FLUORINE EFFECT ON FUNCTION OF THE PITUITARY-THYROID SYSTEM IN THE BODY OF HEALTHY PERSONS AND PATIENTS WITH THYROPATHIES

It is known that fluorine and iodine can exhibit antagonistic effects in certain processes in humans, animals and plants [7, 10, 14].

Residents of central Ukraine who use the water from the Buchaksko-Kanevsk water-bearing horizon, in connection with its high fluorine content (79-526 _mol/L), can consume fluorine in an amount from 2.5 to 50 _mol per kg of body weight per day, compared to the norm of 1-2.3 _mol/kg. The concentration of fluorine in drinking water according to GOST [All-Union State Standard] 2874-73 can be up to 1.5 mg/L, i.e., up to 79 _mol/L[1] [4, 7, 9, 13].

The results of studies of the effect of fluorine on the functional status of the thyroid are unclear. There is a report [8] indicating that long-term consumption of water that has a high fluorine content had a depressive effect on the functional status of the thyroid in white rats, beginning with a fluorine concentration in drinking water of 263-268 _mol/L, which corresponded to 13-18 _mol per kg of body weight. The effect of fluorine in doses of 18-26 _mol/kg (368-526 _mol/L) was manifested not in depression, but rather, in activation of the thyroid function.

A number of authors [2, 6, 8] showed that a fluorine concentration in drinking water from 102 to 421 _mol/L did not have a significant effect on the activity of the thyroid in humans: enlargement of the thyroid, accumulation of radioactive iodine in the thyroid, or an increase of the rate of disease of this organ were not seen. A. S. Kas'yanenko [7] suggests possible disruption of iodine metabolism and depression of the thyroid function when there is elevated ingestion of fluorine (79-526 _mol/L). It was also noted that thyroid disorders are seen significantly more often among people consuming an elevated quantity of fluorine [11, 12].

In connection with the fact that disruption of thyroid function is seen in people who are at the foci of endemic fluorosis, it is important to investigate the concentration of fluorine not just in the drinking water, but also in the blood and urine, which is necessary for a more accurate judgment concerning the kinetics of this chemical element in the body.

Our goal was a simultaneous study of the functional status of the pituitary-thyroid system and identification of a correlation between the concentration of fluorine in the drinking water and the concentration of fluoride in the body of healthy subjects and patients with hypo- and hyperfunction of the thyroid who are permanent residents in areas with different concentrations of fluorine in the drinking water.

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[1] In the further exposition the concentration of fluorine in milligrams per liter or in milligrams per kg is given in micromoles per liter or in micromoles per kg, in accordance with the International System of Units.

Materials and Methods

123 subjects were studied: 26 with pathology of the thyroid: 43 with thyroid hyperfunction (ages 18 to 58), 33 with thyriod hypofunction (ages 20 to 55); the control group consisted of 47 essentially healthy subjects aged 19 to 59 years. The subjects lived in two regions. Region I had a normal level of fluorine in the drinking water; while region II had an elevated concentration of fluorine.

The intrathyroid phase of iodine metabolism (absorption of ^{131}I by the thyroid) was investigated by the generally accepted technique. The hormonal activity of the pituitary (concentration of thyrotropic hormone – TSH) was determined using the TSHK-PR test kit (Cea Sorin). The concentration of thyroid hormones in the blood was investigated: total thyroxin (T_4) using a kit from the Buk-Mallinckrodt Co. (SPAC-T_4), and triiodothyronin (T_3) using the TRIK-PEG kit (Cea Sorin).

The determination of the concentration of fluorine in the drinking water, erythrocytes, blood serum and urine was carried out in accordance with L. A. Golovanova [5] using the EF U-1 fluorine-selective electrode.

Results and Discussion

The results (Table 1) indicated hyperfunction of the thyroid in 43 patients (elevation of concentration of T_3 and T_4 in the blood serum in combination with elevated absorption of radioactive ^{131}I) and hypofunction in 33 patients (reduction of concentration of T_3 and T_4 in blood serum in combination with depression of absorption of ^{131}I).

In the control group a decrease of the concentration of T^3 ($P<0.005$) with increased accumulation of ^{131}I ($P<0.005$) in the thyroid tissue and an increase of the TSH concentration in the blood serum ($P<0.005$) was established in the control group among people living in region II. This indicated stress in the pituitary-thyroid system connected with disruption of iodine metabolism (a reduction of the formation or increased degradation of T_3 at the tissue level), since the concentration of T_4 in the serum of the healthy people living in both regions was practically the same ($P<0.5$).

Thus, the effect of fluorine on iodine metabolism produced more frequent disruption of iodine metabolism among the residents of region II. However, since an analogous disruption of iodine metabolism is also seen among individual persons who live in the region with normal fluorine concentration in the drinking water, it can be suggested that among these people there are other key factors in the disruption of the thyroid function or this disruption was due to the personal threshold concentration of fluorine in the drinking water being exceeded.

The concentration of fluorine in the drinking water consumed by healthy subjects in region I was in the range of 26-75 _mol/L, while the level of fluoride in the drinking water of region II was substantially higher (P<0.05) and was 87-184 _mol/L.

The concentration of fluoride in the urine and blood serum of the healthy people residing in region II was reliably elevated (P<0.05) over that of the residence of region I. The concentration of fluorine in the blood erythrocytes among the essentially healthy people residing in regions I and II did not differ significantly (P<0.1).

Table 1. Characteristics of the pituitary-thyroid system in healthy subjects and patients with thyropathies residing in regions with different levels of fluorine in the drinking water

① Группа обследованных	② Регион проживания	③ Число обследованных	Поглощение щитовидной железой ^{131}I через 24 ч, % ④	⑤ Содержание гормонов в сыворотке крови		
				⑥ T_4, нмоль/л	⑦ T_3, нмоль/т	⑧ ТТГ, мЕД/л
⑨ Больные с гиперфункцией щитовидной железы	I	21	61±7 P<0,05	250±16 P<0,05	5,2±0,7 P<0,05	0,8±0,12 P<0,05
	II	22	72±13 P_1<0,05	261±23 P_1<0,05	7,1±1,8 P_1<0,05	0,6±0,08 P_1<0,05
1) Больные с гипофункцией щитовидной железы	I	14	8,5±2,7 P<0,05	26±7 P<0,05	1,1±0,4 P<0,05	51±11 P<0,05
	II	19	9,8±1,3 P_1<0,05	29±2 P_1<0,05	1,0±0,1 P_1<0,05	58±17 P_1<0,05
1! Контрольная	I	17	24±3	97±8	2,8±0,3	2,4±0,2
	II	30	33±4 P<0,05	94±6 P>0,5	2,0±0,2 P<0,05	4,3±0,6 P<0,05

Note. Here and in Table 2: P – reliability of differences compared to healthy subjects residing in region I; P_1 – reliability of differences compared to healthy subjects residing in region II.

Key:
1 Group of subjects
2 Region
3 Number of subjects
4 Absorption of ^{131}I over 24 h by thyroid
5 Concentration of hormones in blood serum
6 T_4, _mol/L
7 T_3, _mol/L
8 TSH, mU/L
9 Patients with thyroid hyperfunction
10 Patients with thyroid hypofunction
11 Control

The investigation of the availability of fluorine to patients with hypo- and hyperactivity of the thyroid as a function of the peculiarities of the region of residence establish the following: the concentration of fluorine in the urine of patients with thyroid hyperactivity who consume

drinking water with elevated fluorine content (87-184 _mol/L) is elevated (P<0.05) compared to the level in the hyperthyroid patients residing in region I. Excretion of fluorine with the urine among patients with thyroid hypofunction consuming drinking water with elevated fluorine content (87-300 _mol/L) was also elevated (P<0.05) over the characteristics of the residents of region I.

The determination of fluorine in urine taken in a 24-hour period established a clear tendency toward elevation of the urine content in the body when there is a dysfunction of the thyroid (Table 2). At the same time, the determination of fluorine in the urine in micromoles per liter shows a leveling of the differences in the concentration of fluorine in the body. The concentration of fluorine in the blood serum and in the erythrocytes did not reflect differences in the concentration of fluorine in the drinking water, and for this reason the information about the content of fluorine in the urine collected in a 24-hour period has the greatest level of information.

Table 2. Concentration of fluorine in drinking water and in the body of essentially healthy subjects and patients with thyropathies residing in regions with different fluorine levels

① Группа обследованных	Регион проживания ②	Число обследованных ③	④ Содержание фтора				
			в питьевой воде, мкмоль/л ⑤	в моче, мкмоль/л ⑥	в моче, ⑦ мкмоль/сут	в сыворотке крови, мкмоль/л ⑧	в эритроцитах мкмоль/л ⑨
1) Больные с гиперфункцией щитовидной железы	I	21	63±8	78±11	112±23	9,5±0,5	24±1,5
			$P>0,1$	$P>0,5$	$P>0,5$	$P>0,05$	$P>0,5$
	II	22	114±11	153±27	203±49	10±0,5	27±5
			$P_1>0,5$	$P_1>0,2$	$P_1>0,2$	$P_1<0,05$	$P_1>0,2$
			$P_2<0,05$	$P_2<0,05$	$P_2<0,05$	$P_2>0,2$	$P_2>0,2$
1! Больные с гипофункцией щитовидной железы	I	14	58±5	74±8	82±11	12±1	29±5
			$P>0,05$	$P>0,5$	$P>0,2$	$P>0,5$	$P>0,5$
	II	19	134±24	146±22	194±38	15±1	32±0,8
			$P_1>0,5$	$P_1>0,2$	$P_1>0,1$	$P_1>0,2$	$P_1>0,5$
			$P_2<0,05$	$P_2<0,05$	$P_2<0,05$	$P_2>0,05$	$P_2>0,5$
1 Контрольная	I	17	52±5	78±9	98±15	11±0,5	29±5
	II	30	122±5	124±9	140±12	13±0,5	32±1,5
			$P<0,05$	$P<0,05$	$P<0,05$	$P<0,05$	$P>0,1$

Note: P_2 – reliability of differences compared to patients with thyropathies residing in region I.

Key:
1 Group of subjects
2 Region
3 Number of subjects
4 Fluorine content
5 In drinking water, _mol/L
6 In urine, _mol/L
7 In urine, _mol/day
8 In blood serum, _mol/L
9 In erythrocytes, _mol/L
10 Patients with thyroid hyperfunction
11 Patients with thyroid hypofunction
12 Control

Thus, the increase of the fluorine concentration in the drinking water of region II up to 87-300 _mol/L significantly changed the level of ingestion of it into the body by comparison with region I, but not it did not significantly change in the blood serum or in the erythrocytes of the subjects. It is known that fluorine is mainly deposited in the bone tissues, and the excess of it is removed from the body with the urine due to the protective mechanism of the kidneys [1, 3, 4].

Analysis of the results from the study of the concentration of fluorine in various media of the body among the healthy subjects and patients whom we investigated and a comparison of the level of informativeness of the characteristics of the forming concentration in the erythrocytes, blood serum and urine suggests that the quantity of the element entering the body is most adequately reflected by its level in the daily urine. The data we obtained indicating a higher concentration of fluorine in the erythrocytes than in the blood serum among all of the subjects indicate the existence of a membrane mechanism of active transport of fluorine against a concentration gradient, due to which a higher concentration of fluorine is maintained in the erythrocytes than in the plasma. The identified membrane gradient of fluorine concentration is less than that of potassium, but nevertheless significant and probably, biologically necessary.

Based on the results of these studies, one can conclude that an elevated concentration of fluorine in drinking water (87-300 _mol/L) contributed to the development of thyroid dysfunction in individual persons.

Excess quantities of fluorine getting in to the body disrupt iodine metabolism and cause a functional stress in the pituitary-thyroid system. When stress arises in this system, further injury may be either to hyperfunction or to hypofunction of the thyroid, depending on a combination of other factors, which provides a basis for attributing excess ingestion of fluorine to risk factors for this pathology.

Findings

1. Consumption of drinking water with elevated fluorine content (122 ± 5 _mol/L) leads to stress of the functional status of the pituitary-thyroid system in healthy people, as is indicated by a decrease of the concentration of T_3, an increase of production of TSH in the blood serum, more intensive absorption of ^{131}I by thyroid tissue; this makes it possible to categorize excess ingestion of fluorine among risk factors creating a basis for the development of thyroid dysfunction.

2. If the concentrations of fluorine in the urine, erythrocytes, blood serum and the drinking water are determined, the greatest level of informativeness concerning fluorine kinetics is offered by the characteristics of the fluorine level in the urine.

3. The concentration of fluorine in the erythrocytes is higher than in the blood serum among healthy subjects and patients with thyropathies, which may indicate the presence of a mechanism of active transport of fluorine through the membrane of the cells.

References

1. A. P. Avtsyn and A. A. Zhavaronkov. Pathology of Fluorosis [in Russian]. Novosibirsk, 1981.

2. N. V. Verzhikovskaya. In: Goiter [in Russian]. Edited by A. K. Gorchakov, Kiev, 1959, Vol. 2, pp. 241-244.

3. R. D. Gabovich and G. D. Ovrutskii. Fluorine in Stomatology and Hygiene [in Russian]. Kazan, 1969.

4. R. D. Gabovich and A. A. Minkh. Hygiene problems of fluorination of drinking water [in Russian}. Moscow, 1979.

5. G. A. Golovanova. Gig. druda, 1977, No. 4, pp. 55-57.

6. L. G. Zherdienko. The role of nutrition and fluorination in prevention of dental caries in children. Author's summary of dissertation for degree of Candidate of Medical Sciences [in Russian]. Kharkov, 1970.

7. A. S. Kas'yanenko. Vrach. delo, 1978, No. 10, pp. 125-129.

8. V. A. Knizhnikova, Gig. i san., 1959, No. 1, pp. 20-25.

9. N. I. Gkovgan, In: Hygiene of Populated Areas [in Russian]. Kiev, 1974, Issue 13, pp. 130-131.

10. L. A. Porteyanko. In: Trace Elements in the Environment [in Russian]. Edited by P. A. Valsyuk. Kiev, 1980, pp. 39-42.

11. V. D. Sidora, et al., In: Urgent Problems of Experimental and Clinical Endocrinology [in Russian]. Kiev, 1982, pp. 270-271.

12. v. D. Sidora, et al., Probl. endokrinol., 1983, No. 4, pp. 32-35.

13. V. I. Smolyar. In: Rational Nutrition [in Russian]. Kiev, 1974, Issue 10, pp. 85-90.

14. *Galber W. L., Leong P. A.*— J. dent. Res., 1980, vol. 59, p. 135.