Topic: NORMAL SERUM TSH & LIPIDS

Title: The association between TSH within the reference range and serum lipid concentrations in a population-based study: the HUNT study.

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SUMMARY

Objective: The association between TSH and serum lipids in people with no apparent thyroid disease is insufficiently understood. The authors have studied the association between normal thyroid function, defined as TSH within the reference range of a general population, and concentrations of serum lipids.

Design: Cross-sectional, population-based study with 30,656 individuals without known thyroid disease.

Methods: Using general linear models, the authors calculated mean concentrations of total serum cholesterol, LDL-cholesterol, non-HDL-cholesterol, HDL-cholesterol, and triglycerides across categories of TSH.

Results: Within the reference range of TSH, there was a linear and significant (P for trend < 0.001) increase in total serum cholesterol, LDL-cholesterol, non-HDL-cholesterol, and triglycerides, and a linear decrease (P for trend < 0.001) in HDL-cholesterol with increasing TSH. Subgroup analyses showed statistically significant associations for all lipids in men above 50 years of age, and for triglycerides in all age groups. For women, associations were statistically significant in all age groups except for HDL-cholesterol below 50 years of age. The associations with triglycerides and HDL-cholesterol were stronger among overweight than normal weight individuals.

Conclusion: Within the range of TSH that is considered clinically normal, the authors found that increasing level of TSH was associated with less favourable lipid concentrations. The association with serum lipids was linear across the entire reference range of TSH.

COMMENT

An important clinical consequence of hypothyroidism is its association with an increased risk of cardiovascular disease, which is thought to be mediated in part by the changes in serum lipids that often accompany hypothyroidism. For instance in subclinical hypothyroidism (SCH), defined as increased serum TSH (usually between 4-10 µU/ml) with normal serum free T4 levels, the benefit of early treatment with thyroxine has only been clearly demonstrated when serum lipids abnormalities are present. In such patients, studies have shown that thyroxine administration may be beneficial to reduce total serum cholesterol and LDL-cholesterol. A meta-analysis (in 1996) concluded that normalization of serum TSH in patients with SCH was associated with a decrease in serum cholesterol by 0.4 mMol/L on average (Tanis et al., Clin Endocrinol., 44:643, 1996). A more recent
meta-analysis also concluded that normalization of serum TSH decreased serum LDL-cholesterol by 0.26 mMol/L (Danese et al., JCEM 85:2993, 2000). Reduction in serum total and LDL-cholesterol may be larger in individuals with higher cholesterol levels prior to treatment. The observed decrease in LDL-cholesterol is estimated to decrease the risk of cardiovascular mortality by 9-31% (Meier et al., JCEM 86:4860, 2001).

The main finding of present study was to show a consistent, linear, and significant increase in concentrations of total serum cholesterol, LDL-cholesterol, non-HDL-cholesterol, and triglycerides, in both men and women, with increasing concentration of serum TSH within the reference range of 0.5-3.5 µU/ml. There was also a consistent reduction in HDL-cholesterol with increasing TSH. In a separate analysis, an additional interesting finding of present study was that, in the context of this population study, the authors had a database concerning 2,007 patients with SCH. When the data from patients with SCH were analysed with those of the normal subjects, there was a continuum for further increases in total serum cholesterol, LDL-cholesterol, non-HDL-cholesterol, and triglycerides, but no clear association with decreased HDL-cholesterol.

In conclusion, TSH levels representative of normal thyroid function may have long-term harmful effects on cardiovascular health through the association with serum lipids. However, the strengths of the associations were modest, and their clinical significance remains to be determined in prospective studies of variations of normal thyroid function related to risk of cardiovascular disease.

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See Figures below