Acta Paediatrica Hungarica 27 (4), pp. 317—321 (1986)

Thyroid hormones and thyroglobulin autoantibodies in insulin dependent diabetes mellitus

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Serum T_4, FT_4, T_3, and TSH were measured in a group of children with insulin dependent diabetes mellitus and a control group. In the insulin dependent diabetes mellitus group, serum T_3 concentration was significantly lower than the control values. Serum T_4, FT_4 and TSH level did not differ. The difference in serum T_3 concentration was significant between diabetic children with good or poor control.

Thyroglobulin antibodies were investigated in diabetic children by Serono's "hTg antibodies" kit. Thyroglobulin antibodies were present in 14.5%. TSH concentration did not differ in antibody positive and negative cases, but one child with diabetes had evidence of moderately impaired thyroid reserve.

During the last few years a considerable amount of evidence has been obtained for abnormal thyroid function in insulin dependent diabetes mellitus (IDDM) [1,4,7,10,12,13]. Abnormalities in circulating thyroid hormone levels, referred to as the low T_3 syndrome, have been described in uncontrolled and poorly controlled patients with IDDM. In addition, diabetes as an autoimmune endocrinopathy is frequently associated with presence of thyroid autoantibodies in serum [6, 11, 14].

We have attempted to (i) compare the serum concentration of T_4, FT_4, T_3 and TSH in a group of children with IDDM and in healthy controls; (ii) investigate the possible relationship between thyroid hormone abnormalities and the degree of metabolic control of the diabetic state; (iii) determine the frequency of thyroglobulin antibodies detected in sera of IDDM patients; (iv) compare thyroid function in IDDM patients with or without thyroid antibodies.

Material and Methods

Thirty diabetic children and adolescents (13 boys and 17 girls) and 11 healthy controls (5 boys and 6 girls) participated in the study. Mean age $\pm$ SD of diabetic patients and healthy controls were not significantly different (10.6 ± 4.3 years vs. 10.8 ± 2.7 years). The duration of diabetes at the time of the study was 1 to 11 years (mean $\pm$ SD $= 4.3 \pm 3.8$). The diabetic subjects were treated by two daily injections of Monotard MC and Actrapid MC insulin. Insulin dosage was prescribed according to the glucose quantity in three urine fractions collected during 8 hour periods, and blood glucose concentration measured after breakfast with the glucose

oxidase method. The groups of poorly and well controlled diabetic patients were divided according to their urinary glucose concentrations [8]. Children with well controlled diabetes (11 boys and 13 girls) during three months preceding study did not have a urinary glucose concentration exceeding 3%. Patients with poorly controlled diabetes (2 boys and 4 girls) during the preceding three months repeatedly exhibited glucosuria exceeding 3%.

The serum concentrations of T_3 and T_4 were determined by commercial RIA kits. Serum FT_4 was measured by RIA method of Radiochemical Centre (Amersham), TSH was investigated by RIA-mat-TSH kit of Byk Mallinckrodt. The thyroglobulin antibody titres were determined by "hTg antibodies" kit of Serono. The hTg test was performed in 48 diabetic children (20 boys and 28 girls). Statistical analysis was performed by Student's *t* test.

Results

The serum levels of thyroid hormones and TSH in the diabetic patients and in healthy control ones are shown in Table I. Serum T_4 and FT_4 concentrations were almost identical in the two groups. The T_3 level was significantly lower in diabetic subjects than in controls, but T_3 concentrations of IDDM patients were in the normal range. TSH levels did not differ in the two groups.

Statistically significant difference in thyroid hormones and TSH was not found between the hormone concentrations of boys and girls, neither in the diabetic nor in the control group.

The influence of metabolic control is demonstrated in Table II. There was a considerable difference in serum T_3 concentrations of well and poorly controlled IDDM patients. It was remarkable that the degree of significance was different between the compared groups.

The frequency of thyroglobulin antibodies in 48 children with IDDM is shown in Table III, together with the different antibody titres: 7 diabetic children (3 boys and 4 girls) had thyroglobulin antibodies.

The serum TSH concentrations measured in antibody positive, antibody negative, and in control groups are shown in Figure 1, and individual serum TSH concentrations in antibody positive and control groups are also demonstrated. TSH concentra-

Table I

Serum concentration of thyroid hormones and TSH in diabetic patients and in healthy controls (mean ± SD)

Groups	T_4 nmol/l	FT_4 pmol/l	T_3 nmol/l	TSH mE/l
Control (n = 11)	131.6 ± 21.2	19.30 ± 3.98	2.69 ± 0.44	1.8 ± 0.7
IDDM (n = 30)	116.4 ± 18.4	18.79* ± 3.60	2.16 ± 0.52	1.9 ± 1.1
t-test (p)	NS	NS	<0.01	NS

NS = non-significant; * = n = 12

TABLE II

Serum T_3 concentration (mean ± SD) in healthy controls and in diabetic patients according to diabetic metabolic control

Groups	(n)	T_3 (nmol/l)	t test (p)
Control	(11)	2.69 ± 0.44	<0.01
IDDM (total)	(30)	2.16 ± 0.52	<0.05
Good metabolic status	(24)	2.30 ± 0.44	<0.001
Poor	(6)	1.64 ± 0.42	<0.01

TABLE III

hTg antibody positivity in 38 children with IDDM

Antibody titre	n	Frequency per cent
1 : 1 000	2	4.17
1 : 10 000	4	8.33
1 : 20 000	1	2.05
Antibody positivity:	7	14.58

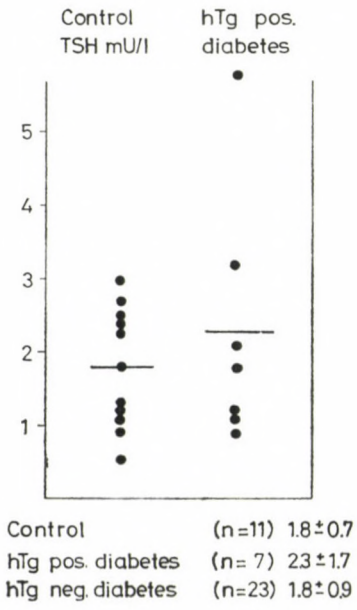

FIG. 1. Serum TSH concentration in healthy controls and in antibody positive and negative diabetic patients

tion did not differ in the compared groups. The TSH level, however, in one of our patients, was 5.8 mU/l. Her thyroglobulin antibody titre was 1 : 20 000 while thyroid hormone concentration showed a normal range.

Discussion

Recently, alterations of circulating thyroid hormones have been demonstrated in IDDM by several authors [1, 4, 7, 10, 12, 13] who found the following characteristics: low serum concentration of T_3, increased rT_3, normal to low T_4, and normal TSH. It has been assumed that these changes were related to glucose utilisation [3], and a good diabetic control has been found to restore it [3, 13]. A recent report on the effects of diabetes mellitus and insulin treatment upon serum thyroid hormone parameter concluded, however, that thyroid hormone concentrations were not influenced by variations of serum glucose [1].

In our study the mean T_3 levels were lower in diabetic children than in healthy controls of the same age, suggesting that the "low T_3 syndrome" [9] existed in our material, too. The T_4 and FT_4 concentrations did not differ, so the low T_3 level may have been a consequence of an impaired peripheral T_3 production from T_4 [10]. The T_3 concentrations strongly depended in diabetic children on the quality of metabolic control. Our findings confirmed the results recently obtained by Dorchy et al. [4].

The relationship between T_3 and metabolic state in IDDM indicates an association between the severity of thyroid abnormalities and diminished glucose metabolism. Since glucose utilisation is related to the degree of insulin deficiency, normal serum T_3 seems to be an index of optimum insulin replacement and the T_3 level can be used as an indirect parameter of metabolic control in IDDM [3]. On the other hand, it is worth considering that thyroid function in diabetic children should be assessed by the measurement of serum T_4 and FT_4 [3, 4].

Patients with IDDM commonly have co-existent autoimmune thyroiditis characterized by the presence of circulating thyroid antibodies [6, 11, 14] and biochemical evidence of impaired thyroid reserve [5]. Serum TSH concentration is accepted as a useful index of an impaired thyroid reserve in symptom-free autoimmune thyroiditis [2]. For this reason, in our study thyroid antibodies and thyroid functions were investigated simultaneously.

The prevalence of thyroglobulin antibodies was similar to that previously reported in children [4, 11]. Thyroid hormones and TSH concentration did not differ in antibody positive and negative cases, but in our study one antibody positive child with IDDM had evidence of moderately impaired thyroid reserve. So, we suggest to determine TSH concentration from time to time in antibody positive cases of IDDM.

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Received 7 January 1986

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