Effect of thyroid substitution on hypercholesterolaemia in patients with subclinical hypothyroidism: a reanalysis of intervention studies

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Authors' objectives
To assess the effect of thyroid substitution on total cholesterol in patients with subclinical or overt hypothyroidism.

Searching
MEDLINE was searched from January 1976 (when a reliable thyrotrophin, TSH, assay became available) until January 1995, using the following index terms: ‘cholesterol’, ‘hypercholesterolaemia’, ‘hyperlipidaemia’, ‘hypothyroidism’, ‘thyrodrophin’ and ‘human’. Additional literature was found by examining the references of retrieved articles and reviews.

Study selection
Study designs of evaluations included in the review
Intervention studies were included (no further information given).

Specific interventions included in the review
Thyroxine (thyroid substitution therapy) of 4 to 106 weeks in duration.

Participants included in the review
Patients with either subclinical or overt hypothyroidism were included.

Outcomes assessed in the review
The outcome was the decrease in total cholesterol after thyroid substitution therapy.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection. Included studies had to report TSH levels before and after treatment, and be written in English, French or German.

Assessment of study quality
The authors do not state that they assessed validity.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction, but data were extracted on the following: year of publication, study design, number of patients enrolled, mean age, duration of therapy, normal range of TSH levels, TSH levels before and after treatment, total cholesterol in plasma before and after treatment.

Methods of synthesis
How were the studies combined?
The mean decrease in total cholesterol and its standard error were calculated for each study, based on the standard deviations of the total cholesterol levels before and after treatment. In homogeneous subsets of studies, pooled estimates and 95% confidence intervals (CIs) were obtained by precision weighting.

How were differences between studies investigated?
Homogeneity between the studies was tested for using the sum of squares of the differences between the estimated
treatment effect and the estimated mean, weighted by the inverse squared standard errors. When heterogeneity between studies was found, the random-effects model of DerSimonian and Laird (see Other Publications of Related Interest) was used to explore the source of heterogeneity in the treatment effects. Studies of patients with subclinical hypothyroidism were analysed separately from those of patients with overt hypothyroidism.

**Results of the review**
Thirty-one studies in total: 13 studies (n=278) and 18 studies (n=372) in patients with subclinical and overt hypothyroidism, respectively.

The precision weighted decrease of cholesterol in patients with subclinical hypothyroidism after thyroid therapy was 0.4 mmol/L (95% CI: 0.2, 0.6).

The effect of thyroid substitution in patients with overt hypothyroidism was highly dependent on pre-treatment levels of total cholesterol. When plasma levels were elevated up to 7.8 mmol/L, therapy decreased cholesterol by 1.2 mmol/L (95% CI: 0.9, 1.5). When plasma levels were higher than 7.8 mmol/L, cholesterol was reduced by 3.4 mmol/L (95% CI: 3.0, 3.7).

**Authors' conclusions**
Thyroid substitution treatment in patients with hypercholesterolaemia and subclinical hypothyroidism decreases total plasma cholesterol by 0.4 mmol/L, but plasma levels remain elevated in most patients. Further treatment with dietary restriction and cholesterol synthesis inhibitors should be considered.

**CRD commentary**
No information is given on the types of study design used in this review, other than that they were intervention studies. Since the analysis compares differences between pre- and post-treatment cholesterol levels, the intervention studies may be of a before-and-after type rather than randomised controlled trials. Therefore, the decreases in cholesterol reported may have been due to factors other than the thyroid substitution therapy, e.g. dietary factors.

**Bibliographic details**

PubMedID
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**Other publications of related interest**
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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.