

Justin Ford, MD;
Jon O. Neher, MD
Valley Family Medicine,
Renton, Wash

Sarah Safranek, MLIS
University of Washington
Health Sciences
Library, Seattle

ASSISTANT EDITOR

Gary Kelsberg, MD
Valley Family Medicine,
Renton, Wash

Q / Medication vs radioablation for Graves' disease: How do they compare?

EVIDENCE-BASED ANSWER

A / **THE BENEFITS ARE SIMILAR**; the risks vary. Treating Graves' disease initially with medication or radioablation (or surgery) produces comparable resolution of hyperthyroidism at 2 years (strength of recommendation [SOR]: **B**, a randomized clinical trial [RCT]). The goal of radioablation is lifelong hypothyroidism.

While radioablation doesn't appear to increase the risk of neoplasia, "theoretical concerns" have led to the recommenda-

tion that it not be used for children younger than 5 years (SOR: **C**, expert opinion).

Radioablation carries a higher risk of thyroid-associated ophthalmopathy (TAO) than medical therapy (SOR: **B**, an RCT and a lower-quality meta-analysis).

Between 9% and 16% of patients are unable to tolerate medical therapy, mainly because of rash but also because of agranulocytosis (SOR: **A**, meta-analysis).

Evidence summary

A prospective RCT found that medical therapy, radioablation with iodine-131 (¹³¹I), and surgery produced similar control of Graves' hyperthyroidism in 179 patients.¹ Investigators stratified patients by age, assigning younger patients (20-34 years; N=60) to antithyroid medication (methimazole and a β -blocker) for 18 months or subtotal thyroidectomy and older patients (35-55 years; N=119) to 18 months of antithyroid medication, subtotal thyroidectomy, or ¹³¹I radioablation.

After 6 weeks, all therapies produced serum triiodothyronine levels of less than 2.5 nmol/L (data extracted from table; no comparison statistic given). Patients were followed for 48 to 121 months (average follow-up time not given). Investigators found no significant differences in sick leave (72 vs 83 days for medical treatment compared with radioablation; no comparison statistic given) or patient satisfaction (95% for both medical treatment and radioablation; no comparison statistic given).

Medication (initially methimazole) was changed in 16% of patients because of adverse effects. More than a third of patients relapsed after medications were stopped (time to relapse 1-57 months); 21% relapsed after a single ¹³¹I treatment (time to relapse 5-16 months).

In another study, radioablation outperforms medication

A retrospective case series found that radioablation resolved hyperthyroidism more often than medical therapy among 194 consecutive Saudi Arabian patients (mean age 32 years) diagnosed with Graves' disease and followed for an average of 50 months.² One dose of radioiodine (13-15 mCi) cured hyperthyroidism in 83% of patients, whereas 18 months of medical therapy produced remission lasting at least 6 months past the end of therapy in only 26% of patients (no comparison statistic given).

The presence of TAO at diagnosis increased the likelihood of radioablation failure (odds ratio for failure to respond to single dose

of radioiodine=6.4; 95% confidence interval [CI], 1.51-24.4; $P<.01$). A major weakness of the study was that the investigators didn't describe the medication therapy clearly.

More patients develop TAO after radioablation than medical therapy

An RCT found that radioablation is more commonly associated with development of TAO than medical therapy.³ When investigators randomized 313 patients to receive ¹³¹I radioablation or medical therapy for 18 months and followed them for as long as 4 years, more patients receiving radioablation developed TAO (38% compared with 18% for medical therapy, using intention-to-treat analysis; $P<.001$; number needed to harm [NNH]=5). Twenty-five percent of patients initially receiving medical therapy later underwent radioablation, but these patients didn't develop TAO at a higher rate.

An earlier meta-analysis of 2 RCTs (N=189) also found an increased risk of TAO with radioablation compared with medical therapy.⁴ Patients receiving radioablation were more likely to develop TAO (18% vs 4%; relative risk [RR]=4.2; 95% CI, 2.0-8.8; NNH=7) and more likely to develop severe TAO (10% vs 1.6%; RR=4.4; 95% CI, 1.3-15; NNH=12). Adjunctive use of steroids with radioablation didn't alter the risk of new TAO. However, steroid prophylaxis in patients with preexisting TAO significantly reduced the risk of progression after radioablation (RR=0.03; 95% CI, 0.00-0.24). The authors of the meta-analysis didn't evaluate the quality of the RCTs.

Despite low neoplasia risk, radioablation isn't for young children

Expert guidelines state that the goal of radioablation is to induce lifelong hypothyroidism, which is managed with thyroid hormone replacement.⁵ The risk of neoplasia after radioablation is believed to be low with appropriate dosing. However, based on "theoretical concerns," experts don't recommend using radioiodine in children younger than 5 years and advise limited use in children 5 to 10 years of age.⁵

Medication adverse effects include rashes, transient agranulocytosis

A Cochrane review with 7 RCTs (N=620) describing withdrawal rates for patients receiving medication for Graves' disease found that 9% to 16% of patients discontinued treatment because of adverse effects.⁶ Rashes were the most common adverse effect (6%-10% of patients), but as many as 3% of patients developed transient agranulocytosis. In addition, patients on medication need frequent blood tests to monitor for thyroid activity and potential toxicity.

Recommendations

The guidelines of the American Thyroid Association and the American Association of Clinical Endocrinologists state that overt Graves' hyperthyroidism may be treated with any of the following: ¹³¹I radioablation, antithyroid medication, or thyroidectomy.³ Patient characteristics (pregnancy, mild disease, goiter compression symptoms) should help determine the appropriate option in any given case. **JFP**

>
Patients on medication need frequent blood tests to monitor for thyroid activity and potential toxicity.

References

1. Törring O, Tallstedt L, Göran W, et al. Graves' hyperthyroidism: treatment with antithyroid drugs, surgery, or radioiodine—a prospective, randomized study. *J Clin Endocrinol Metab*. 1996;81:2986-2993.
2. Alfadda A, Malabu UH, El-Desouki MI, et al. Treatment of Graves' hyperthyroidism—prognostic factors for outcome. *Saudi Med J*. 2007;28:225-230.
3. Träisk F, Tallstedt L, Abraham-Nordling M, et al. Thyroid-associated ophthalmopathy after treatment for Graves' hyperthyroidism with antithyroid drugs or iodine-131. *J Clin Endocrinol Metab*. 2009;94:3700-3707.
4. Acharya SH, Avenell A, Philip S, et al. Radioiodine therapy (RAI) for Graves' disease (GD) and the effect on ophthalmopathy: a systematic review (structured abstract). *Clin Endocrinol*. 2008;69:943-950.
5. Bahn RS, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid Association and American Association of Clinical Endocrinologists. *Endocr Pract*. 2011;17:456-520.
6. Abraham P, Avenell A, McGeoch SC, et al. Antithyroid drug regimen for treating Graves' hyperthyroidism. *Cochrane Database Syst Rev*. 2010;(1):CD003420.



Visit us @ jfponline.com

THE JOURNAL OF
**FAMILY
PRACTICE**