Short Communication

Subclinical hypothyroidism: When to treat

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KEY WORDS : Hypothyroidism, subclinical, TSH

Subclinical hypothyroidism (SCH)is a conditionin which there is a persistent elevation in thyroid-stimulatinghormone (TSH) (12 weeks or longer) in the setting of FT4/T4concentrations that are repeatedly found within the referenceinterval.[1] Subclinical hypot hyroidism may be categorized as grade 1 when TSH level sare between the upper limit of the reference range and 9.9mIU/L and as grade 2 if serum TSH levels are10mIU/L or higher.As multiple factors, such as subacute thyroiditis,recovery from nonthyroidal illness, andmedication (e.g., amiodarone and lithium), cancause transient abnormalities in the serum TSH level,subclinical hypothyroidism is diagnosed after excluding all other causes of elevated TSH levels.[2]

Risk of Progression to Overt Disease

The natural history of subclinical hypothyroidism depends onseveral other factors like underlying cause and the characteristicsof each patient. It can be reversible, or it can progress to overthypothyroidism. Progression has been reported to occur inapproximately 2–6% of affected patients per year.[2] There is increased risk of progression to overt hypothyroidismin patients who are older, female, and positive for anti-TPO (thyroidperoxidase) antibodies, goiter, neck irradiation orradioactive iodine exposureserum TSH values >10 mIU/L.[3]

Clinical impact of subclinical hypothyroidism

Many patients with subclinical hypothyroidismare asymptomatic. Risk of hypothyroid symptoms are more when TSH level is more than 10 mIU/L.

Cardiovascular risk: Subclinical hypothyroidism has been associated with increasedcardiovascular risk by different mechanisms affecting serumcholesterol, heart rhythm and rate, ventricular function, riskof coronary artery disease and cardiovascular mortality. Theseoperate by inducing left ventricular diastolic dysfunction, reduced systolic function, increased vascular resistance, stiffening of arteries and endothelial dysfunction.[4] Thyroid dysfunction, that is, both high and suppressed TSH, is one of the exacerbating condition in heart failure and American Heart Association (AHA) recommend its determination as a precipitating factor in heart failure patients. Sub clinical hypo thyroidism, particularly among persons with TSH levels of more than 7 mIU/L, has also been associated with increased risks of congestive heart failure and fatal stroke.[2,5]

Should subclinical hypothyroidism be treated at all?

Treatment of asymptomatic patients with serum TSH concentrations less than 10 mIU/Lremains unclear. Retrospective study conducted by Razvi et al.[6] of individuals with mild subclinical hypothyroidism reported an association of levothyroxine treatment, compared with non treatment, with lower all-cause mortality and reduced ischemic heart disease events in patients who were younger (40-70 years), but not in patients older than 70 years. In another similarly designed study by Anderson et al.[7] levothyroxine treatment was associated with a reduction in all-cause mortality in patients younger than 65 years but not myocardial infarction or cardiovascular death in this age group and not with these outcomes in older patients.

Initiationof treatment can be considered for patients with a TSH level of 7.0 to 9.9 mIU/L based on observational data indicating increasedcardiovascular risk, and a therapeutic trial of levothyroxinecan be considered for patients with TSH 4.5 to 6.9 mIU/L who have substantial symptoms of hypothyroidism.

Patients whose serum TSH levels exceed 10 mIU/L are at increasedrisk for heart failure and cardiovascular mortality and should be considered for treatment with levothyroxine.[8]

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General therapeutic approach to the management of subclinical hypothyroidism in nonpregnant adults[8]

TSH levels	Patients < 65 years	Patients > 65 years
o.4-4.4 mIU/L	Normal thyrotropin reference range	
4.5-6.9mIU/L	• Measure thyroid peroxidase (TPO) antibodies • Annual follow-up TSH measurementof asymptomatic patients • Consider treatment with levothyroxine (LT4)in patients with, o Multiple symptoms of hypothyroidism o Positive TPO antibodies o Progressively increasing TSH levels o Planning for pregnancy o Goiter	Treatment is not recommended
7.0-9.9 mIU/L	Treat with LT4 to reduce risk of fatal stroke and coronary heart disease (CHD) mortalitya	Consider treatment with LT4 to reduce risk of CHD mortalitya
>10 mIU/L	Treat with LT4 to reduce risk of progression to overt hypothyroidism, heart failure, CHD events, and CHD mortalitya	
a: Recommendation is based on anassociation of subclinicalhypothyroidism with increasedrates to the outcomes listedand is not based on clinical trialevidence that treatment can reducethese outcomes.		

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