

Subclinical hypothyroidism: to treat or not to treat?

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Prescribing levothyroxine has increased remarkably during the last decade, and these are mostly done for subclinical hypothyroidism. Subclinical hypothyroidism (SH) is diagnosed when both serum-free thyroxine (FT4) and free triiodothyronine (FT3) are within the normal range, whereas the serum thyroid-stimulating hormone (TSH) is elevated⁽¹⁾. The prevalence of SH in the population varies between 4% and 20%. Although SH is considered an asymptomatic disorder, some patients may present with non-specific symptoms, which can overlap with the symptoms of overt hypothyroidism (OH)^(2,3). In the US Colorado Thyroid Disease Prevalence Study, which included 20,862 subjects, patients with SH more frequently reported symptoms compared to euthyroid subjects but less frequently than patients with OH⁽²⁾. SH can progress to OH around 4% per year in the presence of Thyroid peroxidase antibodies, and 2% per year if antibodies are negative^(3,4).

As TSH screening is used widespread in primary care, it has increased the number of patients being diagnosed with SH⁽¹³⁾. However, management of SH is still controversial, due to uncertainties related to the magnitude of its clinical benefit. A TSH cutoff level of 10 mIU/L is commonly used to distinguish between mild and more severe SH^(4,5). Approximately 75% of patients with SH have a TSH level of less than 10 mIU/L^(3,4,5). Current guidelines recommend that treatment is warranted when TSH >10 mIU/L^(5,6,7,9). In those with milder forms, treatment could be considered with levothyroxine in cases with repeated measures of elevated TSH, and symptoms compatible with hypothyroidism. On the other hand, some clinicians recommend that most patients with SH should be treated, including those with a serum TSH value below 10 mIU/L^(14,15).

Those who favour treating SH prefer treating as some studies have shown that SH could be associated with increased risk of cardiovascular disease (CVD), mood disorders and cognitive dysfunction as well as impaired neuromuscular function^(3,4,7,8).

Patients with SH are believed to be at increased risk of atherosclerosis and disturbed blood coagulation. Thyroid hormones exert a direct influence on the heart and blood vessels and lipid status.^(10,11,12) In SH there is a disruption of the systolic and diastolic function of the left ventricle. In the blood vessels, there are also changes in the form of increased

vascular resistance, increased arterial stiffness and endothelial dysfunction. Many studies have shown that patients with SH have increased level of total cholesterol and low-density lipoprotein (LDL) compared to euthyroid patients⁽¹²⁾. Despite these results, a clear connection between lipids and SH has not been established because some studies have shown that the lipid profiles of patients with SH were not significantly different compared to euthyroid patients⁽¹²⁾. However, the lipid profile was more impaired in patients whose TSH is >10 mIU/L. Due to the extreme heterogeneity of the studies, we are unable to make any accurate conclusions about the influence of SH on CV system. Hence currently there is no evidence that a mild form of SH (TSH values are from 4.0 to 10.0 mIU/L) may have consequences for patient's cardiovascular system. Similarly recent studies have shown that levothyroxine treatment in milder forms rarely affects cognition, mood, neuromuscular function, weight, or quality of life^(13,16).

Recent results from a large randomized clinical trial suggest that levothyroxine treatment doesn't benefit older adults with SH. Serum TSH levels rise as people without thyroid disease age due to physiological adaptation. This phenomenon can lead to an overestimation of the true prevalence of SH in persons older than 70 years⁽¹⁵⁾. Therefore levothyroxine therapy may be associated with iatrogenic thyrotoxicosis, especially in elderly patients, and currently there is no evidence that it is beneficial in persons aged 70 years or older⁽¹⁵⁾.

SCH should be treated in specific conditions, namely: pregnancy and infertility. Treatment with levothyroxine should be commenced in SH (TSH > 4.0 mIU/L) in females planning pregnancy and if found during ongoing pregnancy, since normal thyroid function decreases the risk of miscarriage and other pregnancy complications. Nevertheless, before initiation of levothyroxine therapy in SH, a repeated measurement of TSH level after 3 months is imperative. This is important, as a transient elevation of TSH levels that normalizes within 3 months has been reported in 60% of cases, and after 5 years in 62% of cases⁽¹⁵⁾.

If a symptomatic response is not reached 3–4 months after TSH normalization, treatment should be stopped⁽⁴⁾. This is invariably difficult, as hypothyroid symptoms are unspecific, and the decision to treat or not has to be individualized.

Therefore until enough evidence become available each patient's thyroid function test should be assessed on an individual basis with the entire clinical picture in mind to decide whether to treat or not. Monitoring also needs to be vigilant, targets for treatment should be reassessed continually

and treatment withdrawn if no favorable response is achieved after treating for considerable time. Similarly patients in whom treatment is deferred, periodic reassessment of TSH should be done to decide whether treatment needs to be initiated⁽¹⁷⁾.

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