

The analysis of the disturbances in a morphological structure and a hormonal function of thyroid gland in women in perimenopausal period

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Abstract

It has been found out that there is a similarity between the symptoms of hyperthyroidism and perimenopausal period. The similarity between the symptoms of ovarian function suppression and excessive thyrocytes activity significantly prolongs the time of making proper diagnosis in women in perimenopausal period. The aim of this study was to evaluate the relation between the morphological structure of thyroid gland and the frequency of hyperthyroidism during the perimenopausal period. The comparison of thyroid hormonal disturbances was made in two groups of women in perimenopausal period: those suffering from nodular goiter and those with immunological Graves-Basedow disease. The analysis of the group of 146 women in age 46-54 in perimenopausal period was made. All of the patients have visited endocrinologist for 10 years. Our studies points to a high percentage of activation of thyroid gland during the perimenopausal period. The women with the neutral nodular goiter are particularly predisposed to hyperthyroidism during the perimenopausal period.

Graves- Basedow disease in the past with a long period of remission was a rare reason of the resume of hyperthyroidism in a menopausal period. The most frequent morphological changes, which caused the hyperthyroidism, were hot nodules and warm nodules-single and coexisting with cold nodules. In ten years time of observation, the morphological changes in scintigraphy were observed. The most frequent form of changes was the development of hot and warm nodules on the basis of warm, cold and cool areas. The patients during perimenopausal period should be very well diagnosed because of the similarity of the symptoms in hyperthyroidism and menopausal period.

Keywords: hyperthyroidism, perimenopausal period, Graves- Basedow disease

Introduction

It has been found out that there is a striking similarity between the symptoms of hyperthyroidism and perimenopausal period. Among them are heart problems, mood swings, increased sweating, hot flashes, irregular periods, and sleeplessness.

Not infrequently, it is very difficult to find the real reason of a patient's complaint on the basis of the medical interview and the physical examination. The similarity between the symptoms of ovarian function suppression and excessive thyrocytes activity significantly prolongs the time of making proper diagnosis in women in perimenopausal period. In order to find the answer to this problem, a group of women in perimenopausal period were examined in this clinical study.

Nodular goiter and Graves- Basedow disease are the most frequent pathologies of thyroid gland. In both diseases, the symptoms are caused by high level of thyroxine and triiodothyronin in the patient's blood.

The aim of this study was to evaluate the relation between the morphological structure of thyroid gland and the frequency of hyperthyroidism during the perime-

nopausal period. The comparison of thyroid hormonal disturbances was made in two groups of women in perimenopausal period: those suffering from nodular goiter and those with immunological Graves- Basedow disease.

Materials and methods

The analysis of the group of 146 women in age 46-54 in perimenopausal period was made. All of the patients have visited endocrinologist for 10 years.

The observation was made in a group of 120 patients in euthyrosis with neutral nodular goiter and a group of 26 patients suffering from Graves- Basedow disease (in remission).

The patients were divided into several groups: the group I with multinodular goiter, IA with cold and cool nodules (n=14), IB with warm and cold nodules (n=47), IC with warm nodules (n=16). The second group of patients with single nodule contains the group IIA with cold nodule (n=19), IIB with warm nodule (n=21) and IIC with hot nodule (n=3).

The patients with low level of TSH and normal level of fT4 and fT3 in blood tests were diagnosed as the pa-

tients suffered from subclinical hyperthyroidism.

Clinical hyperthyroidism was diagnosed in women who had low level of TSH and high level of fT4 and/or fT3 in blood tests.

If the level of the hormones was proper, the nodular changes were observed and the clinical symptoms of hyperthyroidism were absent, the neutral nodular goiter was diagnosed.

The comparative analysis of scintigraphy was made in these patients at the beginning of the treatment and ten years later.

Graves-Basedow disease was diagnosed in patients who had the symptoms of hyperthyroidism in the past (clinical symptoms and the levels of thyroid hormones were considered), exophthalmic goiter, exophthalmos. The results of ultrasound examination, scintigraphy of thyroid gland, and the level of TSI antibodies were also used in the process of making diagnosis.

The level of FSH, TSH, fT4, fT3 in blood were measured by automatic, quantity immunoenzymatic test in VIDAS system. The sets of BioMerieux Company were used.

The level of TSI antibodies in blood was measured by radioreceptor RRA test (BRAHMS).

The 10 MHz sonde was used in ultrasonography of thyroid glands in patients.

In scintigraphy examination, the technetium isotope (^{99m}Tc) was used.

Fine needle aspiration biopsy (FNAB) of thyroid glands under USG guidance was done on all thyroid nodules. Then thin smears on a glass slides, fixed with Cytofix were done. The preparations were stained with hematoxylin and eosin.

The patients were divided into several groups:

The results were analyzed in statistic software SPSS PL v. 12.

As critical significance level of tested differences $P_{\alpha} = 0,05$ was accepted. The statistical values $P < P_{\alpha}$ were considered as statistically significant.

Results

A group of 146 patients was analyzed. Among them 52.7% of women suffered from multinodular goiter, 29.5% had single nodule and 17.8% suffered from Graves-Basedow disease.

The diagnosis of nodular goiter was made for 120 patients. In this group 64.2% of women had multinodular goiter and 35.8% had single nodule. The majority of size of the first group above the second was statistically significant [Figure 1].

Among 120 patients with nodular goiter, about 54.2% had symptoms of hyperthyroidism. Comparatively in a group of 26 women suffering from Graves-Basedow disease only in 2 patients the symptoms of hyperthyroid-

ism appeared. The difference between these two groups of patients was statistically significant [Figure 2].

Fig. 1. The structure of the group of patients suffered from nodular goiter

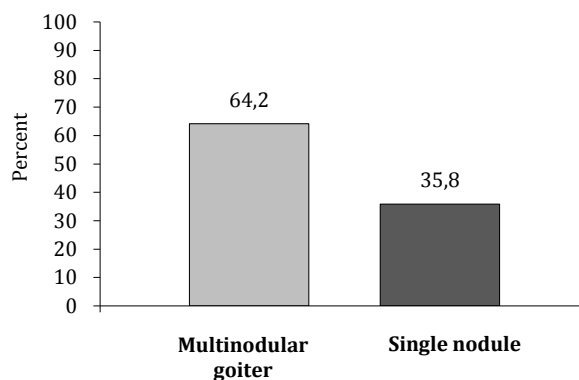


Fig. 2. Hyperthyroidism in patients suffered from Graves-Basedow disease or nodular goiter

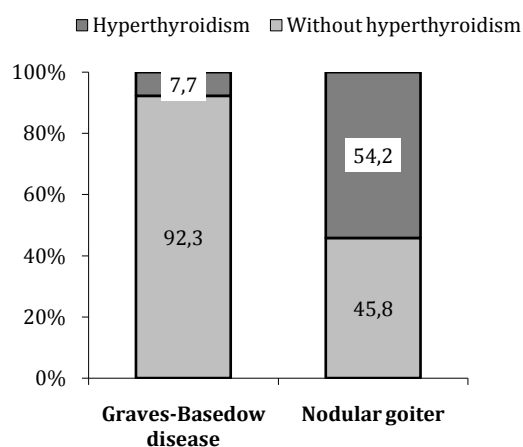
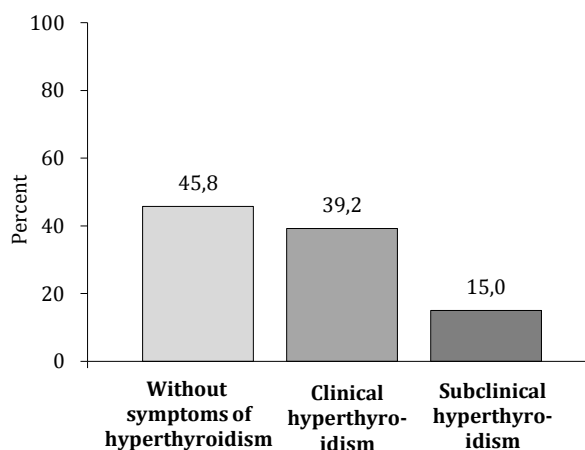


Figure 3. Hormonal activity of thyroid gland in patients suffered from nodular goiter



Among 120 patients with diagnosis of nodular goiter the clinical symptoms did not appear in 45.8% of them. The clinical hyperthyroidism was diagnosed in 39.2% and subclinical hyperthyroidism in 15.0% of patients [Figure 3].

The statistical analysis of incidence of clinical hyperthyroidism symptoms compared to subclinical hyperthyroidism was done in a group of 65 patients with nodular goiter, who had the symptoms of hyperthyroidism. In this group,

the clinical hyperthyroidism was diagnosed in 72.3% of women with nodular goiter and the subclinical hyperthyroidism appeared only in 27.7% of examined patients (the difference was statistically very significant).

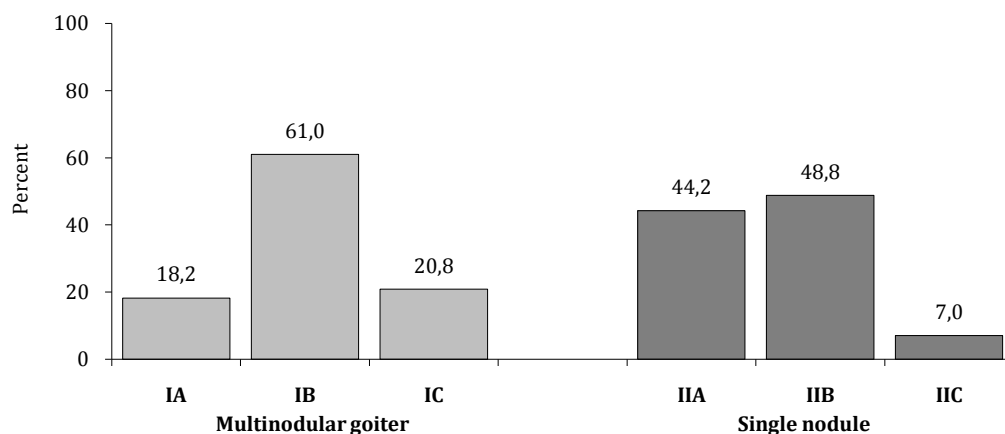
Table 1. The results of hormone levels tests (TSH, fT4, fT3, FSH) in a group of patients with nodular goiter

	TSH mU/ml	fT4 pmol/l	fT3 pmol/l	FSH mIU/ml
Group with nodular goiter without hyperthyroidism	0.9–4.2	10.3–18.2	4–7.6	30–84
Group with nodular goiter with hyperthyroidism	0.01–0.15	21–28	6–11	32–92
Group with nodular goiter with subclinical hyperthyroidism	0.01–0.05	15.2–19.1	4.8–7.2	37–90

Table 2. The results of hormone level tests (TSH, fT4, fT3, FSH) and antibodies TSI in a group of patients with Graves-Basedow disease

	TSH mU/ml	fT4 pmol/l	fT3 pmol/l	FSH mIU/ml	TSI IU/l
Group with Graves Basedow disease without hyperthyroidism	1.1–3.8	9.5–16	4.5–7	41–75	0.3–0.7
Group with Graves Basedow disease with hyperthyroidism	0.01–0.1	22–31	6.8–8.1	42–90	2.5–9

Fig.4. The structure of morphological changes of the thyroid glands in scintigraphy examination in patients with a multinodular goiter and a single nodule



Among 77 patients with multinodular goiter, particular types of nodules appeared with diversified frequency. The most frequent types were IB- cold and warm nodules, which were diagnosed in 61% of women. The type IC-warm nodules (20.8%) and the type IA-cold and cool nodules (18.2%) were diagnosed rarely. In a group of 43 examined patients diagnosed with single nodule, particular types of nodules appeared with uneven frequency. The type IIB-warm nodule was diagnosed in 48.8% of patients. The nodule type IIA-cold was diagnosed in 44.2% of women and the nodule type IIC-hot was observed only in 7% of patients [Figure 4].

The results of a comparative analysis of a thyroid gland scintigraphy examination in patients with nodular goiter over ten years.

The results of scintigraphy examination in ten years time in patients with nodular goiter show that in 24.17% of women (29 results, out of 120 examined patients) the image of isotope detection changed. In the same group,

the morphological changes of some warm nodules (the group IIB) into hot nodules (the group IIC) were observed. The change of cold and cool nodules (the group IA) and single cold nodule (the group IIA) into warm and cold (the group IB) and warm (the group IC) was too observed [Table 3].

The results show the fact, that in 25% of patients in a group of nodular goiter, after ten years of observations, the changes of isotope detection image appeared. This fact indicates the morphological changes in some warm nodules into hot nodules and a group of cold and cool into warm and cold nodules.

The results indicate the increased activity of thyroid gland. This situation can predispose to a hyperactive goiter. The cold areas in a gland present the elements of degeneration and the reverse changes such as cysts, fibromatosis and calcification. It is a common morphological image in a long-term goiter.

Table 3. The structure of morphological changes of the thyroid gland in a group of patients with multinodular and single nodule, who had symptoms of hyperthyroidism and without these symptoms

Group		Patients with hyperthyroidism symptoms			Patients without hyperthyroidism symptoms			Altogether		
		n	%w	%k	n	%w	%k	n	%w	%k
	IA cold and cool nodules	6	42.9	13.0	8	57.1	25.8	14	100.0	18.2
	IB cold and warm nodules	26	55.3	56.5	21	44.7	67.7	47	100.0	61.0
	IC warm nodules ^c	14	87.5	30.4	2	12.5	6.5	16	100.0	20.8
Altogether multinodular goiter		46	59.7	100.0	31	40.3	100.0	77	100.0	100.0
	IIA cold nodule	5	26.3	26.3	14	73.7	58.3	19	100.0	44.2
	IIB warm nodule	11	52.4	57.9	10	47.6	41.7	21	100.0	48.8
	IIC hot nodule	3	100.0	15.8	–	–	–	3	100.0	7.0
Altogether single nodule ^c		19	44.2	100.0	24	55.8	100.0	43	100.0	100.0

%w — the percentage participation in a line, %k — the percentage participation in a column

Table 4. The structure of morphological changes of the thyroid gland in scintigraphy examination in patients with multinodular goiter and single nodule

Group	Type of nodule	n	%
	IA cold and cool nodules	14	18.2
	IB cold and warm nodules	47	61.0
	IC warm nodules	16	20.8
Altogether multinodular goiter		77	100.0
	IIA cold nodule	19	44.2
	IIB warm nodule	21	48.8
	IIC hot nodule	3	7.0
Altogether single nodule		43	100.0

Table 5. The comparison of scintigraphy examination results in particular groups in ten years time

Group	Scintigraphy I	Scintigraphy II
IA	29	14
IB	38	47
IC	15	16
IIA	20	19
IIB	18	21
IIC	–	3

The most frequent type of nodule in a group of patients with a single nodule was warm or cold nodule. Only three women had hot nodule diagnosed. The autonomic activity of hot nodules was always the cause hyperthyroidism. All of the patients examined in this research diagnosed with hot nodules had symptoms of hyperthyroidism.

It was observed that in the first results of scintigraphy, the patients did not have hot nodules and a thyroid parenchyma was activated after ten years of observation in patients with nodular goiter.

Discussion

The observation of natural history of nodular goiter shows that there is a strong mechanism stimulating a thyroid gland during the menopausal period which causes morphological changes of the gland.

Many authors emphasize the role of antagonism between estrogens and thyroid hormones[1]. In contrast to thyroid hormones, estrogens block tissue oxidation. As a

result, estrogens increase the organism's demand for these hormones in order to balance the oxidation processes[9].

The research carried by Brenty and others [4] proves that the fluctuation of the level of thyroid hormones may influence the level of globulin and sex hormones.

The high level of thyroid hormones in hyperthyroidism lowers SHBG (sex hormone-binding globulin) level [5]. This effect of estrogens is associated with the symptoms of menopause.

The fall of estrogens concentration causes the fall of TBG (Thyroid Binding Globulin) and the increase of free fraction of thyroid hormones in blood [3]. As a result of this process, the hyperthyroidism symptoms increase during the perimenopausal period [10]. On account of the similarity of the symptoms in these two disorders, it is necessary to examine the hormonal function of the thyroid gland during the perimenopausal period [7]. The interdependence of the pituitary-gonadal axis and the pituitary-thyroid axis is direct and results in the direct influ-

ence on the clinical state of the organism [8].

One of the examined groups of patients included the women who suffered from Graves- Basedow disease. It is an immunological disease in which the thyroid antibodies against TSH receptor are produced. This leads to the stimulation of the function and hypertrophy of the thyroid gland dependent on cAMP [2]. The regularities mentioned above have been described by many authors, among them in the collective work by Costaglioli and others [6].

In the presented results of this research, in a group of patients with Graves- Basedow disease, in two cases, hyperthyroidism was preceded by a strong stress reaction. In the first case, the stress was caused by a car accident and in the second by the death of the husband. In comparison with more frequent hyperthyroidism during the observed period in the group with nodular goiter, a greater predisposition can be clearly observed in patients with a single nodule rather than with Graves-Basedow disease (in a clinical interview). During the ten-year-long period of observation of the patients it has been found in this research that hyperthyroidism appeared more often in women with nodular goiter than with Graves-Basedow disease, which can be connected with the different pathogenesis of the disease.

This interesting observation may be pointing to different mechanisms which accelerate the thyroid gland during the menopausal period concerning these two analysed diseases.

Clearly, the patients with nodular goiter were more predisposed to hyperthyroidism than those with Graves – Basedow disease. This suggests that the incorrect immunisation which appears in Graves- Basedow disease, does not have a significant influence on the activity of the thyroid gland during the menopausal period.

Conclusions

1. The women with the neutral nodular goiter are particularly predisposed to hyperthyroidism during the perimenopausal period. In the analyzed group of the nodular goiter, the hyperthyroidism appeared in 54,2% of patients.
2. Graves- Basedow disease in the past with a long period of remission was a rare reason of the resume of hyperthyroidism in a menopausal period. All cases of the reactivation of this disease (7% of women in this group) were preceded by a strong stress reaction.
3. The most frequent morphological changes, which caused the hyperthyroidism, were hot nodules and warm nodules-single and coexisting with cold nodules.
4. In ten years time of observation, the morphological changes in scintigraphy were observed. The most frequent form of changes was the development of hot and warm nodules on the basis of warm, cold and cool areas.
5. The patients during perimenopausal period should be very well diagnosed because of the similarity of the symptoms in hyperthyroidism and menopausal period.

The study reported above points to a high percentage of activation of thyroid gland during the perimenopausal period. Because there is such a striking similarity between the symptoms of hyperthyroidism and menopause, family doctors and gynaecologists should take it into consideration and conduct a thorough interview and diagnose their patients properly.

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