Subclinical Hypothyroidism Is a Frequent Finding in Children and Adolescents With Type 1 Diabetes

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SUMMARY • • • • • • • • • • • • •

Background

Subclinical hypothyroidism (SCH), defined by an increased serum TSH along with normal free T_4 and free T_3 , is a frequent finding in adults with type 1 and type 2 diabetes. In obese nondiabetic children, SCH is more frequent (>10%) than in normal children (1% to 2%) (1). Studies on the prevalence of SCH in children and adolescents (<25 years old) with type 1 diabetes are scarce (2). This large study adds considerable new knowledge to the subject.

Methods

In 1995, a large surveillance database for children and adolescents with type 1 diabetes was established in Germany and Austria (3). Various data from all patients were collected twice yearly. The data from patients with a serum TSH of more than 5 mU/L but less than 25 mU/L were analyzed. In addition to thyroid tests, a lipid profile was obtained in the same blood sample. If multiple samples from the same patient were available, only the last one was considered. Patients with decompensated diabetes or those taking possibly interfering drugs, particularly lipid-lowering substances, were excluded, as were patients affected by familial hypercholesterolemia. A total of 22,747 patients with type 1 diabetes fulfilled the required criteria.

Results

Of the 22,747 children and adolescents with type 1 diabetes type, 19.2% had either anti-TPO and/or anti-thyroglobulin antibodies, and 7.2% had SCH (TSH, >5

and <25 mU/L; normal free T₄ and free T₃). Arranging the patient data according to quartiles of rising serum TSH revealed a stepwise increase of total cholesterol and LDL cholesterol levels. These increments were already evident with serum TSH levels between 2 and 4 mU/L. There were also increases, albeit very modest ones, in body-mass index (BMI) and highdensity lipoprotein (HDL) cholesterol. Patients with higher serum TSH also had significantly higher total cholesterol and low-density lipoprotein (LDL) cholesterol (serum TSH, <4 mU/L: total cholesterol, 173.3 mg/dl [4.54 mmol/L]; TSH: >5 to <25 mU/L: 178.7 mg/dl [4.63 mmol/L]; LDL, 93.7 mg/dl [2.43 mmol/L] for TSH <4 mU/L vs. 97 mg/dl [2.51 mmol/L] for TSH >5 to 25 mU/L). Although BMI was higher in the group with hypothyroidism, there was no difference in mean height. The prevalence of 7.2% of SCH in this study is clearly higher than in a comparable investigation on young healthy adults in which SCH occurred in approximately 2% of subjects (Figure 3 in National Health and Nutrition Survey [NHANES] III) (4).

Clinical

THYROIDOLOGY

Conclusions

In children and adolescents with type 1 diabetes, thyroid antibodies are present in 19.2% and subclinical hypothyroidism is present in 7.2%, a value clearly much higher than in a comparable healthy population. With increased serum TSH, there was a gradual increase of serum total and LDL cholesterol reaching significance in SCH. Yet the increase in lipid levels was modest in view of the rather high serum TSH values. In addition, there was a trend toward increased BMI.

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ANALYSIS AND COMMENTARY • • • • •

The results are remarkable, since they were obtained from a very large population base of young patients with type 1 diabetes. Compared to similar studies in normal subjects, this group of patients had a highly increased incidence of SCH and even a higher incidence of thyroid antibodies. SCH in adults is associated with an increased lipid profile, and most studies suggest an increased cardiovascular risk. Here the authors prove that in a considerable fraction of even a young population with type 1 diabetes, serum lipids are significantly increased. These novel data are therefore an important addition to our knowledge about the connection of diabetes and thyroid disease. In this respect, young patients are not different from adult patients with type 1 diabetes.

One might wonder why the effects of SCH on the lipid profile are so small. This is particularly puzzling, since the range of SCH was defined by a TSH as high as 4 to 25 mU/L. The authors give no information on how many of these patients had a serum TSH in the lower range, for instance between 4 and 10, or 11 and 15 mU/L, etc. However, one may safely guess that the whole sample of study patients contained only a few individuals with a serum TSH as high as 24 mU/L and still normal thyroid hormone levels. At least in adults, it is unusual to find a patient with a serum TSH of 15 mU/L and still normal thyroid hormone levels, and this is even more unlikely for a TSH of 24 mU/L. I suspect that the large majority of the patients included in this study had serum TSH in the low range defined for SCH. If so, this may explain the small effect of SCH on the lipid profile; still, screening for SCH in young patients with type 1 diabetes seems to be highly advisable.

The study also revealed a high prevalence of euthyroid patients with positive thyroid antibodies. The risk of hypothyroidism cannot be neglected in such patients.

Also, the study does not provide arguments as to the question of whether rigorous treatment with thyroxine may improve the lipid profile. It is hoped that the authors will provide data on these important points in a few years. Based on the evidence from adults, it seems reasonable to treat the patients with SCH described here with T_4 , particularly if the serum TSH is repeatedly above 7 to 10 mU/L. Some endocrinologists recommend starting treatment even if serum TSH is above 4 mU/L, but there are not data showing benefit from such a treatment.

References

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