Effectiveness of thyroid hormone suppressive therapy in benign solitary thyroid nodules: a meta-analysis

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Authors' objectives
To review the evidence from randomised, controlled trials (RCTs) on the effectiveness of thyroid hormone suppressive therapy in patients with benign, solitary thyroid nodules.

Searching
MEDLINE was searched from January 1985 to April 2001; the search terms were provided. In addition, the references from all the identified articles were handsearched.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) with or without a placebo control group were eligible for inclusion.

Specific interventions included in the review
Studies of thyroid hormone suppression with thyroid hormone therapy, and which had a treatment duration and follow-up of at least 6 months, were eligible for inclusion. The specific doses of levothyroxine (L-T4) varied from 1.5 to 3 microg/kg.

Participants included in the review
Participants with a diagnosis of single thyroid nodule by palpation, which was proven benign by fine-needle aspiration biopsy, were eligible for inclusion. The majority of the participants were female (90%), and the mean age ranged from 34 to 48 years.

Outcomes assessed in the review
Studies that assessed the measurement of thyroid volume by ultrasound, and in which the response to suppressive therapy was defined as greater than a 50% reduction in nodule volume from baseline, were included.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

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

Data extraction
One reviewer extracted the data and a second reviewer subsequently checked the extraction. The relative risk (RR) and its 95% confidence intervals (CIs) were calculated for each study using the number of patients assigned to treatment versus control group whose nodule volume decreased by more than 50%, as determined by ultrasonic measurement.

Methods of synthesis
How were the studies combined?
The RRs were pooled using a random-effects model.

How were differences between studies investigated?
Heterogeneity was investigated formally using the chi-squared test, and also by visual examination of a plot of the effect sizes. Both one- and two-way sensitivity analyses were performed to evaluate the impact of each selected study.
on the overall results of the meta-analysis.

Results of the review
Six RCTs (total n=346: 175 intervention group and 171 control group) were included.

Five of the 6 included studies showed no statistically significant response to L-T4 suppressive therapy by the end of the study period, although the proportion of patients whose nodule volume decreased by more than 50% was higher in the L-T4 treated groups (22%) than in the control groups (10%). The results of the meta-analysis showed an overall RR of 1.9 (95% CI: 0.95, 3.81) in favour of the treatment group. However, there was considerable heterogeneity between the different study results.

Authors' conclusions
Suppressive thyroid hormone therapy for longer than 6 months is associated with a trend towards a reduction of more than 50% in the volume of benign thyroid nodules, but this trend fails to reach statistical significance.

CRD commentary
The review had a clear objective with defined inclusion criteria for the participants, interventions, study designs and outcomes. The literature search was based on just one electronic database and reference searching. No attempts were made to find unpublished material, and it was unclear whether foreign language articles were eligible for inclusion. It is therefore possible that some relevant studies might have been missed. The quality of the studies did not appear to have been formally assessed, thus making it difficult to assess the potential effect on the results. Aspects of the review methodology, such as the study selection and data extraction processes, were not described in full. It is therefore difficult to assess any potential bias in the review process. The data were appropriately combined in a meta-analysis and differences between the studies were thoroughly explored. Overall, the authors' conclusions appear appropriate, but the results of this review are based on a small number of patients and may, therefore, be subject to bias.

Implications of the review for practice and research
Practice: The authors stated that although, on the basis of the results of the study, suppression therapy cannot be generally recommended for the treatment of single benign thyroid nodules, with the expectation of achieving significant reduction in their sizes, it may still be reasonable to offer this option to carefully selected patients whose risk for development of potential adverse effects is low.

Research: The authors stated that more studies involving a larger number of patients are needed before the effects of thyroid hormone suppressive therapy can be properly delineated.

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Other publications of related interest
This additional published commentary may also be of interest. Hoermann R. Thyroid-hormone suppressive therapy in

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