Early Changes in Thyroid-Stimulating Antibody Activity following Radioiodine Therapy

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Key Words
Graves’ disease · Hyperthyroidism · Thyroid autoimmunity · Thyroid-stimulating hormone receptor antibody stimulating activity · Thyroid-stimulating antibody · Radioiodine therapy

Abstract
Objective: The aim of this study was to determine whether or not the titre of thyroid-stimulating hormone receptor antibody with stimulating (TRAb-S) activity changes in patients with Graves’ disease (GD) or toxic multinodular goitres (TMNG) 3 months after treatment with sodium iodide (131I).

Subjects and Methods: Serum specimens were obtained from 21 hyperthyroid patients (15 with GD and 6 with TMNG) at a median 0.5 months before and 3 months after 131I treatment using a standard ablative dose of 555 MBq. TRAb-S activity was measured in a sensitive and specific luminescent bioassay employing the lulu cell line and expressed as a stimulation index (SI; normal ≤1.5).

Results: The mean TRAb-S in the GD patients was 2.72 SI (95% CI: 1.51–4.03) 0.5 months before administration of 131I and 3.98 SI (95% CI: 1.20–6.76) 3 months after administration of 131I. The difference was not statistically significant at p < 0.8. It was not elevated in the TMNG patients before (0.57 SI; 95% CI: 0.41–0.73) and after (1.00 SI; 95% CI: 0.74–1.26) treatment either. Conclusions: Radioiodine therapy for GD or TMNG did not induce a significant change in TRAb-S activity at 3 months after treatment with 131I, probably due to effective antithyroid therapy or the timing of samples.

Introduction
Sodium iodide-131 (131I) is increasingly advocated as the definitive treatment of choice in patients with hyperthyroidism [1]. Changes that occur in thyroid autoimmunity after treatment of Graves’ disease (GD) with 131I include a rise in thyroid-stimulating hormone receptor antibody with stimulating (TRAb-S) activity [2, 3]. Long-term changes in the titre of TRAb-S that may influence thyroid function have been noted years after 131I treatment [4]. Chiovato et al [5] observed a significant increase in TRAb-S 6 months after 131I treatment in patients who later developed hypothyroidism, and they postulated that the release of thyroid-stimulating hormone receptor (TSH-R) molecules from follicular cells as a consequence of radioiodine-induced thyroid cell damage may boost the immune response and result in the increased TRAb-S activity. Thus the TRAb-S status following 131I treatment...
may be predictive of the clinical outcome of thyroid function and could influence the further management of the patient.

The aim of this study was to determine whether or not the autoimmune changes in TRAb-S activity in serum of hyperthyroid patients treated with an ablative dose of $^{131}$I appear earlier than previously reported by using a highly sensitive and specific human TSH-R bioassay.

**Subjects and Methods**

Twenty-one hyperthyroid subjects, 15 with GD and 6 with toxic multinodular goitres (TMNG), were included in the study. GD was diagnosed on clinical features plus the presence of elevated serum thyrotropin-binding-inhibiting immunoglobulin (TBII) titres (>15% inhibition), and TMNG was also diagnosed on clinical features plus undetectable TBII titres. A $^{131}$I thyroid scan performed on the day of ablative treatment was used as additional evidence for diagnosis and to confirm a 4-hour uptake >4% as indicative of satisfactory iodide trapping. Carbimazole was used as the antithyroid therapy of choice to render patients euthyroid, maintained up to 5 days prior to $^{131}$I therapy, resumed 72 h after treatment and finally discontinued 6 weeks later. Each patient was given a standard ablative dose of 555 MBq (15 mCi). Paired serum samples were obtained at a median 0.5 months before and 3 months after $^{131}$I treatment, and TRAb-S activity was measured in a luminescent bioassay using the lulu cell line (Chinese hamster ovary cells stably transfected with human TSH receptor and a cyclic-adenosine-monophosphate-dependent luciferase-responsive reporter) [6]. Lulu cells were seeded in 96-well plates, and serum was added at 10%. Luciferase expression was quantified as emission of light in the presence of luciferin. Results were expressed as a stimulation index (SI) of light output from a subject’s serum to light output from control serum. The 97.5 percentile of euthyroid serum (1.5 SI) was used as the cut-off. The Mann-Whitney U test was used to assess statistical significance.

**Results**

The mean TRAb-S activity in the patients with GD was 2.72 (1.51–4.03) and 3.98 (1.20–6.76) at 0.5 months before and 3 months after $^{131}$I therapy, respectively. The corresponding SI values for patients with TMNG were 0.57 (0.41–0.73) and 1.00 (0.74–1.26; fig. 1). The difference in titre before and after treatment was not statistically significantly different ($p < 0.8$). In the GD group, 8 of the 15 subjects had elevated TRAB-S activity before radioiodine treatment. Seven continued to have a raised activity at 3 months whilst 1 returned to normal. Two subjects with normal pretreatment TRAB-S developed increased activity after treatment. None of the 6 patients with TMNG had elevated TRAB-S activity either before or after treatment.

**Discussion**

Three months after a standard ablative dose of $^{131}$I had been administered to patients with GD pretreated with carbimazole, TRAB-S activity as measured in a sensitive and specific human TSH-R bioassay showed no significant change probably due to effective antithyroid drug therapy and/or earlier sampling of serum than previously reported [5]. It seems that changes in the titre of TRAB-S do not occur 3 months after ablative treatment with $^{131}$I; however, further studies will be required to confirm this observation.

An increase in TRAB-S titres has been reported following $^{131}$I treatment in some patients with TMNG and variously interpreted as the induction of autoimmunity by $^{131}$I-induced thyroid cell damage, the unmasking of pre-existing GD or a temporary side-effect without further clinical relevance [7, 8]. In this study, we did not observe a similar effect on TMNG patients as the serum sampling was done earlier than 6 months. It should also be noted that the sample size of this study was small.
Conclusion

In this study on 21 hyperthyroid patients, a significant change in TRAb-S activity was not noticed 3 months after treatment with $^{131}I$, probably due to effective antithyroid therapy or the timing of samples.

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References