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ORIGINAL ARTICLE

THE ROLE OF THE LABORATORY SERVICE IN THE TIMELY ASSESSMENT OF RISK FACTORS IN PATIENTS WITH THYROID NODULES AS A TOOL TO PREVENT POSTOPERATIVE COMPLICATIONS

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Abstract

Aim: To study of thyroid hormones with one-time determination of risk factors in the laboratory.

Material and methods: The examination included the following researches: questionnaire, ultrasound examination with fine-needle aspiration (FNA), cytological examination, determination of the concentration of thyroid hormones and determining the body mass index.

Results and conclusions: the size and area of the tumor according to ultrasound (H = 2.30, p> 0.05 and H = 1.92, p> 0.05, respectively). At the same time, patients of the 1st group were younger in age than (when) compared with patients of other groups. For benign thyroid tumors (group I) are characterized by the following data: the level of free thyroxine (FT4) in the serum of 66.7% of patients did not exceed normal and averaged 14.0 (8.0-16.29) pmol/l. Group with suspected tumor malignancy include: very low concentration of FT4 in serum (1.94 (1.44-7.00) pmol/l); high level of FT3 production in 40.0% of cases with a shift of the mean values to the upper limit of the reference interval. Thyroid status of patients with malignant thyroid tumors (group III) is characterized by elevated levels of TSH compared with benign tumors (p <0.05) and suspected malignancy of the tumor (p <0.1). A significant decrease in the production of FT4 in the serum (7.4 times compared with the benign course; p <0.001) against the background of average regulatory levels of FT3.

Key words

thyroid cancer,
laboratory diagnostics,
body mass index,
risk factors,
fine-needle aspiration

INTRODUCTION

In the last few decades, the incidence of thyroid cancer has increased sharply, and now it is the most common cancer in women, especially young people [1-3]. However, the incidence of thyroid cancer is also increasing in men [4].

The relationship between patient factors and postoperative complications is complex and influenced by intrinsic disease factors, patient comorbidities, and operative management. Select studies have revealed an increased risk of complications in outpatient total thyroidectomy associated with male sex, thyrotoxicosis, presence of malignancy, extent of resection, and revision surgery [5].

Treatment of patients with thyroid tumors causes clinical problems and social stress [6]. In particular, for many years the main problem remains the search for a powerful tool that can distinguish between benign and malignant follicular lesions, and minimize the diagnostic search [7].

In general, studies to prevent postoperative complications of the thyroid gland are based on the experience of endocrine surgeons. However, an important component is to identify risk factors during a fine-needle aspiration biopsy visit. The diagnostic link remains limited. For many years, it consists only of cytological examination and quality control with the help of pathomorphological inference. The terms of the latter can have wide variations.

As the incidence of thyroid cancer increases and surgical resection is the mainstay of treatment for patients with thyroid cancer, the number of thyroid surgeries is also increasing [8, 9].

It is especially important to determine the body mass index at the preoperative stage, because it is associated with many pathological features of thyroid cancer, such as larger tumors, extrathyroid invasion, advanced stage of TNM, lymph node metastasis (LN) and tumor multiplicity [10, 11].

Despite the achievement of surgical methods aimed at minimizing adverse effects for patients, thyroid surgery still has risks [12, 13]. Postoperative complications are not uncommon, so it is important to initiate a combined diagnosis using analysis of risk factors and a basic study of thyroid hormones.

THE AIM

The aim of the research is to study of thyroid hormones with one-time determination of risk factors in the laboratory.

MATERIAL AND METHODS

All research was performed in accordance with relevant guidelines and regulations. The prospective study included 60 patients aged 21 to 83 years (mean age 54.6 ± 1.9 years), who according to ultrasound of the thyroid gland were classified as TR-4 category of nodular thyroid tumor on the TIRADS scale (4-6 points, suspected malignant thyroid changes). The research program, information for the patient and the form of informed consent to participate in the study were considered and approved at a meeting of the commission on ethics of the clinical department of Kharkiv National Medical University. The patient confirmed his voluntary decision to participate in the study with a signature in the form of informed consent. The examination included the following researches: questionnaire, ultrasound examination with fine-needle aspiration puncture biopsy (FNA), cytological examination, determination of the concentration of thyroid hormones and determining the body mass index. The research of thyroid status was accomplished on the levels of TSH, free thyroxine (FT4), triiodothyronine free (FT3) and antibodies to thyroperoxidase by immunochemical method with electrochemiluminescent detection on a Cobas e 411 automatic analyzer from Roche Diagnostics, Germany. Ultrasound of the thyroid gland was accomplished using a Toshiba SSA-580A using the TIRADS classification system. A 23G needle (0.6x25 mm) was used for FNA. The puncture material on the slide was air dried and fixed with methanol for 5 minutes, staining for 30 minutes by the method of Romanovsky. The results of the cytological examination were evaluated by the Bethesda System (BSRTC) using a standard cytological protocol. Weight was measured in light clothing and absence of shoes with an accuracy of 0.1 kg, and height was measured with an accuracy of 0.1 cm using a digital scale. Body mass index (BMI) was calculated by dividing body weight (in kilograms) by the square of height (in square meters), and the equivalent of excess weight was 25.0-29.9 kg/m^2 according to specific criteria of Ukraine.

Depending on the cytological conclusion, patients with thyroid pathology were divided into three groups: group I consisted of 18 patients with benign thyroid tumors (Benign); group II included 20 patients suspected thyroid cancer (Suspicious for Malignancy (SFM); group III was formed by 22 patients with malignant thyroid cancer (Malignant). Exclusion criteria: age less than 18 years; pregnant women; reluctance of the patient to participate in the study; refusal of the patient to re-take material and patients with a history of surgery (reoperation, final thyroidectomy) for recurrence of the disease or non-radical primary operations in non-specialized medical institutions, known cardiovascular disease and the use of any medication that alters body weight and composition (e.g., corticosteroids, insulin, sulfonylureas).

Statistical processing of the research results was performed using generally accepted in biomedical research methods of statistical analysis using software products MedCalc v.14.8.1. (MedCalc Software) and Microsoft Excel 2016 (Microsoft). Parametric or non-parametric methods of analysis were used taking into account the law of distribution of quantitative data (Shapiro-Wilk test). To describe and compare data sets with normal distribution, we used the arithmetic mean and its standard error (M ± m), one-way analysis of variance ANOVA (F) with a posteriori comparison of groups with each other according to the Tukey criterion (HSD); with abnormal data distribution – median (Me), interquartile range (25-75%), nonparametric analysis of Kruskal-Wallis ANOVA (H) followed by pairwise comparison of Multiple Comparisons (MS) groups. Comparison of nominal data was performed using the Pearson Chi-square test (χ^2). The relationship between the various factors was determined by analysis of variance and Spearman's rank correlation coefficients (r). The level of significance $p < 0.05$ was considered statistically significant for all statistical analysis procedures, the trend was determined at $p < 0.1$.

RESULTS

A comparative analysis of the studied indicators (Table 1) showed that the selected groups probably did not differ in the gender of patients ($\chi^2 = 2.21$, $p > 0.05$), body mass index ($F = 0.25$, $p > 0.05$). All subjects included in the study had a mean body mass index (BMI) of 28.0 ± 0.6 kg/m², of which more than half (60.0%) were overweight or grade I-II obesity. The size and area of the tumor according to ultrasound ($H = 2.30$, $p > 0.05$ and $H = 1.92$, $p > 0.05$, respectively). At the same time, patients of the 1st group were younger in age than (when) compared with patients of other groups ($p < 0.05$ according to the HSD criterion).

Assessment of thyroid status of patients with thyroid tumors showed a probable correlation between the degree of malignancy in the thyroid gland and TSH levels (according to the analysis of Kraskel-Wallis $H = 7.30$, $p < 0.05$), FT4 ($H = 17.64$, $p < 0.001$)

Table 1. General characteristics of patients and thyroid tumors.

Indicator	Research groups			General difference between the groups
	Group 1 (n=18)	Group 2 (n=20)	Group 3 (n=22)	
Gender, % - female/male	88,9/ 11,1	100/ 0	90,9/ 9,1	χ2=2,21, p=0,331
Age, years, M±m	46,6±3,7	58,7±3,1*	57,4±2,4*	F=4,51, p=0,015
BMI, kg/m^2, M±m	28,7±1,3	27,5±1,4	27,8±0,8	F=0,25, p=0,777
Maximum diameter of formation, mm, Me (25-75%)	15,0 (13,0-17,0)	11,0 (10,0-20,0)	12,0 (10,0-27,0)	H=2,30, p=0,316
Area of formation, mm^2, Me (25-75%)	135,0 (112,0-225,0)	106,0 (60,0-312,0)	120,0 (70,0-513,0)	H=1,92, p=0,383

Note: * – p <0.05 compared to group 1 (by HSD criterion)

Table 2. Thyroid hormone levels of patients of the research groups.

Indicator	Group	Min – max	Me (25-75%)	General difference between the groups	Deviation from the norm [%]	Reference values
Thyroid-stimulating Hormone, μmol / l	I	0,01 – 3,0	1,45 (0,95-1,97)	H=7,30, p=0,026	11,1	0,27- 4,2
	II	0,30 – 2,75	1,39 (1,13-2,27)		–	
	III	0,95 – 2,66	2,00 (1,76-2,30)*		–	
Free Thyroxine, FT4 pmol / l	I	2,10 – 18,63	14,00 (8,00-16,29)	H=17,64, p<0,001	33,3	12,0-22,0
	II	1,12 – 13,5	1,94 (1,44-7,00)**		90,0	
	III	1,07 – 22,1	1,90 (1,21-9,00)**		90,9	
Free Triiodthyronine, FT3 pmol / l	I	4,67 – 6,30	5,67 (5,10-6,20)	H=12,41, p=0,002	–	3,1-6,8
	II	3,9 – 8,3	6,30 (5,40-8,00)		40,0	
	III	3,87 – 7,5	4,90 (4,00-5,30)*#		18,2	
Anti -thyroid peroxidase autoantibodies, IU / ml	I	13,7 – 47,9	23,0 (18,1-24,0)	H=0,20, p=0,903	11,1	До 34
	II	14,9 – 60,9	19,0 (18,1-23,3)		10,0	
	III	11,0 – 75,2	21,9 (16,9-25,8)		9,1	

Notes: * – p <0, 05, ** – p <0,001 in comparison with group I;
– p <0.001 compared to group II (by MC criterion)

and FT3 (H = 12.41, p <0.01). So, despite the fact that the values of TSH in the serum of most patients (96.7%) did not exceed normal, the average in the presence of malignancy was higher than in the benign nature of the tumor and suspected malignancy of the tumor – 2.0 (1.76 -2.30) μIU / l *vs.* 1.45 (0.95-1.97) μIU / L (p <0.05) and 1.39 (1.13-2.27) μIU / L (p < 0.1), respectively (Table 2). From the described data it is clear that patients with the highest concentration of TSH and borderline results of cytological examination need more careful examination compared to patients in whom TSH levels are low. Thus, the increase in TSH even within the reference values correlates with an increased risk of malignancy of the node (r = 0.34, p <0.05) and this indicator can be regarded as an independent predictor for thyroid cancer.

The research of the level of free T4 (FT4) in the serum of thematic patients showed an inverse correlation between the indicators and the potential for malignancy of the tumor – r = -0.45; p <0.001. In benign thyroid disease (group I), the level of FT4 in only one third of patients (33.3%) was below normal, ranged from 2.10 to 18.63 pmol / l and averaged 14.0 (8.0-16, 29) pmol / l (Table 2). In contrast, the vast majority of patients in groups II and III (90%) had a very low concentration of this hormone in the serum – the median rate was 7.2-7.4 times lower than in group I (p <0.001). Therefore, low levels of FT4 may serve as a differential diagnostic criterion and indicate a potentially malignant origin of the tumor.

In contrast to the previous hormone, the concentration of free T3 (FT3) in the serum of most patients

with thyroid tumors (80.0%) did not exceed the reference range. At the same time, a probable shift of FT3 values depending on the degree of malignancy of the node was established. Thus, for benign tumors and suspected malignancy of the tumor, the hormone level mostly approached the upper limit of normal or exceeded it, while in metastatic thyroid disease it's value was within the reference range ($p < 0.05$ compared with previous groups) (Table 2).

Regarding the levels of AT-TPO, the study did not show significant differences between groups of patients ($H = 0.20$, p & gt; 0.05), no process of immunogenic destruction of the thyroid gland. Therefore, autoimmune status is not prognostic factor of malignancy.

DISCUSSION

Timely detection of risk factors at the preoperative stage plays an important role in the prevention of complications after surgery. With the help of laboratory monitoring, it is possible to improve the quality of medical care for patients diagnosed with thyroid cancer.

Some studies have found an increased risk of complications of outpatient total thyroidectomy associated with male gender, thyrotoxicosis, the presence of malignancies, the degree of resection and revision surgery [14, 15].

The study of thyroid hormones in peripheral blood is important, especially recent studies report a positive relationship between TSH and blood pressure [16].

Epidemiological studies report a positive association between obesity and thyroid cancer risk and body mass index [17-19].

This single-center study indicates that the determination of risk factors and body mass index at the same time as the study of thyroid hormones significantly helps in the prevention of complications in the postoperative period.

CONCLUSIONS

1. Analysis of risk factors is especially important in the study of thyroid hormones. To prevent complications after surgery, our studied indicators are considered in the dynamics, which is important in the individual attitude to the patient;
2. Body mass index is positively correlated with thyroid tumors and together with risk factors acts as a mediator;
3. For benign thyroid tumors (group I) are characterized by the following data: the level of free thyroxine (FT4) in the serum of 66.7% of patients did not exceed normal and averaged 14.0 (8.0-16.29) pmol / l; the concentration of FT3 in all cases corresponded to the reference values, but with a shift of the average levels to the upper limit of normal (5.67 (5.10-6.20) pmol / l). Benign thyroid disease (category II BSRTC) is likely to be associated with younger patients (46.6 ± 3.7 years);
4. Group with suspected tumor malignancy include: very low concentration of FT4 in serum (1.94 (1.44-7.00) pmol / l); high level of FT3 production in 40.0% of cases with a shift of the mean values to the upper limit of the reference interval (6.30 (5.40-8.00) pmol / l;
5. Thyroid status of patients with malignant thyroid tumors (group III) is characterized by elevated levels of TSH compared with benign tumors ($p < 0.05$) and suspected malignancy of the tumor ($p < 0.1$), but within the reference range; a significant decrease in the production of FT4 in the serum (7.4 times compared with the benign course; $p < 0.001$) against the background of average regulatory levels of FT3.

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CONFLICT OF INTEREST

Authors declare no conflict of interest.

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