1. Front Endocrinol (Lausanne). 2016 May 23;7:48. doi: 10.3389/fendo.2016.00048. eCollection 2016.

Which Is the Ideal Treatment for Benign Diffuse and Multinodular Non-Toxic Goiters?

Knobel M[1].

Abstract

Patients with large benign goiters often present local compressive symptoms that require surgical treatment, including dysphagia, neck tightness, and airway obstruction. In contrast, patients with such goiters who remain asymptomatic may be observed after exclusion of malignancy. The use of levothyroxine (LT4) to reduce the volume of the goiter is still a controversial treatment for large goiters, and the optimal surgical procedure for multinodular goiter is still debatable. Radioiodine is a safe and effective treatment option when used alone or in combination with recombinant human TSH. This review discusses current therapeutic options to treat diffuse and multinodular non-toxic benign goiters.

2. Clin Endocrinol (Oxf). 2015 Nov;83(5):702-10. doi: 10.1111/cen.12654. Epub 2014 Dec 29.

Recombinant human thyrotropin before (131)I therapy in patients with nodular goitre: a meta-analysis of randomized controlled trials.

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Abstract

BACKGROUND:

Recombinant human thyrotropin (rhTSH) can be used to enhance radioiodine therapy for shrinking multinodular goitre. The aim of this meta-analysis was to compare the effectiveness of rhTSH pretreatment and radioiodine therapy with that of radioiodine alone for treating benign nodular goitre.

METHODS:

The PubMed, EMBASE, Cochrane Library, Scopus and ClinicalTrials.gov databases were searched to identify studies published before September 2014. A meta-analysis was performed to calculate the pooled effect size using random-effects models. The primary outcome was the reduction in thyroid volume. Secondary outcomes included thyroid function, extent of tracheal compression, radioactive iodine uptake, incidence of hypothyroidism and other complications.

RESULTS:

Nine RCTs including 416 patients were selected. The reductions in thyroid volume were significantly greater in the rhTSH pretreatment groups than those in the radioiodine alone groups at 12 months (weighted mean difference: 14·42%; 95% CI: 4·51-24·34% in high-dose rhTSH vs radioiodine alone; weighted mean difference: 19·66%; 95% CI: 3·67-35·65% in low-dose rhTSH vs radioiodine alone). The incidence of hypothyroidism in the high-dose rhTSH groups was significantly higher than that in the radioiodine alone groups. No significant difference in the incidence of hypothyroidism occurred between the low-dose rhTSH groups and the radioiodine alone groups.

CONCLUSIONS:

The overall results indicated that using rhTSH before radioiodine therapy resulted in a greater thyroid volume reduction than radioiodine therapy alone. An increased incidence of hypothyroidism was observed in patients receiving high-dose rhTSH. Low-dose rhTSH before radioiodine therapy is more efficacious than radioiodine therapy alone for treating nontoxic benign thyroid nodules.

3. Thyroid. 2014 Apr;24(4):727-35. doi: 10.1089/thy.2013.0370. Epub 2014 Mar 4.

Long-term efficacy of modified-release recombinant human thyrotropin augmented radioiodine therapy for benign multinodular goiter: results from a multicenter, international, randomized, placebo-controlled, dose-selection study.

Fast S[1], Hegedüs L, Pacini F, Pinchera A, Leung AM, Vaisman M, Reiners C, Wemeau JL, Huysmans DA, Harper W, Rachinsky I, de Souza HN, Castagna MG, Antonangeli L, Braverman LE, Corbo R, Düren C, Proust-Lemoine E, Marriott C, Driedger A, Grupe P, Watt T, Magner J, Purvis A, Graf H.

Abstract

BACKGROUND:

Enhanced reduction of multinodular goiter (MNG) can be achieved by stimulation with recombinant human thyrotropin (rhTSH) before radioiodine ((131)I) therapy. The objective was to compare the long-term efficacy and safety of two low doses of modified release rhTSH (MRrhTSH) in combination with (131)I therapy.

METHODS:

In this phase II, single-blinded, placebo-controlled study, 95 patients (57.2 ± 9.6 years old, 85% women, 83% Caucasians) with MNG (median size 96.0 mL; range 31.9-242.2 mL) were randomized to receive placebo (n=32), 0.01 mg MRrhTSH (n=30), or 0.03 mg MRrhTSH (n=33) 24 hours before a calculated (131)I activity. Thyroid volume (TV) and smallest cross-sectional area of trachea (SCAT) were measured (by computed tomography scan) at baseline, six months, and 36

months. Thyroid function and quality of life (QoL) was evaluated at three-month and yearly intervals respectively.

RESULTS:

At six months, TV reduction was enhanced in the 0.03 mg MRrhTSH group (32.9% vs. 23.1% in the placebo group; p=0.03) but not in the 0.01 mg MRrhTSH group. At 36 months, the mean percent TV reduction from baseline was 44 ± 12.7% (SD) in the placebo group, 41 ± 21.0% in the 0.01 mg MRrhTSH group, and 53 ± 18.6% in the 0.03 mg MRrhTSH group, with no statistically significant differences among the groups, p=0.105. In the 0.03 mg MRrhTSH group, the subset of patients with basal (131)I uptake <20% had a 24% greater TV reduction at 36 months than the corresponding subset of patients in the placebo group (p=0.01). At 36 months, the largest relative increase in SCAT was observed in the 0.03 mg MRrhTSH group (13.4 ± 23.2%), but this was not statistically different from the increases observed in the placebo or the 0.01 mg MRrhTSH group (p=0.15). Goiter-related symptoms were reduced and QoL improved, without any enhanced benefit from using MRrhTSH. At three years, the prevalence of permanent hypothyroidism was 13%, 33%, and 45% in the placebo, 0.01 mg, and 0.03 mg MRrhTSH groups respectively. The overall safety profile of the study was favorable.

CONCLUSIONS:

When used as adjuvant to (131)I, enhanced MNG reduction could not be demonstrated with MRrhTSH doses ≤ 0.03 mg, indicating that the lower threshold for efficacy is around this level.

4. Thyroid. 2014 Feb;24(2):181-9. doi: 10.1089/thy.2013.0291. Epub 2014 Jan 20.

American Thyroid Association statement on optimal surgical management of goiter.

Chen AY[1], Bernet VJ, Carty SE, Davies TF, Ganly I, Inabnet WB 3rd, Shaha AR; Surgical Affairs Committee of the American Thyroid Association.

Abstract

BACKGROUND:

Goiter, or benign enlargement of the thyroid gland, can be asymptomatic or can cause compression of surrounding structures such as the esophagus and/or trachea. The options for medical treatment of euthyroid goiter are short-lived and are limited to thyroxine hormone suppression and radioactive iodine ablation. The objective of this statement article is to discuss optimal surgical management of goiter.

METHODS:

A task force was convened by the Surgical Affairs Committee of the American Thyroid Association and was tasked with writing of this article.

RESULTS/CONCLUSIONS:

Surgical management is recommended for goiters with compressive symptoms. Symptoms of dyspnea, orthopnea, and dysphagia are more commonly associated with thyromegaly, in particular, substernal goiters. Several studies have demonstrated improved breathing and swallowing outcomes after thyroidectomy. With careful preoperative testing and thoughtful consideration of the type of anesthesia, including the type of intubation, preparation for surgery can be optimized. In addition, planning the extent of surgery and postoperative care are necessary to achieve optimal results. Close collaboration of an experienced surgical and anesthesia team is essential for induction and reversal of anesthesia. In addition, this team must be cognizant of complications from massive goiter surgery such as bleeding, airway distress, recurrent laryngeal nerve injury, and transient hypoparathyroidism. With careful preparation and teamwork, successful thyroid surgery can be achieved.

5. Cochrane Database Syst Rev. 2015 Aug 7;(8):CD010370. doi: 10.1002/14651858.CD010370.pub2.

Total or near-total thyroidectomy versus subtotal thyroidectomy for multinodular non-toxic goitre in adults.

Cirocchi R[1], Trastulli S, Randolph J, Guarino S, Di Rocco G, Arezzo A, D'Andrea V, Santoro A, Barczyński M, Avenia N.

Abstract

BACKGROUND:

Total thyroidectomy (TT) and subtotal thyroidectomy (ST) are worldwide treatment options for multinodular non-toxic goitre in adults. Near TT, defined as a postoperative thyroid remnant less than 1 mL, is supposed to be a similarly effective but safer option than TT. ST has been shown to be marginally safer than TT, but it may leave an undetected thyroid cancer in place.

OBJECTIVES:

The objective was to assess the effects of total or near-total thyroidectomy compared to subtotal thyroidectomy for multinodular non-toxic goitre.

SEARCH METHODS:

We searched the Cochrane Library, MEDLINE, PubMed, EMBASE, as well as the ICTRP Search Portal and ClinicalTrials.gov. The date of the last search was 18 June 2015 for all databases. No language restrictions were applied.

SELECTION CRITERIA:

Two review authors independently scanned the abstract, title or both sections of every record retrieved to identify randomised controlled trials (RCTs) on thyroidectomy for multinodular non-toxic goitre for further assessment.

DATA COLLECTION AND ANALYSIS:

Two review authors independently extracted data, assessed studies for risk of bias and evaluated overall study quality utilising the GRADE instrument. We calculated the odds ratio (OR) and corresponding 95% confidence interval (CI) for dichotomous outcomes. A random-effects model was used for pooling data.

MAIN RESULTS:

We examined 1430 records, scrutinized 14 full-text publications and included four RCTs. Altogether 1305 participants entered the four trials, 543 participants were randomised to TT and 762 participants to ST. A total of 98% and 97% of participants finished the trials in the TT and ST groups, respectively. Two trials had a duration of follow-up between 12 and 39 months and two trials a follow-up of 5 and 10 years, respectively. Risk of bias across studies was mainly unknown for selection, performance and detection bias. Attrition bias was generally low and reporting bias high for some outcomes. In the short-term postoperative period no deaths were reported for both TT and ST groups. However, longer-term data on all-cause mortality were not reported (1284 participants; 4 trials; moderate quality evidence). Goiter recurrence was lower in the TT group compared to ST. Goiters recurred in 0.2% (1/425) of the TT group compared to 8.4% (53/632) of the ST group (OR 0.05 (95% CI 0.01 to 0.21); P < 0.0001; 1057 participants; 3 trials; moderate quality evidence). Re-intervention due to goitre recurrence was lower in the TT group compared to ST. Re-intervention was necessary in 0.5% (1/191) of TT patients compared to 0.8% (3/379)of ST patients (OR 0.66 (95% CI 0.07 to 6.38); P = 0.72; 570 participants; 1 trial; low quality evidence). The incidence of permanent recurrent laryngeal nerve palsy was lower for ST compared with TT. Permanent recurrent laryngeal nerve palsy occurred in 0.8% (6/741) of ST patients compared to 0.7% (4/543) of TT patients (OR 1.28, (95% CI 0.38 to 4.36); P = 0.69; 1275 participants; 4 trials; low quality evidence). The incidence of permanent hypoparathyroidism was lower for ST compared with TT. Permanent hypoparathyroidism occurred in 0.1% (1/741) of ST patients compared to 0.6% (3/543) of TT patients (OR 3.09 (95% CI 0.45 to 21.36); P = 0.25; 1275 participants: 4 trials; low quality evidence). The incidence of thyroid cancer was lower for ST compared with TT. Thyroid cancer occurred in 6.1% (41/669) of ST patients compared to 7.3% (34/465)of TT patients (OR 1.32 (95% CI 0.81 to 2.15); P = 0.27; 1134 participants; 3 trials; low quality evidence). No data on health-

related quality of life or socioeconomic effects were reported in the included studies.

AUTHORS' CONCLUSIONS:

The body of evidence on TT compared with ST is limited. Goiter recurrence is reduced following TT. The effects on other key outcomes such as re-interventions due to goitre recurrence, adverse events and thyroid cancer incidence are uncertain. New long-term RCTs with additional data such as surgeons level of experience, treatment volume of surgical centres and details on techniques used are needed.

6**. Multinodular Goiter [Internet].**

Medeiros-Neto G[15].

Editors

In: De Groot LJ[1], Chrousos G[2], Dungan K[3], Feingold KR[4], Grossman A[5], Hershman JM[6], Koch C[7], Korbonits M[8], McLachlan R[9], New M[10], Purnell J[11], Rebar R[12], Singer F[13], Vinik A[14], editors.

Endotext [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000-.
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Excerpt

Multinodular goiter (MNG) is the most common of all the disorders of the thyroid gland. MNG is the result of the genetic heterogeneity of follicular cells and apparent acquisition of new cellular qualities that become inheritable. Nodular goiter is most often detected simply as a mass in the neck, but sometimes an enlarging gland produces pressure symptoms. Hyperthyroidism develops in a large proportion of MNGs after a few decades, frequently after iodine excess. Diagnosis is based on the physical examination. Thyroid function test results are normal, or indicate subclinical or overt hyperthyroidism. Imaging procedures are useful to detect details such as distortion of the trachea, and to provide an estimation of the volume before and after therapy. From 4 to 17% of MNGs fulfill the criteria of malignant change, however, the majority of these lesions are not lethal. If a clinical and biochemically euthyroid MNG is small and produces no symptoms, treatment is controversial. T4 given to shrink the gland or to prevent further growth is effective in about one third of patients. If the clinically euthyroid goiter is unsightly, shows subclinical hyperthyroidism or is causing pressure symptoms, treatment with ^{131}I preceded by recombinant human TSH is successful but causes hypothyroidism in varying degrees. This treatment can lead to 45-65% shrinkage of the MNG, even if in an intrathoracic position, with a relatively low cost, thus it is considered a good alternative to surgery. However, surgery is an acceptable option. The efficacy of T4 treatment after surgery, to prevent regrowth, is debatable although frequently usedt.