Can thyroid stimulating hormone levels by TSH (IRMA) predict relapse of thyrotoxicosis following carbimazole treatment?

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Summary: Serum thyrotrophin receptor antibody (TRAb) and thyroid stimulating hormone (TSH) (IRMA) levels were measured in 38 patients at one month after the end of a course of carbimazole/T₃ therapy for Graves' disease. Despite the increased sensitivity of the IRMA assay a TSH measurement at this stage was found to be of no predictive value, in contrast to estimation of serum TRAb levels which correctly predicted relapse and remission in 90% of patients.

Introduction

Following treatment of Graves' disease with antithyroid drugs, some patients will enter remission while others relapse. Previous studies^{1,2} have assessed the value of thyrotrophin receptor antibodies (TRAb) in identifying patients likely to relapse. These have met with varying degrees of success. While in our experience an elevated TRAb index was associated with relapse² this test is time consuming and is not routinely used in the majority of laboratories. Dahlberg *et al.*³ claimed that a normal thyroid stimulating hormone (TSH) response to a thyrotrophin releasing hormone (TRH) test was a useful indicator of remission. As it has been suggested⁴ that sensitive TSH measurements can replace the TRH test we decided to assess the ability of thyroid stimulating hormone (TSH) levels, estimated using a recently developed commercial immunoradiometric assay (IRMA) to indicate potential relapse and remission after carbimazole treatment of Graves' disease.

Material

The study group comprised 38 patients with clinically and biochemically diagnosed Graves' disease. These patients were treated for 12 months as follows; 0–1 month 45 mg/day of carbimazole, 1–2 months 30 mg/day of carbimazole, 2–12 months 20 mg/day of carbimazole plus 60–80 µg of triiodothyronine (T₃). The

patients were followed for a minimum of 12 months after treatment. Samples for TSH estimation were obtained 1 month after the end of treatment to avoid the suppressive effect of T₃ on TSH Levels. TSH (IRMA) levels were measured using the Sucrosep assay system (Boots Celltech) in which within and between assay coefficients of variation were 1.5% at 20 mU/l, 4% at 2 mU/l and 10% at 0.3 mU/l. The levels of TSH (IRMA) in euthyroid controls ranged from 0.3 to 6.0 mU/l. TRAb levels were measured as described previously² at the end of carbimazole/T₃ treatment.

Statistics

Results are expressed as mean $\pm$ s.d. Data was analysed using a Wilcoxon Rank test.

Results

Thirteen of 38 patients relapsed within the first year. The results (Figure 1) showed 9/38 patients to have undetectable TSH (IRMA) values. Of these, 3 relapsed and 6 remained in remission. Of the 29 patients with detectable TSH (IRMA) values 10 relapsed and 19 remained in remission. There was no significant difference in mean TSH IRMA levels between those who relapsed and those who remained in remission (1.26 ± 1.5 vs 1.8 ± 2.5 , $P > 0.1$).

Twenty three of the 38 patients had TSH levels less than 0.08 mU/l and of these 9 relapsed. This TSH level

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Figure 1 TSH levels at 1 month off carbimazole/T₃ therapy.

was selected as it has been suggested that patients with TSH (IRMA) levels less than 0.08 mU/l would not be expected to respond to a TRH test.⁵

Of the 13 patients who relapsed 11 had elevated

TRAb levels. Of the 25 who remained in remission 23 had TRAb levels within the normal range ($P < 0.05$).

Discussion

In an earlier study Dahlberg *et al.*³ investigated the prognostic value of a TRH test in thyrotoxicosis and found that 74% of patients who developed a normal TSH response to TRH during therapy would remain in remission compared to the 29% who did not. The authors, however, made no mention of whether basal TSH levels differed significantly between groups.

One of the main advantages of the sensitive TSH (IRMA) test is that the lower limit of the normal range can be defined and as a result patients with suppressed circulating levels of TSH can be distinguished. Therefore it might have been anticipated that patients likely to have a relapse of thyrotoxicosis after carbimazole treatment would have suppressed TSH levels measured by an IRMA assay. This small study has shown this not to be the case. All patients in this study received T₃ therapy. After 1 month off carbimazole/T₃ TSH levels ranged from undetectable to 10.6 mU/l. This makes it unlikely that TSH levels are suppressed by the previous T₃ treatment.

TRAb levels were measured in these patients following a 12 month course of antithyroid drugs and were found to predict cases of relapse and remission in 90% of patients. This is in keeping with previous studies.

The results from this study would suggest that TSH (IRMA) levels obtained at 1 month after the end of antithyroid drug therapy are of little use in identifying patients likely to relapse or remain in remission.

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