NORMAL SERUM TRIODOOTHYRONINE CONCENTRATION AND THE LACK OF TSH RESPONSE TO TRH IN PATIENTS WITH EUTHYROID GRAVES' DISEASE

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Synopsis

In four patients with euthyroid Graves' disease, serum T3 concentration and TRH response were tested. All four patients showed T3 concentration within normal range, albeit representing TRH-refractoriness. The results suggest the possibility that thyroid hormone concentration is not a sole determinant of TRH-responsiveness in Graves' disease, implying currently undetermined pathologic process underlying the abnormality.

It was well documented that TRH failed to stimulate TSH secretion in patients with thyrotoxic Graves' disease. In view of the fact that TRH-responsiveness can be restored when the patients become euthyroid state, it is possible that thyroid hormone excess is in part a cause of TRH-refractoriness in thyrotoxic patients. In this context, we sought to determine the relation between TRH-responsiveness and thyroid hormone concentration in patients with euthyroid Graves' disease.

Materials and Methods

Four female patients with euthyroid Graves' disease Group I (Liddle, et al., 1965) were investigated. All those patients had diffuse goiter and eye signs of Graves' disease. They all had no history or clinical evidence of hyperthyroidism.

Serum total thyroxine (T4) was measured with the method described by Murphy and 131I-triiodothyronine resin sponge uptake (131I-T3-RSU) with Triosorb (Dainabot Laboratories, Tokyo). Serum T3 concentration was measured with the radioimmunoassay by Sephadex G25 column recently developed in our laboratory (Shimizu, et al., 1973).

Synthetic TSH-releasing hormone (TRH), 500μg, was injected intravenously into patients under study. Blood specimens were obtained before 30, 60, 90, and 120 min after injection of TRH. TSH concentration of each specimen was measured by radioimmunoassay employing two antibody technique.

T3-suppression test was performed by the measurement of 131I-24hr-thyroidal uptake before and after administration of T3 75μg per day for 7 days. Anti-thyroglobulin antibody titer of the serum was measured by hemagglutination, employing thyroglobulin hemagglutination test kit (Wellcome Research Laboratories).

LATS activity of serum IgG from patients was measured by McKengie bioassay modified as described previously (Shishiba, et al., 1973).

Results and Discussion

Table 1 summarizes the data obtained in four patients with euthyroid Graves' disease. As shown, all the patients had goiter and eye signs of Graves' disease. Their normal T4, T3-RSU, failure of suppression of thyroidal radiiodine uptake by T3 and their lack of history of hyperthyroidism indicate that the patients under study belonged in euthyroid Graves' disease Group I (Liddle, et al., 1965).
Three of the patients were tested for TRH-induced TSH increase. All showed no elevation of TSH. In all four patients, T₃ concentration measured by radioimmunoassay was within normal limits.

Anti-thyroglobulin antibody measured by hemagglutination and LATS activity by McKenzie assay were negative in all four patients.

Relevant to the present findings, Lawton reported the normal T₃ concentration and TRH-refractoriness in two patients with euthyroid Graves’ disease. However, one of his patients had an overt history of hyperthyroidism and received thyroidectomy. In the other patient, eye signs were not described. Thus, his study mainly dealt with euthyroid Graves’ disease Group II (Lawton, et al., 1971). At any event, normal T₃ concentration combined with TRH-refractoriness found in both studies makes the possibility unlikely that thyroid hormone excess is a sole determinant of TRH-refractoriness in Graves’ disease. Currently undetermined pathologic process may underlie the pituitary gland which results in TRH-refractoriness.

References