NATURAL HISTORY OF SUBCLINICAL HYPERTHYROIDISM

Vadiveloo T, Donnan PT, Cochrane L, Leese GP. The Thyroid Epidemiology, Audit, and Research Study (TEARS): the natural history of endogenous subclinical hyperthyroidism. J Clin Endocrinol Metab. October 6, 2010 [Epub ahead of print].

SUMMARY • • • • • • • • •

BACKGROUND

Patients with subclinical hyperthyroidism have subnormal serum thyrotropin (TSH) with normal free thyroxine (FT₄) and free triiodothyronine (FT₃) or total T_3 concentrations, usually with no typical features of hyperthyroidism. The prevalence varies widely in different reports, ranging from 0.7% to 12.4%. The rate of development of overt hyperthyroidism in these patients has been estimated at 1% to 5% per year. The purpose of this study was to determine the rate of conversion to overt hyperthyroidism and the rate of conversion to the euthyroid state.

METHODS

The study included a population of almost 600,000 people in Tayside, Scotland, starting in 1993; eventually 46% had a TSH measurement. The patients included in the study were over age 18, nonpregnant, not receiving therapy for thyroid disease, and not taking drugs that could affect thyroid function. They had at least two measurements of TSH separated by 4 months or more that were <0.4 mU/L with normal thyroid hormone levels. Thyroid function was followed at 2, 5, and 7 years.

RESULTS

Approximately three fourths of the patients were women. The prevalence of subclinical hyperthyroidism

increased with time so that it was about 0.6% in 2006–2008. The patients were further subdivided into two groups: those with a TSH of <0.1 mU/L (417 patients) and those with a TSH of 0.1 to 0.4 mU/L (1507 patients). A third group of 100 patients could not be classified because the TSH fluctuated between the two categories. The mean (\pm SD) age at baseline was 66 ± 16 years. Of those with a TSH of <0.1 mU/L, 96% had measurement of FT₄ and 84% serum T₃, but for those with a TSH of 0.1 to 0.4 mU/L, only 20% had measurement of FT₄ and 15% serum T₃.

Frank hyperthyroidism developed within 1 year of diagnosis in 10% of those with a TSH of <0.1 mU/L. Of the patients with a TSH of <0.1 mU/L, 17% were receiving treatment for hyperthyroidism at 2 years, 37% at 5 years, and 44% at 7 years. Conversely, in this group, 51%, 40%, and 37% had no improvement at 2, 5, and 7 years, respectively. Of the group with a TSH of 0.1 to 0.4, 2.5%, 11%, and 17% were receiving treatment for hyperthyroidism at 2, 5, and 7 years; 72%, 55%, and 50% had no improvement at 2, 5, and 7 years. In the two groups together, 17%, \sim 30%, and 30% to 38% reverted to normal at 2, 5, and 7 years.

CONCLUSIONS

The authors conclude that very few patients with subclincal hyperthyroidism develop overt hyperthyroidism and that the majority revert to normal or remain subclinically hyperthyroid.

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COMMENTARY • • • •

The strengths of this study are that it follows the largest number of subjects with subclinical hyperthyroidism reported to date and that it classifies these subjects into the two groups. The authors conclude that the rate of development of overt hyperthyroidism, 10%, is small in those with a TSH of <0.1 mU/L, but they ignore the even higher proportion in this category who were given therapy for hyperthyroidism. They base the diagnosis of hyperthyroidism on raised FT₄ and T₃ levels, but it is likely that the physicians caring for these patients decided that the TSH of <0.1 mU/L together with whatever thyroid hormone levels the patients had was a sufficient basis for the initiation of therapy. When the authors ignored those under therapy, the progression to overt hyperthyroidism was 6.1% of all patients at 1 year. They consider these patients as having incipient hyperthyroidism and

differentiate them from those with stable subclinical hyperthyroidism.

The authors tend to emphasize that most patients remain subclinically hyperthyroid or revert to normal, but I think the take-home message is that in 10% hyperthyroidism will develop within 1 year and that clinical judgment will dictate an intervention in an even higher proportion of patients as they are followed. Clearly, most of those who have slightly subnormal serum TSH levels make up the 2.5% of subjects below the lower 95% confidence limit and will probably not require intervention, but this study provides good evidence that those with serum TSH <0.1 mU/L must be followed carefully. The findings reinforce the recommendations of the Task Force on subclinical thyroid disease (1).

- Jerome M. Hershman, MD

Reference

1. Surks MI, Ortiz E, Daniels GH, et al. Subclinical thyroid disease: scientific review and guidelines for diagnosis and management. JAMA 2004;291:228-38.