Magnesium, Zinc and Copper Concentrations in the normal and diseased Thyroid Gland

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Zusammenfassung

Die Konzentrationen von Magnesium, Zink und Kupfer wurden in 156 Gewebsproben aus dem rechten Schilddrüsenlappen atomabsorptionsspektralphotometrisch gemessen. 80 Gewebsproben wurden normalen Schilddrüsen entnommen, 43 einer euthyreoten Struma nodosa colloides, 11 einer euthyreoten Struma diffusa colloides, 9 einem euthyreoten follikulären Schilddrüsenadenom, 4 einer hyperthyreoten Struma nodosa, 3 einem hyperthyreoten Schilddrüsenadenom, 2 einer Thyreoiditis, eine einem follikulären Schilddrüsenkarzinom, eine einer Plattenepithelkarzinommetastase und eine einem Infiltrat eines malignen Non-Hodgkin-Lymphoms.
Im Vergleich mit der normalen Schilddrüse ist der Magnesiumgehalt in der euthyreoten nodulären und diffusen Struma colloides statistisch signifikant erniedrigt. Im hyperthyreoten Adenom wurden ebenfalls statistisch signifikant höhere Zink- und in der nodulären hyperthyreoten Struma höhere Kupferkonzentrationen gemessen.
Eine Deutung dieser Befunde ist derzeit nicht möglich, da pharmakologische Interaktionen zwischen der Schilddrüsenfunktion und dem Mineralstoffwechsel nicht beschrieben werden.

Summary

The concentrations of magnesium, zinc and copper were examined in 156 consecutively collected specimens of the right lobe of the thyroid gland using atmoic absorption spectral photometry. 80 specimens were from normal thyroid glands, 43 from non-toxic nodular goitre, 11 from non-toxic colloid goitre, 9 from non-toxic thyroid adenoma, 4 from toxic nodular goitre, 3 from toxic thyroid adenoma, 2 from thyroiditis, one from a follicular thyroid cancer, one from a metastasis of a squamous cell carcinoma and one from a malignant Non-Hodgkin-lymphoma.
In relation to the normal thyroid gland, the magnesium concentration of thyroid tissue is statistically significant decreased in non-toxic nodular and colloid goitres. In the toxic thyroid adenomas we find statistically significant increased zinc concentrations and in the toxic nodular goitre increased copper concentrations.
The reasons of these changes are unknown, because interactions between the function of the thyroid gland and the mineral metabolism were not described.

Résumé

Les concentrations de Mg, Zn, Cu étaient mesurées dans 156 prélèvements de tissus du lobe droit de la glande thyroide. L'analyse quantitative s'était effectuée dans un spectrophotomètre d'absorption atomique. 80 prélèvements de tissus étaient pris aux glandes thyroides normales, 43 à un euthyroidisme goitre colloide noueux, 11 à un euthyroidisme goitre diffus parenchymateux, 9 à un euthyroidisme adénome thyroidien, 4 à un hyperthyroidisme goitre noueux, 3 à un hyperthyroidisme adénome thyroidien, 2 à un thyroidite, 1 à un carcinome thyroidien folliculaire et 1 à un lymphe maligne Non-Hodgkin.
La concentration en Mg de faible niveau du point de vue statistique s'est relevée dans l'euthyroidisme goitre colloide noueux et diffus en comparaison de la glande thyroide normale.
Des concentrations élevées en Zn étaient enregistrées — statistique assurées — dans l'adénome thyroidien en hyperthyroidisme et des concentrations élevées en Cu dans l'hyperthyroidisme goitre noueux.
Actuellement l'interprétation de ces constatations n'est pas possible, parce que des interactions pharmacologiques entre la fonction de la glande thyroide et le métabolisme d'électrolytes ne sont pas décrites.

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Introduction

Minerals, especially nutritional important electrolytes and trace elements, have a demonstrable biochemical and physiological function in the metabolism of the human body [9]. Although disturbances of the mineral metabolism are clinically recognizable, yet they do not show any diagnostic histological changes in the tissues. So we tried to use the method of quantitative mineral pathology [2] to examine mineral changes in autopsy and biopsy specimens in an often investigated organ: the thyroid gland.
It is known that thyroid hormones influence the absorption of electrolytes, magnesium is one of them [7]. Hypomagnesemia was noted in hyperthyroid patients [11]. So changes in mineral concentrations could be expected in the diseased thyroid gland.

Material and Methods

156 consecutively collected samples of the right lobe of thyroid glands were examined. A part of each specimen was fixed in formaline, embedded in paraffin and after cutting in 5 µm-slides stained with hematoxylin and eosin. The other part of the specimen was used for quantitative mineral analysis. The dried tissue was analysed after acid digestion by atomic absorption spectral photometry (for detail [3]: Atom-

ic absorption spectral photometer *Beckman* 1236).
For the statistical analysis we applied the analysis of the variance and the Kruskal-Wallis-Test, a non-parametric variance analysis.

Results

According to the histological examination the following groups were identified:
80 specimens were associated with a normal histological picture, no functional abnormalities were clinically detected.
In 43 patients we found a non-toxic colloid goitre, in 11 patients a non-toxic nodular goitre, 9 patients had non-toxic adenoma, 4 toxic nodular goitre and 3 toxic thyroid adenoma. In two cases we found thyroiditis and in another one a follicular thyroid cancer. One case was a metastasis of a squamous cell cancer of the lung and another a malignant lymphoma of the thyroid gland.
So we had 7 cases showing hyperthyroid changes and the rest showed normal thyroid function.
86 specimens were from females and 70 from males. The patient's age ranged between 13 week fetus and 87 years old.

I. Histological normal thyroid Gland

80 specimens of the thyroid gland showed normal histological structures. 35 specimens were from females and 45 from males (Tab. 1). There was no statistical significant difference in the mineral concentration of the thyroid tissue between males and females.
Children's thyroid gland, including fetus and newborns, had a higher magnesium concentration than the adult thyroid gland ($p < 0.05$). In the older patients, there was a slight decrease in copper concentration in the sixty years old. There were no statistical differences in copper (Cu)-, zinc (Zn)- and magnesium (Mg)-concentration in relation to age.
Cu, Zn and Mg-concentrations in the histological normal thyroid gland are listed in table 1.

Tab. 1: Mineral concentrations (mmol/kg dry weight; x = mean value, SD = standard deviation) in this histological normal thyroid gland. Age-related changes are not seen in the adults. Magnesium-concentration in the children is higher than in the adults.

Age	Number	Sex		Copper		Zinc		Magnesium	
		F	M	x	SD	x	SD	x	SD
— 9	23	11	12	0.096	0.052	2.478	1.545	18.885	7.118
20 – 29	2	—	2	0.096	0.009	1.071	0.214	13.166	2.345
30 – 39	1	—	1	0.074	—	3.365	—	11.932	—
40 – 49	6	2	4	0.096	0.030	2.952	1.117	15.305	3.209
50 – 59	9	2	7	0.083	0.030	2.448	0.948	15.223	3.580
60 – 69	9	4	5	0.079	0.025	2.295	0.704	14.441	3.168
70	30	16	14	0.088	0.036	2.631	0.704	15.347	4.608

Tab. 2: Sex and age distribution in the cases of diseased thyroid glands.

	Number	Sex		Age		
		F	M	0 – 39	40 – 59	> 60
Non-toxic nodular goitre	43	28	15	5	19	19
Non-toxic colloid goitre	11	4	7	4	5	2
Non-toxic thyroid adenoma	9	8	1	2	5	2
Toxic nodular goitre	4	3	1	3	1	—
Toxic thyroid adenoma	3	2	1	—	3	—
Thyroiditis	2	1	1	1	1	—
Thyroid cancer	1	1	—	—	—	1
Metastases	1	1	—	—	1	—
Malignant lymphoma	1	1	—	—	1	—

Tab. 3: Mineral content of the thyroid gland in histological normal specimens and diseased thyroid glands (in mmol/kg dry weight)

	Copper		Zinc		Magnesium	
	x	SD	x	SD	x	SD
Normal thyroid gland	0.083	0.024	2.295	0.918	14.400	3.292
Non-toxic nodular goitre	0.082	0.035	2.295	0.916	12.755	3.292
Non-toxic colloid goitre	0.072	0.024	2.141	1.124	12.755	4.937
Non-toxic thyroid adenoma	0.105	0.022	2.907	1.530	17.692	5.349
Toxic nodular goitre	0.345	0.321	2.601	1.071	16.869	2.880
Toxic thyroid adenoma	0.127	0.061	4.895	1.377	21.806	6.994
Thyroiditis	0.096	—	1.989	—	12.343	—
Thyroid cancer	0.082	—	1.683	—	28.389	—
Metastasis	0.112	—	2.907	—	13.577	—
Malignant lymphoma	0.046	—	2.601	—	40.732	—

II. The thyroid Gland with morphological Changes with and without functional Abnormalities

The sex and age distribution of the patients are listed in table 2.

The mineral content in the diseased thyroid gland is described in table 3.

II.a. Non-toxic nodular Goitre

Cu and Zn-concentrations in the nodular non-toxic goitre are similar to the normal thyroid glands. Magnesium had a concentration of 12.7 mmol/kg dry weight of tissue which was statistically significant lower than the normal thyroid's magnesium concentration of 14.4 mmol/kg dry weight ($p < 0.05$).

II.b. Non-toxic colloid Goitre

There were no statistical significant differences in the concentrations of Cu and Zn in relation to the normal thyroid. The concentration of Mg was statistically lower than in the histological normal thyroid tissues ($p < 0.05$).

II.c. Non-toxic thyroid Adenoma

In this group, there were no statistical significant differences comparing the concentrations of the three elements ($p > 0.05$).

II.d. Toxic nodular Goitre

The Cu-concentration in these cases were markedly increased. The difference between the levels in measured samples and normal thyroid tissues were statistically significant ($p < 0.05$; 0.345 versus 0.083 mmol copper/kg dry weight). Zn and Mg-concentrations were nearly increased, but these differences were not statistically significant ($p > 0.05$).

II.e. Toxic thyroid Adenoma

In toxic thyroid adenoma Cu-concentration was normal. Zn-concentration was statistically significant increased ($p < 0.05$). There was no significant difference in the concentration of Mg.

III. Mineral Concentrations in Inflammation and Tumors

The two cases of thyroiditis have nearly normal mineral content (Tab. 3). We noted an abnormal high magnesium content in the case of a follicular thyroid cancer and in that of malignant lymphoma.
The Cu-concentration in the case of malignant lymphoma was relatively lower than in the normal thyroid glands, but the difference was not statistically significant ($p > 0.05$).

Discussion

In a literature search covering the last 25 years, we only found two russian studies [5, 8], dealing with the mineral content of the thyroid glands.
Bredichin [5], using a spectrophotometric method, examined the changes of copper and other trace elements in blood, urine and thyroid dissue. The authors described an increase in Cu-concentration in relation to the severity of hyperthyroidism.
In our series we noted an increase in the Cu-concentration of toxic nodular goitre in relation to the severity of hyperthyroidism too, but we did not see similar changes in toxic thyroid adenoma. The increased thyroid function and activity is obviously asociated with copper mineral metabolism disturbances.
Manjuch and *Neciporenka* [8] studied trace element concentrations, using a method described by *Babenko* [1], in the thyroid nodules and the surrounding (paranodular) tissues. The authors noted an increase in the nodule's Cu-concentration in relation to the Cu-content of the surrounding tissue. The paranodular Cu-concentrations were higher than the Cu-concentrations in the nodules.
This may suggest, that paranodular mineral concentration may influence the nodular mineral concentration.
In our study, using atomic absorption spectral photometry [2], the normal adult thyroid gland had a Cu-concentration of 0.083 mmol, a Zn-concentration of 2.29 mmol and a Mg-concentration of 14.4 mmol/kg dry weight. Our results are different from the two russian studies, probably due to the different techniques used.
Comparing the copper, zinc and magnesium values in the histological normal thyroid gland with other organs (like liver, skeletal muscle, heart muscle, brain or ovary [2], we found a lower Mg-concentration in the thyroid gland than in the other organs. The thyroid gland had a higher Cu-concentration than other tissues but the ovary.
The difference in Cu-concentration in various organs is probably due to the changes of the amount of Cu-binding proteins in these organs.
Further biochemical studies are required to explain the increase of the Cu-concentration in toxic nodular goitre and the increase of the Zn-concentration in toxic thyroid adenoma.
Demko [6] demonstrated, that iodine alone does not improve hypothyroidism induced in rats due to defiency in I, Cu and Mg.
The relative higher Mg-concentration in thyroid cancer is probably caused by the high cellularity and the minimal colloid content in the tumor tissue.
Thyroid tissue has a similar magnesium content as a well perfused tissue like myokardium [3].
Metastases seem to have a mineral content similar to the host organ [4]. In the present study, the metastasis of a lung cancer had mineral concentrations similar to the thyroid gland.
Clinical and biochemical studies are still necessary to understand the unknown interactions be-

tween mineral metabolism and certain diseases, which can be described as quantitative mineral pathology [3] and as a part of the molecular pathology [10].

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