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Application of neutron activation analysis for the comparison of eleven trace elements contents in thyroid tissue adjacent to thyroid malignant and benign nodules

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Abstract
Aim: Thyroid nodules (TN) are the most common endocrine disorder worldwide. Etiology and pathogenesis of thyroid benign and malignant nodules (TBN and TMN, respectively) are still not enough understood. The present study was performed to clarify the role of some trace elements (TEs) in the origination and development of TN.
Methods: Contents of TEs such as silver (Ag), cobalt (Co), chromium (Cr), iron (Fe), mercury (Hg), iodine (I), rubidium (Rb), antimony (Sb), scandium (Sc), selenium (Se), and zinc (Zn) were prospectively evaluated in thyroid tissue adjacent to TBN (79 patients) and to TMN (41 patients). Measurements were performed using non-destructive instrumental neutron activation analysis. Results of the study were additionally compared with previously obtained data for the same TEs in "normal" thyroid tissue.
Results: I was observed that in thyroid tissue adjacent to TMN the mass fractions of I and Rb were 1.53 and 1.79 times, respectively, higher than those in thyroid tissue adjacent to TBN. The common characteristics of thyroid tissue adjacent to TBN and TMN were similar contents of Ag, Co, Cr, Fe, Hg, Sb, Sc, and Zn, as well as elevated levels of Ag, Co, Hg, I, and Rb, which overdrew those in "normal" thyroid approximately in 32.2, 1.8, 40.9, 1.4, and 1.9 times, respectively.
Conclusions: Role of TEs in etiology and pathogenesis TBN and TMN is similar and exessive accumulation of Ag, Co, Hg, I, and Rb in thyroid tissue may be involved in the TN origination and development.

Keywords: Thyroid; Thyroid benign and malignant nodules; Trace elements; Neutron activation analysis

Introduction

Thyroid benign and malignant nodules (TBN and TMN, respectively) are the most common endocrine disorder worldwide. Moreover, in some parts of the world, especially those of current or former iodine deficiency, thyroid nodules (TN) are still an endemic disease [1]. Incidence of TBN and TMN has been growing steadily over the past four decades, despite the use of iodine prophylaxis in many countries [2]. Some factors causing this higher incidence of TN were described in literature [3] and analysis of these data shown intriguing links between the etiologies of TBN and TMN [2, 3]. In other words, the factors contributing to increases in the incidence of TBN are the same as those contributing to increases in TMN. However, the current state of knowledge regarding TN demonstrates that the etiology and pathogenesis of TBN and TMN are still not enough understood, because there are many not adequately explored chemicals, which induced thyroid hormone perturbations leading to these diseases.

For over 20th century, there was the dominant opinion that TN is the simple consequence of iodine deficiency [4]. However, it was found that TN is a frequent disease even in those countries and regions where the population is never exposed to iodine shortage. Moreover, it was shown that iodine excess has severe consequences on human health and associated with the presence of TN [5-8]. It was also demonstrated that besides the iodine deficiency and excess many other dietary, environmental, and occupational factors are associated with the TN incidence [3, 9-11]. Among these factors a disturbance of evolutionary stable input of many trace elements (TEs) in human body after industrial revolution plays a significant role in etiology of TN [12].

Besides iodine, many other TEs have also essential physiological functions [13]. Essential or toxic (goitrogenic, mutagenic, carcinogenic) properties of TEs depend on tissue-specific need or tolerance, respectively [13]. Excessive accumulation or an imbalance of the TEs may disturb the cell functions and may result in cellular proliferation, degeneration, death, benign or malignant transformation [13-15].

In our previous studies the complex of *in vivo* and *in vitro* nuclear analytical and related methods was developed and used for the investigation of iodine and other TEs contents in the normal and pathological thyroid [16-22]. Iodine level in the normal thyroid was investigated in relation to age, gender and some non-thyroidal diseases [23, 24]. After that, variations of many TEs content with age in the thyroid of males and females were studied and age- and gender-dependence of some TEs was observed [25-41]. Furthermore, a significant difference between some TEs contents in colloid goiter, thyroiditis, thyroid adenoma, and cancer in comparison with normal thyroid was demonstrated [42-47].

The present study was performed to clarify the role of some TEs in the etiology of TBN and TMN. Having this in mind, the aim of this exploratory study was to examine differences in the content of silver (Ag), cobalt (Co), chromium (Cr), iron (Fe), mercury (Hg), iodine (I), rubidium (Rb), antimony (Sb), scandium (Sc), selenium (Se), and zinc (Zn) in thyroid tissue adjacent to TN using a combination of non-destructive instrumental neutron activation analysis with high resolution spectrometry of short-lived radionuclides (INAA-SLR) and long-lived radionuclides (INAA-LLR), and to compare the levels of these TEs in two groups of samples (tissue adjacent to TBN and TMN, respectively). Moreover, for understanding a possible role of TEs in etiology and pathogenesis of TN results of the study were compared with previously obtained data for the same TEs in "normal" thyroid tissue [42-47].

Material and Methods

All patients suffered from TBN (n=79, mean age M±SD was 44±11 years, range 22-64) and from TMN (n=41, mean age M±SD was 46±15 years, range 16-75) were hospitalized in the Head and Neck Department of the Medical Radiological Research Centre (MRRC), Obninsk. Thick-needle puncture biopsy of suspicious nodules of the thyroid was performed for every patient, to permit morphological study of thyroid tissue at these sites and to estimate their trace element contents. In all cases the diagnosis has been confirmed by clinical and morphological results obtained during studies of biopsy and resected materials. Histological conclusions for benign nodules were: 46 colloid goiter, 19 thyroid adenoma, 8 Hashimoto's thyroiditis, and 6 Riedel's Struma, whereas for thyroid malignant tumors were: 25 papillary adenocarcinomas, 8 follicular adenocarcinomas, 7 solid carcinomas, and 1 reticulosarcoma. Samples of visually intact thyroid tissue adjacent to TBN and TMN were taken from resected materials.

"Normal" thyroids for the control group samples were removed at necropsy from 105 deceased (mean age 44±21 years, range 2-87), who had died suddenly. The majority of deaths were due to trauma. A histological examination in the control group was used to control the age norm conformity, as well as to confirm the absence of micro-nodules and latent cancer.

All studies were approved by the Ethical Committees of MRRC. All the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments, or with comparable ethical standards. Informed consent was obtained from all individual participants included in the study

All tissue samples obtained from visually intact tissue adjacent to nodules were divided into two portions using a titanium scalpel to prevent contamination by TEs of stainless steel [48]. One was used for morphological study while the other was intended for TEs analysis. After the samples intended for TEs analysis were weighed, they were freeze-dried and homogenized [49].

To determine contents of the TEs by comparison with a known standard, biological synthetic standards (BSS) prepared from phenol-formaldehyde resins were used [50]. In addition to BSS, aliquots of commercial, chemically pure compounds were also used as standards. Ten certified reference material IAEA H-4 (animal muscle) and IAEA HH-1 (human hair) sub-samples were treated and analyzed in the same conditions that thyroid samples to estimate the precision and accuracy of results.

The content of I were determined by INAA-SLR using a horizontal channel equipped with the pneumatic rabbit system of the WWR-c research nuclear reactor (Branch of Karpov Institute, Obninsk). Details of used nuclear reaction, radionuclide, gamma-energies, spectrometric unit, sample preparation, and the quality control of results were presented in our earlier publications concerning the INAA-SLR of I contents in human thyroid [27,28] and scalp hair [51].

A vertical channel of the same nuclear reactor was applied to determine the content of Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, and Zn by INAA-LLR. Details of used nuclear reactions, radionuclides, gamma-energies, spectrometric unit, sample preparation and procedure of measurement were presented in our earlier publications concerning the INAA-LLR of TEs contents in human thyroid [29, 30], scalp hair [50], and prostate [52, 53].

A dedicated computer program for INAA-SLR and INAA-LLR mode optimization was used [54]. All samples for TEs analysis were prepared in duplicate, and mean values of TEs contents were used in final calculation. Using Microsoft Office Excel software, a summary of the statistics, including, arithmetic mean, standard deviation of mean, standard error of mean, minimum and maximum values, median, percentiles with 0.025 and 0.975 levels was calculated for TEs contents in two groups of tissue adjacent to TBN and TMN. Data for "normal" thyroid were taken from our previous publications [42-47]. The difference in the results between two groups of samples "adjacent to TBN" and "adjacent to TMN", as well as between "normal" and "adjacent to TBN and TMN combined" was evaluated by the parametric Student's *t*-test and non-parametric Wilcoxon-Mann-Whitney *U*-test.

Table 1: Some statistical parameters of Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn mass fraction (mg/kg, dry mass basis) in thyroid tissue adjacent to thyroid benign (TATBN) and malignant (TATMN) nodules

Tissue	Element	Mean	SD	SEM	Min	Max	Median	P 0.025	P 0.975
TATBN	Ag	0.474	0.662	0.130	0.021	3.31	0.282	0.0516	2.07
	Co	0.0728	0.0979	0.0170	0.0051	0.594	0.0525	0.0086	0.219
	Cr	0.575	0.618	0.108	0.0180	3.14	0.401	0.0596	2.19

	Fe	211	140	24	41.5	620	163	58.2	557
	Hg	1.36	0.96	0.17	0.014	4.68	1.21	0.268	4.25
	I	2158	1436	214	343	7912	1917	527	5441
	Rb	10.5	4.3	0.7	4.10	20.0	9.80	4.74	19.4
	Sb	0.131	0.174	0.030	0.0076	0.757	0.0759	0.0269	0.749
	Sc	0.0057	0.0147	0.0020	0.0002	0.0654	0.0002	0.0002	0.0468
	Se	1.95	0.87	0.15	0.647	4.34	1.65	0.906	3.66
	Zn	105	68	12	34.2	344	86.4	42.8	304
TATMN	Ag	0.503	0.450	0.103	0.079	2.00	0.303	0.0984	1.53
	Co	0.0707	0.0581	0.0120	0.0152	0.205	0.0455	0.0170	0.201
	Cr	0.556	0.468	0.094	0.0512	1.58	0.457	0.0589	1.56
	Fe	244	137	27	95.2	752	213	104	591
	Hg	2.19	1.92	0.38	0.0160	7.78	1.43	0.158	6.50
	I	3183	1673	301	563	8240	2982	853	7766
	Rb	18.8	17.0	3.3	5.00	67.0	11.9	5.69	65.6
	Sb	0.247	0.416	0.085	0.0069	1.77	0.0634	0.0159	1.38
	Sc	0.0059	0.0134	0.0030	0.0002	0.0539	0.0002	0.0002	0.0442
	Se	3.08	1.67	0.33	0.704	6.91	2.56	0.942	6.89
	Zn	111	56	11	20.4	272	110	28.8	215

M – arithmetic mean, SD – standard deviation, SEM – standard error of mean, Min – minimum value, Max – maximum value, P 0.025 – percentile with 0.025 level, P 0.975 – percentile with 0.975 level.

Table 2: Differences between mean values (M±SEM) of Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn mass fraction (mg/kg, dry mass basis) in thyroid tissue adjacent to thyroid benign (TATBN) and malignant (TATMN) nodules

Element	Thyroid tissue adjacent to thyroid nodules				Ratio
	TATBN	TATMN	Student's t-test *p*≤	U-test *p*	TATMN/TATBN
Ag	0.474±0.130	0.503±0.103	0.864	>0.05	1.06
Co	0.0728±0.0170	0.0707±0.0120	0.918	>0.05	0.97
Cr	0.575±0.108	0.556±0.094	0.898	>0.05	0.97
Fe	211±24	244±27	0.358	>0.05	1.16
Hg	1.36±0.17	2.19±0.38	0.057	>0.05	1.61
I	2158±214	3183±301	**0.0074**	**≤0.01**	1.47
Rb	10.5±0.7	18.8±3.3	**0.022**	**≤0.01**	1.79
Sb	0.131±0.030	0.247±0.085	0.208	>0.05	1.89
Sc	0.0057±0.0020	0.0059±0.0030	0.964	>0.05	1.04
Se	1.95±0.15	3.08±0.33	**0.0033**	**≤0.01**	1.58
Zn	105±12	111±11	0.708	>0.05	1.06

M – arithmetic mean, SEM – standard error of mean, Statistically significant values are in **bold**.

Table 3: Some statistical parameters of Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn mass fraction (mg/kg, dry mass basis) in in thyroid tissue adjacent (TTA) to thyroid benign and malignant nodules (combined)

Tissue	Element	Mean	SD	SEM	Min	Max	Median	P 0.025	P 0.975
TTA	Ag	0.486	0.576	0.086	0.021	3.31	0.297	0.0709	1.93
	Co	0.072	0.083	0.011	0.0051	0.594	0.0467	0.0115	0.202
	Cr	0.567	0.554	0.073	0.018	3.14	0.429	0.0566	1.88
	Fe	225	138	18	41.5	752	184	68.3	583
	Hg	1.72	1.50	0.20	0.0140	7.78	1.30	0.117	5.37
	I	2577	1608	184	343	8240	2400	554	7646
	Rb	14.1	12.4	1.6	4.10	67.0	10.6	4.90	55.1
	Sb	0.180	0.303	0.040	0.0069	1.77	0.075	0.0136	0.971
	Sc	0.0058	0.0141	0.0020	0.0002	0.0654	0.0002	0.0002	0.0490
	Se	2.43	1.38	0.18	0.647	6.91	2.12	0.828	6.45
	Zn	107	62.4	8.1	20.4	344	101	34.0	284

M – arithmetic mean, SD – standard deviation, SEM – standard error of mean, Min – minimum value, Max – maximum value, P 0.025 – percentile with 0.025 level, P 0.975 – percentile with 0.975 level.

Table 4: Differences between mean values (M±SEM) of Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn mass fraction (mg/kg, dry mass basis) in normal thyroid (NT) and thyroid tissue adjacent to thyroid benign and malignant nodules (TTA)

Element	Thyroid tissue				Ratio
	NT	TTA	Student's t-test $p \leq$	U-test p	TTA/NT
Ag	0.0151±0.0016	0.486±0.086	**0.0000019**	**≤0.01**	32.2
Co	0.0399±0.0030	0.0720±0.0110	**0.0056**	**≤0.01**	1.80
Cr	0.539±0.032	0.567±0.073	0.724	>0.05	1.05
Fe	225±11	225±18	0.992	>0.05	1.00
Hg	0.0421±0.0041	1.72±0.20	**0.0000001**	**≤0.01**	40.9
I	1841±107	2577±184	**0.000049**	**≤0.01**	1.40
Rb	7.37±0.44	14.1±1.6	**0.00014**	**≤0.01**	1.91
Sb	0.111±0.008	0.180±0.040	0.094	>0.05	1.62
Sc	0.0046±0.0008	0.0058±0.0020	0.523	>0.05	1.26
Se	2.32±0.14	2.43±0.18	0.608	>0.05	1.05
Zn	97.8±4.5	107±8.1	0.308	>0.05	1.09

M – arithmetic mean, SEM – standard error of mean, Statistically significant values are in bold.

Results

Table 1 presents certain statistical parameters (arithmetic mean, standard deviation, standard error of mean, minimal and maximal values, median, percentiles with 0.025 and 0.975 levels) of the Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn mass fraction in thyroid intact tissue samples of two groups "adjacent to TBN" and "adjacent to TMN".

The ratios of means and the comparison of mean values of Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn mass fractions in pair of sample groups such as "adjacent to TBN" and "adjacent to TMN" is presented in Table 2.

Table 3 depicts certain statistical parameters (arithmetic mean, standard deviation, standard error of mean, minimal and maximal values, median, percentiles with 0.025 and 0.975 levels) of the Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn mass fraction in thyroid tissue adjacent "TTA" to TN (two groups "adjacent to TBN" and "adjacent to TMN" combined).

The ratios of means and the comparison of mean values of Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn mass fractions in pair of sample groups such as normal thyroid tissue "NT" and "TTA" is presented in Table 4.

Discussion

As was shown before [27-30, 51-53] good agreement of the TEs contents in CRM IAEA H-4 and and CRM IAEA HH-1 samples analyzed by instrumental neutron activation analysis with the certified data of these CRMs indicates acceptable accuracy of the results obtained in the study of "adjacent to TBN", "adjacent to TMN", "NT", and "TTA" groups of thyroid tissue samples presented in Tables 1–4.

From Table 2, it is observed that in thyroid tissue adjacent to TMN the mass fractions of I, Rb, and Se are 1.47, 1.79 and 1.58 times, respectively, higher than in thyroid tissue adjacent to TBN. In a general sense Ag, Co, Cr, Fe, Hg, Sb, Sc, and Zn contents found in the "adjacent to TBN" and "adjacent to TMN" groups of thyroid tissue samples were similar (Table 2). It allowed combine data obtained for two groups for the purposes of finding a common TEs composition of TTA to TN and improving statistical characteristics of results for this group of samples (Table 3).

From obtained results it was found that the common characteristics of thyroid tissue adjacent to TBN and TMN were elevated levels of Ag, Co, Hg, I, and Rb, which overdrew those in "normal" thyroid approximately in 32.2, 1.8, 40.9, 1.4, and 1.9 times, respectively (Table 4). Thus, if we accept the TEs contents in "normal" thyroid glands as a norm, we have to conclude that with a nodular transformation the Ag, Co, Hg, I, and Rb contents in thyroid intact tissue adjacent to TN significantly changed.

Characteristically, elevated or reduced levels of TEs observed in thyroid nodules are discussed in terms of their potential role in the initiation and promotion of these thyroid lesions. In other words, using the low or high levels of the TEs in affected thyroid tissues researchers try to determine the role of the deficiency or excess of each TE in the etiology and pathogenesis of thyroid diseases. In our opinion, abnormal levels of some TEs in TN could be and cause, and also effect of thyroid tissue transformation. From the results of such kind studies, it is not always possible to decide whether the measured decrease or increase in TEs level in pathologically altered tissue is the reason for alterations or vice versa. According to our opinion, investigation of TEs contents in thyroid tissue adjacent to TN and comparison obtained results with TEs levels typical of "normal" thyroid gland may give additional useful information on the topic because these data show conditions of tissue in which TN were originated and developed.

Silver

Ag is a TE with no recognized trace metal value in the human body. Food is the major intake source of Ag and this metal is authorised as a food additive (E174) in the EU [55]. Another source of Ag is contact with skin and mucosal surfaces because Ag is widely used in different applications (e.g., jewelry, wound dressings, or eye drops). Ag in metal form and inorganic Ag compounds ionize in the presence of water, body fluids or tissue exudates. The silver ion Ag^+ is biologically active and readily interacts with proteins, amino acid residues, free anions and receptors on mammalian and eukaryotic cell membranes. Besides such the adverse effects of chronic exposure to Ag as a permanent bluish-gray discoloration of the skin (argyria) or eyes (argyrosis), exposure to soluble Ag compounds may produce other toxic effects, including liver and kidney damage, irritation of the eyes, skin, respiratory, and intestinal tract, and changes in blood cells. Experimental studies shown that Ag nanoparticles may affect thyroid hormone metabolism [56]. More detailed knowledge of the Ag toxicity can lead to a better understanding of the impact on human health, including thyroid function.

Cobalt

Health effects of high Co occupational, environmental, dietary and medical exposure are characterized by a complex clinical syndrome, mainly including neurological, cardiovascular and endocrine deficits, including hypothyroidism [57]. Co is genotoxic and carcinogenic, mainly caused by oxidative DNA damage by reactive oxygen species, perhaps combined with inhibition of DNA repair [57]. In our previous studies it was found a significant age-related increase of Co content in female thyroid [29]. Therefore, a goitrogenic and, probably, carcinogenic effect of excessive Co level in the thyroid of old females was assumed. Elevated level of Co in TBN and TMN, observed in the present study, supports this conclusion.

Mercury

In the general population, potential sources of Hg exposure include the inhalation of this metal vapor in the air, ingestion of contaminated foods and drinking water, and exposure to dental amalgam through dental care. Hg is one of the most dangerous environmental pollutants. The growing use of this metal in diverse areas of industry has resulted in a significant increase of environment contamination and episodes of human intoxication. Many experimental and occupational studies of Hg in different chemical states shown significant alterations in thyroid hormones metabolism and thyroid gland parenchyma [58, 59]. Moreover, Hg was classified as certain or probable carcinogen by the International Agency for Research on Cancer [60].

Iodine

To date, it was well established that iodine excess has severe consequences on human health and associated with the presence of TBN and TMN [4-8, 61, 62]. In present study elevated level of I in thyroid tissue adjacent to TBN and TMN was found in comparison with “normal” thyroid. Thus, on the one hand, it is likely that elevated level of I in thyroid tissue might be involved in the TN origination and development. On the other hand, however, elevated level of I in thyroid tissue adjacent to TN may explain by unusually intensive work of this tissue. Compared to other soft tissues, the human thyroid gland has higher levels of I, because this element plays an important role in its normal functions, through the production of thyroid hormones (thyroxin and triiodothyronine) which are essential for cellular oxidation, growth, reproduction, and the activity of the central and autonomic nervous system. As was shown in our previous study, TBN and, particularly, TMN transformation of thyroid gland is accompanied by a significant loss of tissue-specific functional features, which leads to a significant reduction in I content associated with functional characteristics of the human thyroid tissue [43-47]. Because the affected part of gland reduced productions of thyroid hormones, the rest “intact” part of thyroid tries to compensate thyroid hormones deficiency and work more intensive than usual.

Rubidium

There is very little information about Rb effects on thyroid function. Rb as a monovalent cation Rb+ is transfered through membrane by the Na+K+-ATPase pump like K+ and concentrated in the intracellular space of cells. Thus, Rb seems to be more intensivly concentrated in the intracellular space of cells. The sourse of Rb elevated level in thyroid tissue adjacent to TN may be Rb environment overload. The excessive Rb intake may result a replacement of medium potassium by Rb, which effects on iodide transport and iodoaminoacid synthesis by thyroid. The sourse of Rb increase in thyroid tissue adjacent to TN may be not only the excessive intake of this TE in organism from the environment, but also changed Na+K+ -ATPase or H+K+ - ATPase pump membrane transport systems for monovalent cations, which can be stimulated by endocrin system, including thyroid hormones [63]. It was found also that Rb has some function in immune responce and that elevated concentration of Rb could modulate proliferative responses of the cell, as was shown for bone marrow leukocytes [64]. These data partially clarify the possible role of Rb in etiology and pathogenesis of TBN and TMN.

Selinium

The high level of Se content found just in thyroid tissue adjacent to TMN cannot be regarded as pure chance. The seleno-protein characterized as Se-dependent glutathione peroxidase (Se-GSH-Px) is involved in protecting cells from peroxidative damage. This enzyme may reduce tissue concentration of free radicals and hydroperoxides. It is particular important for the thyroid gland, because thyroidal functions involve oxidation of iodide, which is incorporated into thyreoglobulin, the precursor of the thyroid hormones. For oxidation of iodide thyroidal cells produce a specific thyroid peroxidase using of physiologically generated hydrogen-peroxide (H_2O_2) as a cofactor [65]. It follows that the thyroid parenchyma must be continuously exposed to a physiological generation of H_2O_2 and in normal conditions must be a balance between levels of Se (as Se-GSH-Px) and H_2O_2.

The elevated level of Se in thyroid tissue adjacent to TMN was accompanied excessive accumulation of Ag, Co, Hg, I, and Rb in comparison with "normal" values for these elements. Moreover, contents of Ag, Co, Hg, I, and Rb in adjacent tissue were higher than in malignant nodules [47]. Thus, it might be assumed that the elevated level of Se is reaction of adjacent tissue on an increase in concentration of free radicals and hydroperoxides in thyroid gland and that this increase preceded the TMN origination and development.

Limitations

This study has several limitations. Firstly, analytical techniques employed in this study measure only eleven TEs (Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn) mass fractions. Future studies should be directed toward using other analytical methods which will extend the list of TEs investigated in thyroid tissue adjacent to TN. Secondly, the sample size of TBN and TMN group was relatively small and prevented investigations of TEs contents in this group using differentials like gender, functional activity of nodules, stage of disease, and dietary habits of patients with TN. Lastly, generalization of our results may be limited to Russian population. Despite these limitations, this study provides evidence on some TEs level alteration in thyroid tissue adjacent to TN and shows the necessity to continue TEs research of TN.

Conclusion

In this work, TEs analysis was carried out in the thyroid tissue adjacent to TBN and TMN using neutron activation analysis. It was shown that neutron activation analysis is an adequate analytical tool for the non-destructive determination of Ag, Co, Cr, Fe, Hg, I, Rb, Sb, Sc, Se, and Zn content in the tissue samples of human thyroid in norm and pathology. I was found that in thyroid tissue adjacent to TMN the mass fractions of I, Rb, and Se were 1.47, 1.79 and 1.58 times, respectively, higher than those in thyroid tissue adjacent to TBN. The common characteristics of thyroid tissue adjacent to TBN and TMN were elevated levels of Ag, Co, Hg, I, and Rb, which overdrew those in "normal" thyroid approximately in 32.2, 1.8, 40.9, 1.4, and 1.9 times, respectively, and similar contents of Ag, Co, Cr, Fe, Hg, Sb, Sc, and Zn. Thus, from results obtained, it was possible to conclude that the role of TEs in etiology and pathogenesis TBN and TMN is similar and exessive accumulation of Ag, Co, Hg, I, and Rb in thyroid tissue may be involved in the TN origination and development.

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Conflict of Interest

The author has not declared any conflict of interests.

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