Early Treatment of Hypothyroidism after Radioiodine Therapy of Graves’ Disease Prevents Ophthalmopathy

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SUMMARY

Background
Treatment of hyperthyroidism with radioactive iodine (RAI) has been associated with worsening of Graves’ ophthalmopathy (GO). The purpose of the present study was to evaluate risk factors for GO, especially hypothyroidism, after RAI.

Methods
This was a retrospective study of a large cohort of patients treated for Graves’ disease (GD) with RAI at the Mayo Clinic, using a dose of 0.2 mCi $^{131}I$ per gram of thyroid tissue corrected for the thyroid uptake. Patients were evaluated for the presence of GO before therapy and for worsening or onset of GO based on the development of the following features: worsening of proptosis, diplopia, soft-tissue features, or visual acuity; need for systemic or surgical GO therapy; or deterioration of the eyes as assessed by the patient. For the final analysis, patients with GO were divided into two groups: (i) new or worsened GO; and (ii) unchanged or improved GO.

Results
From January 2005 through December 2006, 291 patients with GD received RAI treatment for hyperthyroidism. Ninety-six patients were excluded from the study because of inadequate data or other factors, leaving a cohort of 195 patients, of whom 155 were followed at the Mayo Clinic and 40 were followed by mail and telephone contact. Of the 195 patients 80% were women, the mean age was 50 years, and the median duration of GD was 2 months. The prevalence of GO at baseline was 23.6% (46 of 195), with 38 patients having mild and 8 having moderate to severe GO. The prevalence of smoking was 17.4% (34 of 195).

After 1 year of follow-up, 39 patients had GO (20%), including 15 new cases and 24 preexisting cases. In the 46 patients with GO at baseline, the eye disease subsequently deteriorated in 10. In 9 (19.6%) of the 46 patients, the GO did not progress and in 27 (58.7%), it improved. Altogether, after RAI treatment, GO developed or worsened in 25 (12.8%) of 195 patients.

Hypothyroidism was present at the first follow-up visit in 102 (52.3%) of 195 patients and was strongly associated with the development or deterioration of GO (odds ratio [OR], 3.3; 95% CI, 1.3 to 8.7; P = 0.011). The time to the first visit after RAI therapy was a median of 69 days (interquartile range, 53 to 88). In a multivariate analysis, the duration to first follow-up was a predictor of hypothyroidism, with an OR of 1.05 per day increase in follow-up time (95% CI, 1.03 to 1.07). The multivariate analysis included hypothyroid status at the first follow-up, steroid prophylaxis, smoking status, $FT_4$ at baseline, sex, age, 24-hour RAI uptake, thyroid size, and dose of RAI. The only factors that remained independently significant were the development of hypothyroidism by the first follow-up visit after RAI therapy (OR, 3.6) and preexisting GO (OR, 2.8).

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Although more smokers had new or worse GO than nonsmokers (18% vs. 12%), the difference was not significant. Preexistent GO was associated with a higher risk for worsening as compared with patients who had no GO at baseline; 24% of patients with GO at baseline experienced worsening, but GO developed in only 11% of patients who did not have it at baseline (P = 0.021).

Conclusions

The presence of hypothyroidism at the first assessment of thyroid function after RAI administration is a strong predictor for an adverse outcome of GO, with the highest possibility in patients with preexistent GO. To prevent clinical hypothyroidism and the associated risk for GO, the optimal time for first measurement of FT$_4$ is prior to 6 weeks after RAI therapy.

ANALYSIS AND COMMENTARY

In other studies, hypothyroidism and smoking have been shown to predispose patients to the development of ophthalmopathy after $^{131}$I therapy for GD (1,2). It is well known that RAI therapy exacerbates preexistent ophthalmopathy. Indeed, this knowledge led to the use of prednisone to prevent GO after $^{131}$I therapy (3). Surprisingly, RAI was used in the current study in patients with preexistent GO, including a few with moderate GO. Although some patients received glucocorticoids, systematic data was not presented with regard to their use in the 46 patients with preexistent GO, so the effect of glucocorticoids in preventing exacerbations in this group could not be determined. The authors state that prophylactic steroids were offered only to patients deemed at high risk for deterioration.

The dose of $^{131}$I was relatively large (mean, 15 mCi), resulting in a high prevalence and early onset of hypothyroidism. Forty percent of patients had hypothyroidism at 6 to 8 weeks, and about three fourths had hypothyroidism at 12 to 16 weeks, based on measurements of FT$_4$. It is important to note that TSH may still be suppressed at these early times after RAI therapy of hyperthyroidism, so it is not a reliable marker for hypothyroidism in this context.

Tallstedt et al. noted that early administration of levothyroxine was associated with a reduction in the development of GO (2). In another study of 72 patients with minimally active GO treated with RAI, levothyroxine was started 2 weeks after RAI; there was no deterioration of the GO, and several patients improved during the 12 months of follow-up (4).

The authors of the current study suggest that the first follow-up after RAI to detect and initiate treatment for hypothyroidism should be within 6 weeks, but it might be safer to perform routine follow-up at 4 weeks and initiate therapy for hypothyroidism, if necessary, at this time.

References


