Ablation of the thyroid remnant and I-131 dose in differentiated thyroid cancer

Doi S A, Woodhouse N J

Authors' objectives
To compare the efficacy of remnant ablation following a single low dose versus a single high dose of iodine-131 (I-131) in patients with differentiated thyroid cancer, and to determine whether or not the extent of surgery influences the outcome.

Searching
MEDLINE was searched from inception to June 1999 for studies reported in the English language; the search terms were reported. An internet search of conference abstracts and a manual search of the reference lists of identified articles were also performed. Only published studies were eligible for inclusion in the review.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) and cohort studies were eligible for inclusion in the review. The authors also included a historical cohort of patients seen by one of the authors.

Specific interventions included in the review
Studies that compared a 1,110 (+ or - 185) megabecquerel (MBq) dose of I-131 with higher doses using a similar protocol were eligible for inclusion. In the majority of the included studies, the low dose used was 1,110 MBq (range: 925 to 1,258) and the most commonly used high dose was 3,700 MBq (range: over 1,110 to 3,700).

Participants included in the review
Studies of patients who had received surgery for differentiated thyroid cancer were eligible for inclusion in the review. Patients not eligible for inclusion were: patients with medullary, anaplastic or poorly differentiated carcinomas who were not given radioiodine; patients who presented with distant metastases; and patients who received their first dose of I-131 more than 12 months after surgery. The studies included patients who had received total, near-total and sub-total thyroidectomy.

Outcomes assessed in the review
Studies in which the relative risk of failure of remnant ablation associated with dose levels of I-131 could be calculated were eligible for inclusion. The studies had to have assessed the outcome after the first I-131 ablation post-surgery with clear criteria. The studies also had to have performed whole body scanning between 3 and 12 months after the therapeutic dose of I-131. The criteria for successful ablation used in the included studies varied; details were provided in the paper.

How were decisions on the relevance of primary studies made?
The two authors independently assessed studies for inclusion in the review. They did not state how any disagreements were resolved.

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

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction.

Successful remnant ablation was determined by the various criteria used in the individual studies. The relative risk (RR)
was used as a measure of the relation between I-131 dose levels and the risk of remnant nonablation for each study.

Methods of synthesis
How were the studies combined?
The pooled RR was calculated using both fixed-effect (Mantel-Haenszel) and random-effects (DerSimonian and Laird) models. The 95% confidence interval (CI) around the pooled RR was calculated using the method of Greenland-Robins. Publication bias was assessed using Egger's regression.

How were differences between studies investigated?
Heterogeneity was assessed using the Cochran Q test. Sensitivity analyses were performed based on study design, sample size, risk of failure in the low-dose group and year of publication. The subgroup analysis of RCTs was also re-run excluding a trial that had a worse outcome for patients in the high-dose group.

Results of the review
Eleven published studies (n=809) were included in the review, along with a cohort of patients seen by one of the authors; the cohort (n=158) was split into two groups according to type of thyroidectomy procedure. The 11 published studies comprised 3 RCTs and 8 cohort studies.

The pooled RR of nonablation after the first dose of I-131 was 0.73 (95% CI: 0.61, 0.87), indicating that high-dose patients have a statistically significantly lower risk of nonablation than low-dose patients after the first dose. There was no significant heterogeneity between the studies (Cochran Q test, P=0.76). Assuming the average risk of failure of ablation with low-dose I-131 is about 50%, then the absolute reduction in risk with high-dose I-131 would be 15%. The number of patients that would need-to-be-treated with high dose I-131 in order to prevent one ablation failure would be about seven.

The pooled RR was 0.69 (95% CI: 0.57, 0.84) for the cohort studies and 0.9 (95% CI: 0.6, 1.3) for the RCTs, using both the fixed-effect and random-effects models. Smaller studies, studies in which the risk of failure in the low-dose group was higher, and studies published in 1987 or earlier had a lower pooled RR. However, none of the sensitivity analyses produced significantly different results from the main analysis.

Egger's regression suggested that publication bias was present.

Authors' conclusions
High-dose I-131 (in the region of 2,775 to 3,700 MBq) is more efficient than low dose I-131 for remnant ablation, particularly after less than total thyroidectomy.

CRD commentary
The review question was clear in terms of the study designs, interventions, participants and outcomes of interest. However, the authors stated that only published RCTs and cohort studies were eligible for the review, yet included a cohort of their own patients. The authors undertook a limited search and only studies published in English were included, thereby increasing the potential for language bias and publication bias; an assessment of publication bias suggested that it was present. Two reviewers independently assessed studies for inclusion in the review, which helps reduce the potential for errors and reviewer bias. However, the authors did not state how the data were extracted from the included studies, thus the potential for errors and reviewer bias in this process cannot be assessed. The included studies were not assessed for quality and this may affect the validity of the results. Adequate details of the included studies were presented. The authors assessed statistical heterogeneity and performed sensitivity analyses. The methods used to combine the studies appear appropriate. Owing to the lack of a validity assessment, the potential for reviewer error or bias and language bias, and the presence of publication bias, the authors' conclusions should be interpreted with caution.
Implications of the review for practice and research

Practice: The authors stated that the results of their review suggest that patients with differentiated thyroid cancer should routinely have a total thyroidectomy followed by high-dose I-131 (2,775 to 3,700 MBq) for ablation of the remnant.

Research: The authors did not state any implications for further research.

Bibliographic details

PubMedID
10848882

Indexing Status
Subject indexing assigned by NLM

MeSH
Cohort Studies; Combined Modality Therapy; Humans; Iodine Radioisotopes /administration & dosage /therapeutic use; Radiotherapy Dosage; Randomized Controlled Trials as Topic; Risk; Thyroid Gland /radiation effects; Thyroid Neoplasms /radiotherapy /surgery; Thyroidectomy /methods; Treatment Failure

AccessionNumber
12000001240

Date bibliographic record published
31/10/2006

Date abstract record published
31/10/2006

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.