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Relationships Between Iodine and Some Chemical Elements in Normal Thyroid of Males Investigated by Short Neutron Activation

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Received: Jan 10, 2023
Accepted: Feb 17, 2023
Published Online: Feb 24, 2023
Journal: Annals of Community Medicine and Primary Health Care
Publisher: MedDocs Publishers LLC
Online edition: http://meddocsonline.org/

Keywords: Thyroid; Chemical elements; Age-related changes; Intrathyroidal chemical elements relationships; Neutron activation analysis.

Abstract

Thyroid diseases rank second among endocrine disorders, and prevalence of the diseases is higher in the elderly as compared to the younger population. An excess or deficiency of chemical element contents in thyroid play important role in goitro- and carcinogenesis of gland. The correlations with age of the eight chemical element (ChE) contents (Br, Ca, Cl, I, K, Mg, Mn, and Na), I/Br, I/Ca, I/Cl, I/K, I/Mg,, I/Mn, and I/Na content ratios, and inter relationships between ChE contents and I/ChE content ratios in normal thyroid of 73 males (mean age 37.3 years, range 2.0-80) was investigated by instrumental neutron activation analysis with high resolution spectrometry of short-lived radionuclides. Our data reveal that the I and Ca contents, as well as I/K and I/Mn content ratios increase, while K and Mn decrease in the normal thyroid of male during a lifespan. Therefore, a goitrogenic and tumorogenic effect of excessive I and Ca level in the thyroid of old males and of disturbance in intrathyroidal I/K and I/Mn relationships with increasing age may be assumed. Furthermore, it was found that the levels of Br, Ca, Cl, K, Mg, Mn, and Na in the thyroid gland are interconnected and depend on the content of I in it. Because I plays a decisive role in the function of the thyroid gland, the data obtained allow us to conclude that, along with I, such ChE as Br, Ca, Cl, K, Mg, Mn, and Na, if not directly, then indirectly, are involved in the process of thyroid hormone synthesis.

Introduction

According to the World Health Organization (WHO), thyroid diseases rank second among endocrine disorders after diabetes mellitus. More than 665 million people in the world have endemic goiter or suffer from other thyroid pathologies. At the same time, according to the same statistics, the increase in the number of thyroid diseases in the world is 5% per year [1]. It has been suggested that risk factors for the development of thyroid disorders may be numerous factors, including genetics, radiation, autoimmune diseases, as well as adverse environmental factors, such as an increase in the content of various chemicals in the environment [2].

Chemical elements (ChE) are among these various chemicals, because their levels in the environment have increased significantly over the past hundred years as a result of the industrial revolution and the tremendous technological changes that have taken place in metallurgy, chemical production, electronics, agriculture, food processing and storage, cosmetics, pharmaceuticals and medicine. In connection with these changes, the levels and ratio of ChE entering the human body from the outside have been significantly disturbed, compared with the conditions in which human societies have lived for many millennia.

Cite this article: Zaichick V. Relationships Between Iodine and Some Chemical Elements in Normal Thyroid of Males Investigated by Short Neutron Activation. Ann Community Med Prim Health Care. 2023; 2(1): 1016.

More than 50 years ago, we formulated the postulate about the somatic ChE homeostasis, which is now generally recognized [3]. According to this postulate, under evolutionary environmental conditions, the mechanisms of homeostasis of organisms maintain the levels and ratios of ChE in tissues and organs within certain limits. If the content of ChE in the environment changes significantly, the mechanisms of somatic homeostasis may respond inadequately. Inadequate response of homeostasis mechanisms leads to changes in ChE levels in tissues and organs, which, in turn, can affect their function and lead to the development of pathological conditions. The correctness of this conclusion was illustrated by us earlier on the example of the study of the role of ChE in the normal and pathophysiology of the prostate [4-24]. It was shown, in particular, that a special role in the development of pathological transformations of the prostate is played by disturbances in the relationship between ChE in the tissue and gland secretion. Moreover, it was found that changes in the relationship between ChE can be used as highly informative markers of various prostate diseases, including malignant tumors [25-39]. These findings stimulated our investigations of ChE relationships in thyroid tissue in normal and pathological conditions.

There are many studies regarding ChE content in human thyroid, using chemical techniques and instrumental methods [40-51]. However, among the published data, no works on the relationship of ChE in the normal human thyroid were found.

This work had three aims. The primary purpose of this study was to determine reliable values for the bromine (Br), calcium (Ca), chlorin (Cl), iodine (I), potassium (K), magnesium (Mg), manganese (Mn), and sodium (Na) mass fractions in the normal thyroid of subjects ranging from children to elderly males using instrumental neutron activation analysis with high resolution spectrometry of short-lived radionuclides (INAA-SLR) and calculate individual values of I/Br, I/Ca, I/Cl, I/K, I/Mg, I/Mn, and I/Na. The second aim was to compare the Br, Ca, Cl, I, K, Mg, Mn, and Na mass fractions in thyroid gland obtained in the study with published data. The final aim was to estimate the inter-thyroidal correlations between ChE contents and between I/ChE content ratios in normal thyroid of males and changes of these parameters with age.

All studies were approved by the Ethical Committees of the Medical Radiological Research Centre, Obninsk. 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.

Materials and Methods

Samples of the human thyroid were obtained from randomly selected autopsy specimens of 73 males (European-Caucasian) aged 2.0 to 80 years. All the deceased were citizens of Obninsk and had undergone routine autopsy at the Forensic Medicine Department of City Hospital, Obninsk. The available clinical data were reviewed for each subject. None of the subjects had a history of an intersex condition, endocrine disorder, or other chronic disease that could affect the normal development of the thyroid. None of the subjects were receiving medications or used any supplements known to affect thyroid ChE contents. The typical causes of sudden death of most of these subjects included trauma or suicide and also acute illness (cardiac insufficiency, stroke, embolism of pulmonary artery, alcohol poisoning). All right lobes of thyroid glands were divided into two portions using a titanium scalpel [52]. One tissue portion was reviewed by an anatomical pathologist while the other was used for the ChE content determination. A histological examination was used to control the age norm conformity as well as the unavailability of microadenomatosis and latent cancer.

After the samples intended for ChE analysis were weighed, they were transferred to -20°C and stored until the day of transportation in the Medical Radiological Research Center, Obninsk, where all samples were freeze-dried and homogenized [53]. To determine the contents of the ChE by comparison with a known standard, aliquots of commercial, chemically pure compounds were used [54]. Ten subsamples of the Certified Reference Material (CRM) IAEA H-4 (animal muscle) and IAEA HH-1 (human hair) were analyzed to estimate the precision and accuracy of results. The CRM IAEA H-4 and IAEA HH-1 subsamples were prepared in the same way as the samples of dry homogenized thyroid tissue.

The pounded sample weighing about 100 mg was used for ChE measurement by INAA-SLR. The samples for INAA-SLR were sealed separately in thin polyethylene films washed beforehand with acetone and rectified alcohol. The sealed samples were placed in labeled polyethylene ampoules. The content of Br, 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. The neutron flux in the channel was 1.7×10^{13}n cm^{-2} s^{-1}. Ampoules with thyroid tissue samples, intralaboratory-made standards, and certified reference material were put into polyethylene rabbits and then irradiated separately for 180 s. Copper foils were used to assess neutron flux. The measurement of each sample was made twice, 1 and 120 min after irradiation. The duration of the first and second measurements was 10 and 20 min, respectively. A coaxial 98-cm^3 Ge (Li) detector and a spectrometric unit (NUC 8100), including a PC-coupled multichannel analyzer, were used for measurements. The spectrometric unit provided 2.9-keV resolution at the ^{60}Co 1,332-keV line. Details of used nuclear reactions, radionuclides, and gamma-energies were presented in our earlier publications concerning the INAA-SLR of ChE contents in human prostate and scalp hair [55-58].

A dedicated computer program for INAA-SLR mode optimization was used [59]. All thyroid samples were prepared in duplicate, and mean values of ChE contents were used in final calculation. Using Microsoft Office Excel, 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 ChE contents and I/ ChE content ratios. Pearson's correlation coefficient was used in Microsoft Office Excel to calculate the relationship "age – ChE mass fraction" and "age – I/ChE mass fraction", as well as to identify inter-thyroidal relationships between different ChE contents and between different ChE content ratios.

Results

Table 1 depicts comparison of our data for seven ChE in ten sub-samples of CRM IAEA H-4 (animal muscle) and IAEA HH-1 (human hair) with the corresponding certified values of ChE contents in these materials.

Table 2 represents 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 Br, Ca, Cl, I, K, Mg, Mn, and Na mass fractions, as well as I/Br, I/Ca, I/Cl, I/K, I/Mg, I/Mn, and I/Na mass fraction ratios in normal thyroid of males.

The comparison of our results with published data for the Br, Ca, Cl, I, K, Mg, Mn, and Na contents in the human thyroid is shown in **Table 3.**

To estimate the effect of age on the ChE contents and I/ ChE content ratios Pearson's correlation coefficient was used **(Table 4)**.

The data of inter-thyroidal correlation (values of *r* – Pearson's coefficient of correlation) including all ChE and I/ChE content ratios identified by us are presented in **Tables 5 and 6,** respectively.

Figure 1: NAASLR data of Br, Ca, Cl, I, K, Mg, Mn, and Na contents in certified reference material IAEA H-4 (animal muscle) and IAEA HH-1 (human hair) compared to certified values (mg/kg, dry mass basis).

Element	IAEA H-4 animal muscle	This work results	IAEA HH-1 human hair	This work results
Br	4.1 ± 1.1[a]	5.0 ± 09	4.2 ± 2.1[b]	3.9 ± 1.6
Ca	188 ± 58[b]	238 ± 59	522 ± 160[a]	525 ± 42
Cl	1890 ± 130[b]	1950 ± 230	2265 ± 478[a]	2210 ± 340
I	0.08 ± 0.10[b]	<1.0	20.3 ± 8.9[b]	19.1 ± 6.2
K	15840 ± 1440[a]	16200 ± 3800	9.2 ± 5.2[b]	10.7 ± 4.0
Mg	1050 ± 140[a]	1100 ± 190	62.0 ± 9.6[b]	64.7 ± 18.6
Mn	0.52 ± 0.08[a]	0.55 ± 0.11	0.85 ± 0.25[a]	0.93 ± 0.16
Na	2060 ± 330[a]	2190 ± 140	12.6 ± 4.8[b]	14.0 ± 2.7

M – arithmetical mean, SD – standard deviation, a – certified values, b – information values.

Table 2: Some statistical parameters of Br, Ca, Cl, I, K, Mg, Mn, and Na mass fraction (mg/kg, dry mass basis) as well as I/Br, I/Ca, I/Cl, I/K, I/Mg, I/Mn, and I/Na mass fraction ratios in normal thyroid of male (n=73).

Element	Mean	SD	SEM	Min	Max	Median	P 0.025	P 0.975
Br	13.7	7.8	1.0	1.90	32.3	10.2	2.50	30.7
Ca	1703	1048	131	414	6230	1470	452	4163
Cl	3449	1450	219	1030	5920	3470	1262	5657
I	1786	940	118	220	4205	1742	239	3808
K	6289	2594	329	2440	14300	5670	2622	12670
Mg	306	143	19	99.0	930	287	107	572
Mn	1.31	0.49	0.07	0.510	2.30	1.30	0.534	2.21
Na	6820	1781	214	3050	13453	6680	3861	11350
I/Br	179	133	18	9.81	576	138	28.7	473
I/Ca	1.40	1.26	0.17	0.136	7.45	1.00	0.188	4.53
I/Cl	0.729	0.544	0.082	0.0943	2.64	0.587	0.211	2.21
I/K	0.366	0.287	0.039	0.0209	1.30	0.289	0.0257	1.09
I/Mg	7.76	6.79	0.99	0.551	29.3	6.41	0.712	25.4
I/Mn	1609	1362	199	200	7102	1334	233	5389
I/Na	0.284	0.166	0.021	0.0275	0.728	0.253	0.0357	0.605

Mean – 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 3: Median, minimum and maximum value of means Br, Ca, Cl, I, K, Mg, Mn, and Na contents in normal human thyroid according to data from the literature in comparison with our results (mg/kg, dry mass basis).

Element	Published data [Reference]			This work
	Median of means (n)*	Minimum of means M or M±SD, (n)**	Maximum of means M or M±SD, (n)**	M ± SD
Br	18.1 (11)	5.12 (44) [40]	284 ± 44 (14) [41]	13.7 ± 7.8
Ca	1600 (17)	840 ± 240 (10)[42]	3800 ± 320 (29) [42]	1703 ± 1048
Cl	6800 (5)	804 ± 80 (4)[43]	8000 (-) [44]	3449 ± 1450
I	1888 (95)	159 ± 8 (23)[45]	5772 ± 2708 (50) [46]	1786 ± 940
K	4400 (17)	46.4 ± 4.8 (4) [43]	6090 (17) [47]	6289 ± 2594
Mg	390 (16)	3.5 (-) [48]	840 ± 400 (14) [49]	306 ± 143
Mn	1.82 (36)	0.44 ± 11(12) [50]	69.2 ± 7.2 (4) [43]	1.31 ± 0.49
Na	8000 (9)	438 (-) [51]	10000 ± 5000 (11) [49]	6820 ± 1781

M –arithmetic mean, SD – standard deviation, (n)* – number of all references, (n)** – number of samples.

Table 4: Correlations between age (years) and chemical element content (mg/kg, dry tissue), as well as between age and I/chemical element mass fraction ratios in the normal thyroid of males (*r* – coefficient of correlation).

Element	Br	Ca	Cl	I	K	Mg	Mn	Na
r	0.11	0.41[c]	0.11	0.32[b]	-0.32[a]	0.10	-0.38[b]	-0.10
Ratio	I/Br	I/Ca	I/Cl	I/K	I/Mg	I/Mn	I/Na	-
r	0.15	0.15	0.06	0.40[b]	0.24	0.43[b]	0.23	-

Significant values: [a] $p\leq0.05$, [b]$p\leq0.01$, [c] $p\leq0.001$.

Table 5: Intercorrelations of the chemical element mass fractions in the normal thyroid of male (r – coefficient of correlation).

Element	Br	Ca	Cl	I	K	Mg	Mn	Na
Br	**1.00**	0.06	-0.26[a]	0.05	0.03	-0.08	0.09	-0.08
Ca	0.06	**1.00**	-0.19	0.08	-0.21	0.30[a]	0.03	-0.17
Cl	-0.26[a]	-0.19	**1.00**	0.08	-0.46[b]	0.09	-0.19	0.53[c]
I	0.05	0.081	0.08	**1.00**	-0,20	-0.21	-0.14	-0.10
K	0.03	-0.21	-0.46[b]	-0,20	**1.00**	0.27[a]	-0.05	0.08
Mg	-0.08	0.30[a]	0.09	-0.21	0.27[a]	**1.00**	0.16	0.27[a]
Mn	0.09	0.03	-0.19	0.14	-0.05	0.16	**1.00**	-0.01
Na	-0.08	-0.17	0.53[c]	-0.10	0.08	0.27[a]	-0.01	**1.00**

Significant values: [a] $p\leq0.05$, [b] $p\leq0.01$, [c] $p\leq0.001$.

Table 6: Intercorrelations of the I/chemical element mass fraction ratios in the normal thyroid of male (*r* – coefficient of correlation).

Element	I/Br	I/Ca	I/Cl	I/K	I/Mg	I/Mn	I/Na
I/Br	**1.00**	0.322[a]	0.172	0.395[b]	0.314[a]	0.353[a]	0.446[c]
I/Ca	0.322[a]	**1.00**	0.012	0.434[b]	0.719[c]	0.701[c]	0.423[b]
I/Cl	0.172	0.012	**1.00**	0.185	0.654[c]	0.330[a]	0.771[c]
I/K	0.395[b]	0.434[b]	0.185	**1.00**	0.741[c]	0.568[c]	0.723[c]
I/Mg	0.314[a]	0.719[c]	0.654[c]	0.741[c]	**1.00**	0.637[c]	0.799[c]
I/Mn	0.353[a]	0.701[c]	0.330[a]	0.568[c]	0.637[c]	**1.00**	0.591[c]
I/Na	0.446[c]	0.423[b]	0.771[c]	0.723[c]	0.799[c]	0.591[c]	**1.00**

Significant values: [a] $p\leq0.05$, [b] $p\leq0.01$, [c] $p\leq0.001$

Conclusion

The INAA-SLR is a useful analytical tool for the non-destructive determination of ChE contents in the thyroid tissue samples. This method allows determine means for Br, Ca, Cl, I, K, Mg, Mn, and Na (eight ChE).

Our data reveal that the I and Ca contents, as well as I/K and I/Mn content ratios increase, while K and Mn decrease in the normal thyroid of male during a lifespan. Therefore, a goitrogenic and tumorogenic effect of excessive I and Ca level in the thyroid of old males and of disturbance in intrathyroidal I/K and I/Mn relationships with increasing age may be assumed. Furthermore, it was found that the levels of Br, Ca, Cl, K, Mg, Mn, and Na in the thyroid gland are interconnected and depend on the content of I in it. Because I plays a decisive role in the function of the thyroid gland, the data obtained allow us to conclude that, along with I, such ChE as Br, Ca, Cl, K, Mg, Mn, and Na, if not directly, then indirectly, are involved in the process of thyroid hormone synthesis.

Acknowledgements

We are grateful to Dr. Yu. Choporov, Head of the Forensic Medicine Department of City Hospital, Obninsk, for supplying thyroid samples.

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