



FPIN's Clinical Inquiries

Management of Subclinical Hypothyroidism

Clinical Inquiries provide answers to questions submitted by practicing family physicians to the Family Practice Inquiries Network (FPIN). Members of the network select questions based on their relevance to family medicine. Answers are drawn from an approved set of evidence-based resources and undergo peer review. The strength of recommendations and the level of evidence for individual studies are rated using criteria developed by the Evidence-Based Medicine Working Group (http://www.cebm.net/levels_of_evidence.asp).

This series of Clinical Inquiries is coordinated for *American Family Physician* by John Epling, M.D., State University of New York Upstate Medical University, Syracuse, N.Y. The complete database of evidence-based questions and answers is copyrighted by FPIN. If you are interested in submitting questions to be answered or writing answers for this series, go to <http://www.fpin.org> or contact CI2Editor@fpin.org.

Clinical Question

How should patients with subclinical hypothyroidism be managed?

Evidence-Based Answer

Treatment of subclinical hypothyroidism with levothyroxine may be of most benefit to patients with symptoms suggestive of hypothyroidism and those patients with thyroid-stimulating hormone (TSH) levels higher than 10 μ IU per mL (10 mIU per L) or positive anti-thyroid peroxidase (TPO) antibodies. Levothyroxine is recommended for pregnant patients. For asymptomatic patients with TSH levels between 4.5 and 10 μ IU per mL (4.5 and 10 mIU per L), treatment may not be beneficial, but their thyroid function should be monitored at six- to 12-month intervals. [Strength of recommendation: C, based on expert opinion and systematic reviews with troublesome heterogeneity of disease-oriented evidence]

Evidence Summary

Subclinical hypothyroidism is a laboratory diagnosis that refers to a patient with an elevated TSH level and a normal free thyroxine (FT4) level. About 2 to 5 percent of these patients each year will develop overt hypothyroidism,¹⁻³ but the benefits of detecting and treating the subclinical disease are not well established.

A recent scientific review¹ recognized the paucity of randomized controlled trials on the subject, with scant data related to clinical outcomes such as cardiac dysfunction and neuropsychiatric

symptoms. Most studies separated patients into two groups. For patients with a TSH level between 4.5 and 10 μ IU per mL, evidence regarding benefits of treatment was insufficient or absent. Patients with a TSH level higher than 10 μ IU per mL but a normal FT4 level had a higher risk of developing overt hypothyroidism, but evidence that treatment with thyroid hormone replacement would improve patient-oriented outcomes (i.e., morbidity, mortality, and symptom improvement) was inconclusive. Similarly, the presence of anti-TPO antibodies predicted a higher risk of developing overt disease, but the evidence was insufficient to recommend routine measurement of anti-TPO antibodies.

Other reviews show inconclusive results,^{4,5} and many studies lack clinical relevance because of their focus on disease-oriented or physiologic outcomes.³ Some studies that show improvement in patient-oriented outcomes included patients that were already being treated for thyroid disorders, and therefore these results cannot be applied to the general population.

There are no published trials assessing the benefits of levothyroxine in pregnant women with subclinical hypothyroidism, but the potential benefits of treatment for a thyroid-hormone-deficient mother and fetus, compared to the risks of treatment for an euthyroid mother and fetus, justifies its use.¹

Recommendations from Others

One expert panel recommends that TSH levels between 4.5 and 10 μ IU per mL should not be routinely treated, but patients with these levels should have thyroid function tests repeated at six- to 12-month intervals.¹ Patients with symptoms of hypothyroidism may benefit from a trial of levothyroxine while monitoring symptomatic improvement, although distinguishing a true therapeutic effect from placebo effect may be difficult.

The American Association of Clinical Endocrinologists recommends levothyroxine therapy for patients with TSH levels higher than 10 μ IU per mL, positive anti-TPO antibodies, or goiter; the recommended starting dose of 25 to 50 mcg daily must be adjusted as necessary after repeating the TSH level in six to eight weeks.² Annual evaluation of TSH is appropriate after a level between 0.3 and 3.0 μ IU per mL (0.3 and 3.0 mIU per L) is achieved.

Clinical Commentary

Subclinical hypothyroidism often is diagnosed when thyroid tests are ordered for nonspecific symptoms such as depression, weight gain, or fatigue. The physician must then decide if the patient's symptoms are caused by a relative thyroid hormone deficiency, and whether thyroid hormone replacement would improve the patient's well-being. Lacking clear-cut evidence to guide these decisions, the physician's role is to discuss the uncertain implications of the diagnosis and the potential risks (such as osteoporosis and impaired myocardial contractility) and benefits of levothyroxine therapy to allow a patient to make an informed decision about therapy.

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