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Research Article

Contents of Nineteen Chemical Elements in Thyroid Benign Nodules and Tissue adjacent to Nodules investigated using Neutron Activation Analysis and Inductively Coupled Plasma Atomic Emission Spectrometry

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Abstract

Thyroid benign nodules (TBNs) are the most common diseases of this endocrine gland and are common worldwide. The etiology and pathogenesis of TBNs must be considered as multifactorial. The present study was performed to clarify the role of some chemical elements (ChEs) in the etiology of these thyroid disorders. With this aim thyroid tissue levels of aluminum (Al), boron (B), barium (Ba), calcium (Ca), chlorine (Cl), coper (Cu), iron (Fe), I, potassium (K), lithium (Li), magnesium (Mg), manganese (Mn), sodium (Na), phosphorus (P), sulfur (S), silicon (Si), strontium (Sr), vanadium (V), and zinc (Zn) were prospectively evaluated in nodular tissue and tissue adjacent to nodules of 79 patients with TBNs. Measurements were performed using a combination of non-destructive instrumental neutron activation analysis with high resolution spectrometry of short-lived radionuclides and destructive method inductively coupled plasma atomic emission spectrometry. Results of the study were additionally compared with previously obtained data for the same ChEs in "normal" thyroid tissue. It was observed that mass fractions of Al, B, Cl, Cu, Fe, Li, Mn, Na, P, S, Si, V, and Zn contents in "nodular" tissue were higher, while Ca and I content was lower in comparison with contents of these ChEs in normal gland. Mass fractions of Cl and Na in "adjacent" group of samples were approximately 2.7 and 1.6 times, respectively, higher than in "normal" thyroid. Contents of Al, B, Ba, Br, Ca, Cl, Cu, K, Mg, Mn, Na, P, S, Sr, V, and Zn found in the "nodular" and "adjacent" groups of thyroid tissue samples were very similar, however, mass fraction of Fe was lower, while mass fraction of I was higher in "adjacent" group of samples. At that, level of I in "adjacent" group of samples was over 2 times higher than in nodular tissue and almost equals the normal value. Finally, this study provides evidence on many ChEs level alteration in nodular and adjacent to nodule tissue and shows the necessity to continue ChEs research of TBNs. The little reduced level of I content in nodular tissue could possibly be explored for differential diagnosis of TBNs and thyroid cancer.

Keyword: Thyroid; Thyroid benign nodules; Chemical elements; Neutron activation analysis; Inductively coupled plasma atomic emission spectrometry

Introduction

Thyroid benign nodules (TBNs) are universally encountered and frequently detected by palpation during a physical examination, or incidentally, during clinical imaging procedures. TBNs include non-neoplastic lesions, for example, colloid goiter and thyroiditis, as well as neoplastic lesions such as thyroid adenomas [1-3]. For over 20th century, there was the dominant opinion that TBNs is the simple consequence of iodine deficiency. However, it was found that TBNs is a frequent disease even in those countries and regions where the population is never exposed to iodine shortage [4]. Moreover, it was shown that iodine excess has severe consequences on human health and associated with the presence of TBNs [5-8]. It was also demonstrated that besides the iodine deficiency and excess many other dietary, environmental, and occupational factors are associated with the TBNs incidence [9-11]. Among these factors a disturbance of evolutionary stable input of many chemical elements (ChEs) in human body after industrial revolution plays a significant role in etiology of TBNs [12].

Besides iodine, many other ChEs have also essential physiological functions [13]. Essential or toxic (goitrogenic, mutagenic, carcinogenic) properties of ChEs depend on tissue-specific need or tolerance, respectively [13]. Excessive accumulation or an imbalance of the ChEs 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 ChEs 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 ChEs content with age in the thyroid of males and females were studied and age- and gender-dependence of some ChEs was observed [25-41]. Furthermore, a significant difference between some TEs contents in colloid goiter, thyroiditis, and thyroid adenoma in comparison with normal thyroid was demonstrated [42-45].

To date, the etiology and pathogenesis of TBNs must be considered as multifactorial. The present study was performed to find out differences in ChEs contents between the group of nodular tissues and tissue adjacent to nodules, as well as to clarify the role of some ChEs in the etiology of TBNs. Having this in mind, the aim of this exploratory study was to examine differences in the content of aluminum (Al), boron (B), barium (Ba), calcium (Ca), chlorine (Cl), coper (Cu), iron (Fe), I, potassium (K), lithium (Li), magnesium (Mg), manganese (Mn), sodium (Na), phosphorus (P), sulfur (S), silicon (Si), strontium (Sr), vanadium (V), and zinc (Zn) in nodular and adjacent to nodules tissues of thyroids with TBNs using a combination of non-destructive instrumental neutron activation analysis with high resolution spectrometry of short-lived radionuclides (INAA-SLR) and destructive method such as inductively coupled plasma atomic emission spectrometry (ICP-AES), and to compare the levels of these ChEs in two groups (nodular and adjacent to nodules tissues) of the cohort of TBNs samples. Moreover, for understanding a possible role of ChEs in etiology and pathogenesis of TBNs results of the study were compared with previously obtained data for the same ChEs in "normal" thyroid tissue [42-45].

Material and Methods

All 79 patients suffered from TBNs (46 patients with colloid goiter, mean age M±SD was 48±12 years, range 30-64; 19 patients with thyroid adenoma, mean age M±SD was 41±11 years, range 22-55; and 14 patients with thyroiditis, mean age M±SD was 39±9 years, range 34-50) were hospitalized in the Head and Neck Department of the Medical Radiological Research Centre (MRRC), Obninsk. The group of patients with thyroiditis included 8 persons with Hashimoto's thyroiditis and 6 persons with Riedel's Struma. 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 ChEs contents. For all patients the diagnosis has been confirmed by clinical and morphological/histological results obtained during studies of biopsy and 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 were divided into two portions using a titanium scalpel [46]. One was used for morphological study while the other was intended for ChEs analysis. After the samples intended for ChEs analysis were weighed, they were freeze-dried and homogenized [47]. The pounded samples weighing about 10 mg (for biopsy) and 100 mg (for resected materials) were used for ChE measurement by INAA-SLR. The content of Ca, Cl, I, K, Mg, Mn, and Na 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). After non-destructive INAA-SLR investigation the thyroid samples were used for ICP-AES. The samples were decomposed in autoclaves and aliquots of solutions were used to determine the Al, B, Ba, Ca, Cu, Fe, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractions by ICP-AES using the Spectrometer ICAP-61 (Thermo Jarrell Ash, USA). Information detailing with the NAA-SLR and ICP-AES methods used and other details of the analysis were presented in our earlier publications concerning ChE contents in human thyroid [33,34], prostate [48-52], and scalp hair [53].

To determine contents of the ChE by comparison with a known standard, biological synthetic standards (BSS) prepared from phenol-formaldehyde resins were used [54]. In addition to BSS, aliquots of commercial, chemically pure compounds were also used as standards. Ten sub-samples of certified reference material (CRM) IAEA H-4 (animal muscle) and five sub-samples of CRM of the Institute of Nuclear Chemistry and Technology (INCT, Warszawa, Poland) INCT-SBF-4 Soya Bean Flour, INCT-TL-1 Tea Leaves, and INCT-MPH-2 Mixed Polish Herbs were treated and analyzed in the same conditions that thyroid samples to estimate the precision and accuracy of results A dedicated computer program for INAA-SLR mode optimization was used [55]. All thyroid samples for ChEs analysis were prepared in duplicate and mean values of ChEs contents were used in final calculation. Mean values of ChE contents were used in final calculation for the Ca, K, Mg, Mn, and Na mass fractions measured by two methods. Using Microsoft Office Excel software, a summary of the statistics, including, arithmetic mean, standard deviation, standard error of mean, minimum and maximum values, median, percentiles with 0.025 and 0.975 levels was calculated for ChEs contents in nodular and adjacent tissue of thyroids with TBNs. Data for "normal" thyroid were taken from our previous publications [42-45]. The difference in the results between three groups of samples ("normal", "nodular", and "adjacent") was evaluated by the parametric Student's t-test and non-parametric Wilcoxon-Mann-Whitney U-test.

Results

Table 1: Some statistical parameters of Al, B, Ba, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fraction (mg/kg, dry mass basis) in (nodular and adjacent tissue of thyroid benign nodules (TBN)

Tissue	Element	Mean	SD	SEM	Min	Max	Median	P 0.025	P 0.975
TBN adjacent tissue	Al	25.7	14.3	7.1	16.1	46.7	19.9	16.2	44.8
	B	1.7	0.61	0.35	1	2.1	2	1.05	2.09
	Ba	1.53	1.28	0.64	0.42	3.3	1.2	0.449	3.17
	Ca	1537	1700	380	418	6466	994	442	6312
	Cl	9203	6033	1384	2881	23731	8161	3294	22429
	Cu	10.2	7.9	4	3.6	20.4	8.35	3.65	19.8
	Fe	217	142	24	41.5	620	171	58.2	557
	I	2158	1436	214	343	7912	1917	527	5441
	K	6764	4054	864	3406	18255	5392	3500	18077
	Li	0.035	0.022	0.011	0.0175	0.0666	0.0279	0.018	0.064
	Mg	316	275	59	15	987	292	15	890
	Mn	1.78	1.65	0.36	0.1	5.83	1.1	0.1	5.67
	Na	10850	5541	1209	4663	31343	9642	5548	23981
	P	4361	1095	548	3176	5824	4222	3248	5711
	S	9689	1251	625	8071	11122	9781	8196	11024
	Si	135	65	33	87.1	228	112	87.5	221
	Sr	6.28	5.17	2.59	1.3	13.5	5.15	1.54	12.9
	V	0.17	0.116	0.067	0.079	0.3	0.13	0.082	0.292
	Zn	105	68	12	34.2	344	86.4	44.1	304
TBN nodular tissue	Al	27.3	23.6	4.2	6.6	95.1	19.5	7.07	82.2
	B	1.97	1.69	0.31	0.81	7.3	1	0.875	5.63
	Ba	1.7	2.42	0.43	0.18	11.7	0.96	0.265	0.988
	Ca	1313	860	131	52	4333	1169	120	3536
	Cl	8231	3702	772	1757	16786	8326	2543	15157
	Cu	10.2	9.2	1.7	2.9	35.2	6	3.04	34.9
	Fe	332	332	39	52.3	1360	197	59.9	1285
	I	1086	1219	139	29	8260	700	84.8	3734
	K	7051	3955	577	797	23007	6298	1577	19908
	Li	0.0295	0.0151	0.003	0.0073	0.068	0.0253	0.0096	0.0669
	Mg	344	155	23	15	844	326	66.8	745
	Mn	1.81	1.41	0.21	0.1	6.12	1.44	0.454	5.48
	Na	10675	4434	647	2319	28481	10118	3690	18451
	P	5145	1719	304	2890	9637	5030	2933	9091
	S	10909	2177	385	5591	16706	10719	7353	15361
	Si	90.4	68.3	12.3	7.8	346	83.7	13.4	223
	Sr	5.35	7.09	0.99	0.42	32	2.52	0.788	29.3
	V	0.152	0.066	0.012	0.043	0.37	0.15	0.0606	0.289
	Zn	117.7	48.7	5.8	47	264	110	49.8	253

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 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 Al, B, Ba, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fraction in nodular and adjacent to nodules tissue of thyroid with TBN ("nodular" and "adjacent" group of thyroid tissue samples). The ratios of means and the comparison of mean values of Al, B, Ba, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fractions in pairs of sample groups such as "normal" and "nodular", "normal" and "adjacent", and also "adjacent" and "nodular" are presented in Tables 2, 3 & 4, respectively.

Table 2: Differences between mean values (M+SEM) of Al, B, Ba, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fraction (mg/kg, dry mass basis)) in normal thyroid (NT) and thyroid benign nodules (TBN) (nodular tissue).

Element	Thyroid Tissue				Ratio
	NT	TBN nodular	Student's t-test p ≤	U-test p	TBN nodular/NT
Al	10.5±1.8	27.3±4.2	**0.00059**	**≤0.01**	2.6
B	0.476±0.058	1.97±0.31	**0.00042**	**≤0.01**	4.14
Ba	1.12±0.15	1.70±0.43	0.209	>0.05	1.52
Ca	1682±106	1313±131	**0.031**	**≤0.01**	0.78
Cl	3400±174	8231±772	**2.5E-06**	**≤0.01**	2.42
Cu	4.08±0.14	10.2±1.7	**0.0014**	**≤0.01**	2.5
Fe	223±10	332±39	**0.0085**	**≤0.01**	1.49
I	1841±107	1086±139	**0.00003**	**≤0.01**	0.59
K	6418±290	7051±577	0.33	>0.05	1.1
Li	0.0208±0.0022	0.0295±0.0030	**0.017**	**≤0.01**	1.42
Mg	296±16	344±23	0.092	>0.05	1.16
Mn	1.28±0.07	1.81±0.21	**0.022**	**≤0.01**	1.41
Na	6928±175	10675±647	**8E-07**	**≤0.01**	1.54
P	4290±207	5145±304	**0.023**	**≤0.01**	1.2
S	8259±263	10909±385	**4.1E-07**	**≤0.01**	1.32
Si	50.8±6.2	90.4±12.3	**0.006**	**≤0.01**	1.78
Sr	3.81±0.34	5.35±0.99	0.15	>0.05	1.4
V	0.102±0.005	0.152±0.012	**0.00065**	**≤0.01**	1.49
Zn	94.8±4.2	117.7±5.8	**0.0018**	**≤0.01**	1.24

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

Discussion

As was shown before [33,34,48-53] good agreement of the Al, B, Ba, Br, Ca, Cl, Cu, Fe, I, K, Mg, Mn, Na, P, S, Sr, V, and Zn mass fractions in CRM IAEA H-4, INCT-SBF-4, INCT-TL-1, and INCT-MPH-2 samples determined by both INAA-SLR and ICP-AES methods with the certified data of these CRMs indicates acceptable accuracy of the results obtained in the study of thyroid tissue samples presented in Tables 1–4. The Al, B, Cl, Cu, Fe, Li, Mn, Na, P, S, Si, V, and Zn contents in "nodular" tissue were higher, while Ca and I content was lower in comparison with contents of these ChEs in normal gland (Table 2). Significant differences between ChEs contents of "normal" thyroid and ChEs contents of thyroid tissue adjacent to nodules were found for Cl and Na. Mass fractions of Cl and Na in "adjacent" group of samples were approximately 2.7, and 1.6 times, respectively, higher than in "normal" thyroid (Table 3). In a general sense Al, B, Ba, Br, Ca, Cl, Cu, K, Mg, Mn, Na, P, S, Sr, V, and Zn contents found in the "nodular" and "adjacent" groups of thyroid tissue samples were very similar (Table 4). However, mass fraction of Fe was lower, while mass fraction of I was higher in "adjacent" group of samples (Table 4). At that, level of I in "adjacent" group of samples was over 2 times higher than in nodular tissue (Table 4) and almost equals the normal value (Table 3).

Table 3: Differences between mean values (M±SEM) of Al, B, Ba, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fraction (mg/kg, dry mass basis)) in normal thyroid (NT) and thyroid tissue adjacent to benign nodules (TBN adjacent)

Element	Thyroid Tissue				Ratio
	NT	TBN adjacent	Student's t-test p≤	U-test p	TBN adjacent/NT
Al	10.5±1.8	25.7±7.1	0.12	>0.05	2.45
B	0.476±0.058	1.70±0.35	0.07	>0.05	3.57
Ba	1.12±0.15	1.53±0.64	0.576	>0.05	1.37
Ca	1682±106	1537±380	0.716	>0.05	0.91
Cl	3400±174	9203±1384	**0.00056**	**≤0.01**	2.71
Cu	4.08±0.14	10.2±4.0	0.221	>0.05	2.5
Fe	223±10	217±24	0.827	>0.05	0.97
I	1841±107	2158±214	0.188	>0.05	1.17
K	6418±290	6764±864	0.707	>0.05	1.05
Li	0.0208±0.0022	0.035±0.011	0.288	>0.05	1.68
Mg	296±16	316±59	0.752	>0.05	1.07
Mn	1.28±0.07	1.78±0.36	0.188	>0.05	1.39
Na	6928±175	10850±1209	**0.0042**	**≤0.01**	1.57
P	4290±207	4361±548	0.91	>0.05	1.02
S	8259±263	9689±625	0.1	>0.05	1.17
Si	50.8±6.2	135±33	0.08	>0.05	2.66
Sr	3.81±0.34	6.28±2.59	0.413	>0.05	1.65
V	0.102±0.005	0.170±0.067	0.418	>0.05	1.67
Zn	94.8±4.2	105±12	0.409	>0.05	1.11

M - arithmetic mean, SEM - standard error of mean, statistically significant values are in bold.

Table 4: Differences between mean values (M±SEM) of Al, B, Ba, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn mass fraction (mg/kg, dry mass basis) in nodular (TBN nodular) and thyroid tissue adjacent to benign nodules (TBN adjacent).

Element	Thyroid Tissue				Ratio
	TBN adjacent	TBN nodular	Student's t-test p≤	U-test p	Nodular/adjacent
Al	25.7±7.1	27.3±4.2	0.848	>0.05	1.06
B	1.70±0.35	1.97±0.31	0.588	>0.05	1.16
Ba	1.53±0.64	1.70±0.43	0.828	>0.05	1.11
Ca	1537±380	1313±131	0.583	>0.05	0.85
Cl	9203±1384	8231±772	0.545	>0.05	0.89
Cu	10.2±4.0	10.2±1.7	0.999	>0.05	1
Fe	217±24	332±39	**0.014**	**≤0.01**	1.53
I	2158±214	1086±139	**0.000068**	**≤0.01**	0.5
K	6764±864	7051±577	0.784	>0.05	1.04
Li	0.035±0.011	0.0295±0.0030	0.656	>0.05	0.84
Mg	316±59	344±23	0.662	>0.05	1.09
Mn	1.78±0.36	1.81±0.21	0.946	>0.05	1.02
Na	10850±1209	10675±647	0.899	>0.05	0.98
P	4361±548	5145±304	0.265	>0.05	1.18
S	9689±625	10909±385	0.151	>0.05	1.13
Si	135±33	90.4±12.3	0.274	>0.05	0.67
Sr	6.28±2.59	5.35±0.99	0.754	>0.05	0.85
V	0.170±0.067	0.152±0.012	0.821	>0.05	0.89
Zn	105±12	117.7±5.8	0.351	>0.05	1.12

M - arithmetic mean, SEM - standard error of mean, statistically significant values are in **bold**.

Characteristically, elevated or reduced levels of ChEs 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 ChEs in affected thyroid tissues researchers try to determine the role of the deficiency or excess of each ChEs in the etiology and pathogenesis of thyroid diseases. In our opinion, abnormal levels of many ChEs in TBNs 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 ChEs level in pathologically altered tissue is the reason for alterations or vice versa. According to our opinion, investigation of ChEs contents in thyroid tissue adjacent to nodules and comparison obtained results with ChEs levels typical of "normal" thyroid gland may give additional useful information on the topic because this data show conditions of tissue in which TBNs were originated and developed. For example, results of this study demonstrated that contents of Cl and Na in thyroid "adjacent" tissue in which TBNs were originated and developed were significantly higher the levels which are "normal" for thyroid gland, while content of I was "normal". In turn, in nodular tissue content of Fe was significantly higher, whereas content of I was almost 2 times lower than in tissues adjacent to nodules.

Chlorine and sodium

Cl and Na are ubiquitous, extracellular electrolytes essential to more than one metabolic pathway. In the body, Cl and Na mostly present as sodium chloride. Therefore, as usual, there is a correlation between Na and Cl contents in tissues and fluids of human body. Because Cl is halogen like I, in the thyroid gland the biological behavior of chloride has to be similar to the biological behavior of iodide. The main source of natural Cl for human body is salt in food and chlorinated drinking water. Environment (air, water and food) polluted by artificial nonorganic Cl-contained compounds, for example such as sodium chlorate ($NaClO_3$), and organic Cl-contained compounds, for example such as polychlorinated biphenyls (PCBs) and dioxin, is other source. There is a clear association between using chlorinated drinking water, levels NaClO3, PCBs and dioxin in environment and thyroid disorders, including cancer [56-60]. Thus, on the one hand, the accumulated data suggest that Cl level in thyroid tissue might be responsible for TBNs development. However, on the other hand, it is well known that Cl and Na mass fractions in human tissue samples depend mainly on the extracellular water volume [61]. Nodular and adjacent to nodules thyroid tissues can be more vascularized and can contain more relative volume of colloid that normal thyroid. Because blood and colloid are extracellular liquids, it is possible to speculate that it could be the reason for elevated levels of Cl and Na in TBNs and adjacent tissue. If that is the case the equilibrium between Cl and Na increases has to be, however, in comparison with "normal" thyroid the change of Cl level in TBNs and adjacent tissue is significantly higher than change of Na level. Thus, it is possible to assume that an excessive accumulation of Cl in thyroid tissue is involved in TBNs etiology. Overall, the elevated levels of Cl in thyroid tissue could possibly be explored as risk factor of TBNs.

Iron

It is well known that Fe as TEs is involved in many very important functions and biochemical reactions of human body. Fe metabolism is therefore very carefully regulated at both a systemic and cellular level [62,63]. Under the impact of age and multiple environmental factors the Fe metabolism may become dysregulated with attendant accumulation of this metal excess in tissues and organs, including thyroid [25,26,29-35]. Most experimental and epidemiological data support the hypothesis that Fe overload is a risk factor for benign and malignant tumors [64]. This goitrogenic and oncogenic effect could be explained by an overproduction of ROS and free radicals [65]. Thus, on the one hand, the accumulated data suggest that Fe might be responsible for TBNs development. But, on the other hand, the elevated level of Fe was not found in thyroid tissue adjacent to nodules. It is well known that blood is the main pool for Fe in human body and therefore high vascularisation of nodular tissue may be the reason for Fe elevated levels in TBNs [66].

Iodine

To date, it was well established that I deficiency or excess has severe consequences on human health and associated with the presence of TBNs [5-8,67]. However, in present study neither reduced nor elevated levels of I in thyroid tissue adjacent to nodules in comparison with "normal" thyroid tissue were not found. 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 present study, benign nodular transformation is probably accompanied by a partial loss of tissue-specific functional features, which leads to a modest reduction in I content associated with functional characteristics of the human thyroid tissue. Little reduced level of I content in nodular tissue could possibly be explored for differential diagnosis of TBNs and thyroid cancer, because, as was found in our ealier studies, thyroid malignant trasformation is accompanied by a drastically loss of I accumulation [18, 68-70].

Limitations

This study has several limitations. Firstly, analytical techniques employed in this study measure only nineteen ChE (Al, B, Ba, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn) mass fractions. Future studies should be directed toward using other analytical methods which will extend the list of ChEs investigated in "normal" thyroid and in pathologically altered tissue. Secondly, the sample size of TBNs group was relatively small and prevented investigations of ChEs contents in this group using differentials like gender, histological types of TBNs, nodules functional activity, stage of disease, and dietary habits of patients with TBNs. Lastly, generalization of our results may be limited to Russian population. Despite these limitations, this study provides evidence on many ChEs level alteration in nodular and adjacent to nodule tissue and shows the necessity to continue ChEs research of TBNs.

Conclusion

In this work, ChEs analysis was carried out in the tissue samples of TBNs using a combination of non-destructive INAA-SLR and destructive ICP-AES methods. It was shown that this combination is an adequate analytical tool for the determination of Al, B, Ba, Ca, Cl, Cu, Fe, I, K, Li, Mg, Mn, Na, P, S, Si, Sr, V, and Zn content in the tissue samples of human thyroid in norm and pathology, including needle-biopsy specimens. It was observed that mass fractions of Al, B, Cl, Cu, Fe, Li, Mn, Na, P, S, Si, V, and Zn contents in "nodular" tissue were higher, while Ca and I content was lower in comparison with contents of these ChEs in normal gland. Mass fractions of Cl and Na in "adjacent" group of samples were approximately 2.7 and 1.6 times, respectively, higher than in "normal" thyroid. Contents of Al, B, Ba, Br, Ca, Cl, Cu, K, Mg, Mn, Na, P, S, Sr, V, and Zn found in the "nodular" and "adjacent" groups of thyroid tissue samples were very similar, however, mass fraction of Fe was lower, while mass fraction of I was higher in "adjacent" group of samples. At that, level of I in "adjacent" group of samples was over 2 times higher than in nodular tissue and almost equals the normal value.

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