Mild Serum Thyroid Hormone Increase during and after Five-Day Administration of Human Growth Hormone in Healthy Male Adults

YOSHIYA ITO, AKINORI URAE*, AND AKIMASA OKUNO

Department of Pediatrics, Asahikawa Medical College, Hokkaido 078-8510, and
*Kyushu Clinical Pharmacology Research Clinic, Fukuoka 810-0064, Japan

The effect of GH on the pituitary-thyroid axis is a matter of controversy. GH administration has been reported to exert no distinct alteration in thyroid function [1], but to induce decreased serum TSH responses to thyrotropin releasing hormone [2], increased serum triiodothyronine (T3) with no change in thyroxine (T4) levels [3], and enhanced peripheral conversion of T4 to T3 in GH-deficient patients [4]. In normal men there have been few reports on the effects of GH administration on thyroid function. Grunfeld et al. [5] suggested stimulated peripheral conversion of T4 to T3 during a four-day treatment with GH. Jorgensen et al. [6] also suggested that GH stimulated extrathyroidal conversion of T4 to T3 during a four month trial of GH. But the doses of GH used in these studies were pharmacological [5, 6].

The aim of the present study was to evaluate the early effects of low dose recombinant human GH (rhGH) on thyroid function.

**Materials and Methods**

Six male adults with a mean age of 22.2 years (range, 21 to 25 years) participated in the study. They were not obese and had no signs of hormonal or metabolic disorders.

RhGH (SM9500) was administered subcutaneously at a dose of 0.04 U/kg/day on 0900 for 5 days (days 1 to 5). Blood samples were drawn each morning prior to the injection from day 1 to day 6, and another six times on day 1 and day 5. On day 12, seven days after the last injection, blood samples were also drawn. Serum GH, IGF-I, IGF binding protein-3 (IGFBP-3), TSH and thyroid hormone (T4, T3, free T4 (fT4) and free T3 (fT3)) were measured by radioimmunoassay.

The results are given in the text as the mean ± S.D. Student's t test for paired comparisons was used, and a P value less than 0.05 was considered significant.

**Results**

There are no significant difference in pharmacokinetic parameters of SM9500 between the first day and the fifth day of the injection (Table 1). IGF and IGFBP-3 increased significantly after rhGH treatment and declined to their basal values on day 12 (Table 2).

All six men had a gradual increase in serum TSH during five-day rhGH administration (Table 2). High TSH values were also found on day 12.

Serum thyroid hormones increased significantly on day 6 and day 12 (Table 2), but they were all within the normal range. There was no change in the ratio of T3 to T4 during the observation period.
**Discussion**

In our study, after five days of GH administration, there was a parallel increase in serum T3, T4 and TSH. To our knowledge this is the first report that shows a stimulatory effect of rhGH on the pituitary-thyroid axis. In earlier studies of the effects of GH on GH deficiency, a rise in serum T3 was observed \[3\]. Recent trials in normal men have reported decreased levels of T4 and increased levels of T3 after GH administration \[5, 7\]. These results indicate that GH augments peripheral conversion of T4 to T3. In contrast, the rise in serum thyroid hormone with a simultaneous increase in serum TSH in our study are most easily explained by augmented secretion of TSH caused by administered GH.

These conflicting results may be due to the difference in the GH dose and the time of day of the injection. The GH dose we used was 0.04 U/kg/day, which was much lower than in previous studies \[5, 7, 8\]. Increased secretion of TSH from the pituitary may overcome peripheral conversion of T4 to T3, because Jorgensen et al. \[9\] showed that GH activation of peripheral deiodinase is dose-dependent.

Daytime GH injection, as in our study, may have different effects on thyroid function compared to the conventional night time injection, because GH is secreted mostly at night. The time of GH administration was not mentioned in previous studies \[5, 7\], except in the study of Moller et al. \[8\] where they administered GH at 2000.

In our study, the rise in serum thyroid hormone and TSH were observed even on the seventh day after the last injection. Although serum IGF-I and IGFBP-3 declined to their basal value on day 12, direct effects of GH-IGF-I axis on TSH-thyroid axis cannot be excluded.

In summary, our short-term study suggests that the administration of low dose GH stimulates TSH secretion in normal men. Whether the increase in the thyroid hormone and TSH are dependent solely on the GH dose and the timing of injections are questions that deserve attention in future studies.

**References**


