SUMMARY

Introduction: The effect of RI\textsuperscript{131} therapy amplification by recombinant human (rh) TSH prestimulation in very large goiters has not yet been evaluated in a double-blinded, placebo-controlled study.

Methods: Twenty-nine patients (22 females; age range: 37-87 yrs) with a large multinodular goiter (median of 160 ml) were randomized to receive placebo (n = 15) or 0.3 mg rhTSH (n = 14) 24 hours before RI\textsuperscript{131} administration. Goiter volume was monitored by magnetic resonance imaging.

Results: On average, goiter volume was unchanged one week after therapy in both groups, but the largest deviations from baseline were observed in the rhTSH group. After twelve months, median goiter volume was reduced from \textbf{170 to 121 ml} in the placebo group and from \textbf{151 to 72 ml} in the rhTSH group, respectively (within group: P = 0.001; between group: P = 0.019). This corresponds to reductions of 34.1 ± 3.2 and 53.3 ± 3.3\%, respectively (between group: P < 0.001). In the placebo group, goiter reduction correlated positively with the retained thyroid RI\textsuperscript{131} dose, whereas such a relationship was absent in the rhTSH group. Adverse effects, mainly related to thyroid pain and cervical compression, were more frequent in the rhTSH group. At twelve months, goiter-related complaints were significantly reduced in both groups without any between-group difference. One and three patients in the placebo and the rhTSH group, respectively, developed hypothyroidism.

Conclusions: RhTSH-stimulated RI\textsuperscript{131} therapy improves the reduction of very large goiters by more than 50\%, compared with RI\textsuperscript{131} therapy alone, but at the expense of more adverse effects after therapy. Our data suggest that rhTSH stimulation may work through mechanisms that go beyond the increase in thyroidal RI\textsuperscript{131} uptake.

COMMENT

The use of recombinant human TSH (Thyrogen\textsuperscript{®}) has rapidly grown to become a classical tool in the follow-up of patients with differentiated thyroid cancer after surgery. In the context of malignancy, 2 consecutive daily injections of 0.9 mg of Thyrogen\textsuperscript{®} are used to obtain maximal TSH stimulation in patients on l-T4 suppressive therapy. In the entirely different context of the present study, which deals with the treatment of a benign thyroid condition, lower doses were used, namely only 1 injection of 0.3 mg of Thyrogen\textsuperscript{®}. Serum TSH was not measured after stimulation with Thyrogen\textsuperscript{®}, but the authors had shown previously that this small dose of Thyrogen\textsuperscript{®} allowed for a 75\% increase in intrathyroidal retention of
radioiodine, compared with placebo. In a previous (recent) randomized trial, the same group had shown that the administration of Thyrogen® before RI\textsuperscript{131} treatment in patients with nontoxic nodular goiters (less than 100 ml in size) was accompanied by a 62% goiter reduction, compared with a 46% reduction when using placebo.

In the present study, the authors have investigated the effects of thyroidal stimulation using Thyrogen® in patients with very large goiters (ranging from 99 to 440 ml). The main end point of the study was to assess the degree of goiter reduction, comparing prestimulation with Thyrogen® and placebo. Twelve months after RI\textsuperscript{131} treatment, goiter reduction was clearly more effective in the Thyrogen® arm of the randomized study. However, this beneficial effect was obtained at the expense of more frequent (and severe) adverse effects observed with rhTSH: cervical pain, glandular tenderness, goiter growth sensation, thyroid compression with stridorous respiration in one patient (necessitating hospital admission), and two patients requiring steroid administration for a short period.

In conclusion, prestimulation with Thyrogen® can - beyond doubt - improve goiter reduction resulting from radioiodine therapy. This effect is particularly beneficial in patients with very large goiters, but the risk of adverse effects should not be ignored and clinical vigilance in the early post-therapeutic period is therefore recommended.

(Daniel Glinoer, M.D.; Ph.D.)

See Figure below

![Graph showing goiter reduction after radioiodine therapy](image)

**Fig. 1.** The individual deviation from baseline of the goiter volume 1 wk after \textsuperscript{131}I therapy, stratified according to the randomization. Each bar represents a patient.