.62 $\pm$ 0.02	2.64 $\pm$ 0.03*	13.72 $\pm$ 0.22	13.52 $\pm$ 0.23*
E2-P, $n = 20$	2.74 $\pm$ 0.05°	2.89 $\pm$ 0.06#°*	12.63 $\pm$ 0.17°	12.07 $\pm$ 0.33#°*
E1-M, $n = 18$	2.86 $\pm$ 0.02	3.02 $\pm$ 0.07°*	12.36 $\pm$ 0.09	11.73 $\pm$ 0.24#*
E2-M, $n = 17$	3.01 $\pm$ 0.02°	3.20 $\pm$ 0.07#°*	11.91 $\pm$ 0.10°	10.98 $\pm$ 0.28#°*

**Note:** \* —  $p < 0.05$  compared with the index group rates; # —  $p < 0.05$  compared with pre-treatment rates; ° —  $p < 0.05$  when comparing rates between subgroups 1 and 2.

Drinking balneotherapy is pathogenetically justified in patients with MS and CS. It has been shown that its use in comprehensive rehabilitation programs for combined pathology in MS patients normalizes the carbohydrate and lipid metabolism [24].

The need for taking vitamins is determined by their performance as biocatalysts and antioxidants. Vitamins are involved in the formation of hormones, have the ability to change the sensitivity of the receptors to them, thereby contributing to the normal functioning of the endocrine, nervous, cardiovascular systems of the woman's body [25]. The importance of adequate daily iodine intake can hardly be overestimated. Iodine is necessary for the synthesis of triiodothyronine and thyroxine, which affect all types of metabolism, regulate the balance of reproductive sex hormones [26]. The feasibility of iodine prophylaxis in mature women is also indicated in the literature [27].

The use of low-frequency vibrotherapy is based on its ability to reduce vascular tone, improve microcirculation, tissue trophism due to stimulation of skin mechanoreceptors, primary endings of muscle spindles, and effects on the autonomic nervous system [28]. The use of full-spectrum and selective (green light) chromotherapy is based on their ability to coordinate the activities of the hypothalamic-pituitary system and the endocrine glands due to the effect on melatonin production by affecting the visual analyzer, the extraocular photoneuroendocrine system and the skin [29]. Musical therapy was included in the treatment complex due to the presence of a sedative effect, realized due to the rhythmic effect of melodies on various brain regions. It is shown that it increases the effectiveness of complex therapy for patients with cardiovascular pathology [30]. The use of aromatherapy is based on its ability to regulate the functioning of the endocrine system, to reduce the effects of psycho-emotional stress through the effects on the olfactory sensory system [31]. Aeroionotherapy was included in the program, taking into account the biological effects of negative aeroions

realized by reflex, such as stabilization of the processes of vegetative regulation, beneficial effects on the cardiovascular and endocrine systems.

Thus, in our study, complex programs, including physical therapy effects — A, B and C complexes, were required to preserve the structure and maintain the normal function of the thyroid gland in patients with CS and MS. For patients with moderately severe CS to maintain the functioning of the pituitary-thyroid system, the need for a combined use of the whole range of physical therapy factors (vibrotherapy, chromotherapy, music therapy, aromatherapy, aeroionotherapy — A complex) has been identified. It was found that the standard approach does not reduce the incidence of thyroid diseases.

We explain the positive effect on the thyroid status of the applied programs by a decrease in the load on the thyroid gland as a result of the regression of body mass [32], prophylactic effect of iodine-containing vitamin and mineral preparations, improvement of microcirculation as a cumulative effect of preformed physical factors (vibrotherapy, chromotherapy, music therapy, aeroionotherapy, aromatherapy), which increases with their simultaneous use, that is especially significant for patients with moderately severe CS.

## CONCLUSIONS

The use of complex programs, including physical therapy effects, has a protective effect on the thyroid status in patients with CS and MS. For patients with moderate-severity CS, the programs with simultaneous use of vibrotherapy, chromotherapy, music therapy, aromatherapy, aeroionotherapy have priority.

The developed complex non-drug treatment technology can be applied in practical healthcare in inpatient, outpatient, sanatorium and resort conditions, in the centers of restorative medicine and rehabilitation.

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