Early remission in thyrotoxicosis produced by short courses of treatment

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Abstract. Twenty-eight patients with Graves’ disease were treated with short-term antithyroid drug therapy, i.e. treatment was discontinued as soon as they became euthyroid. This was less than 4 months in all patients. Ten patients remained euthyroid, although in two of these, thyrotoxicosis recurred after the patients had been euthyroid for more than 12 months. The other 18 patients relapsed within 12 weeks of stopping therapy, and only two have become euthyroid after a further 12 month period of treatment. All patients who remitted were thyrotoxic for the first time whereas all patients with a past history of thyroid disease relapsed. Positive thyroid microsomal antibody titres were more frequent in patients who remitted, otherwise there were no indicators of a favourable outcome. The remission rate with antithyroid therapy which is only continued until the patient becomes euthyroid is similar to that for treatment lasting 12–18 months. Short-term therapy has the advantage of savings in both patient and clinician time.

Thyrotoxic patients can be controlled with antithyroid drugs but as there is no certain means of predicting remission, the duration of such therapy is arbitrary. The usual recommendation of 12–18 months is not based on any scientific evidence and both early (Astwood 1947; Frisk 1947) and more recent studies (Greer et al. 1977) have shown that remission occurs when patients are treated for only 3–6 months. Provided remissions with short duration therapy are as frequent and long-lasting as conventional treatment (Greer et al. 1977), this would represent a considerable saving in patient and clinician time. In addition those who relapse could be referred at an earlier stage for other forms of therapy.

In the present study patients with thyrotoxicosis of Graves’ disease were treated with carbimazole until they became euthyroid, therapy was then discontinued. Those patients who failed to go into remission have been re-assessed after longer conventional courses of antithyroid drugs.

Materials and Methods

Patients with diffuse toxic goitre were referred to the endocrine clinic by their family doctor. Diagnosis was confirmed by measurement of plasma thyroxine (>150 nmol/l) and radioiodine or radiotechnetium thyroid scan. Thyroid antibody titres were also measured. Patients were then started on carbimazole 45 mg daily in divided doses and reviewed at 6 week intervals or less according to the clinical circumstances. Treatment was discontinued when patients were euthyroid both clinically and biochemically (i.e. plasma thyroxine <120 nmol/l and plasma triiodothyronine <3.0 nmol/l). Subsequent follow-up was initially at 6 week intervals. If relapse occurred, patients were re-started on antithyroid drugs which were continued for a minimum of 12 months before re-assessment.

Results

Twenty-eight patients (21 female), with Graves’ disease presenting over a 12 month period were studied. Four had a history of one previous episode of thyrotoxicosis although not within 3 years of the study, the others had no past history of thyroid disease (Table 1).

All patients became euthyroid on the above regime within 4 months of starting treatment
(mean interval 76 days, range 6–16 weeks). Ten patients, all with no previous history of thyroid disease remained euthyroid when antithyroid drugs were stopped. Thyrotoxicosis has recurred in two of these after 12 and 16 months during which they were clinically and biochemically euthyroid. The mean follow-up of these 10 patients is 21 (17–24) months. The other 18 patients, including the 4 patients with a previous episode of thyrotoxicosis, all relapsed rapidly on discontinuing treatment. Relapse had occurred in 14 by 6 weeks and in all by 12 weeks. Thus patients in remission have been followed for at least five times the maximum period for relapse.

Ten of the 14 patients with no past history who relapsed have completed a longer (≥ 12 months) course of antithyroid drug treatment. Only two have remained euthyroid, the others relapsed again within 3 months of discontinuing treatment. The remainder are still on therapy at the present time.

There was no difference between those who relapsed and those who remained euthyroid as regards male/female distribution, initial plasma thyroxine or presence of goitre. Significant titres of thyroid microsomal antibodies were found more frequently in patients who remained euthyroid (P < 0.1, > 0.05).

Discussion

Determining remission in thyrotoxicosis is impossible except by stopping antithyroid therapy. Several test have been suggested: return of T₃ suppression and return of TRH stimulation (Alexander et al. 1970) but both have significant false negative rates. Recently it has been shown that by measurement of plasma levels of thyroid stimulating antibody (Davies et al. 1977) and of LATS and LATS-protector (Hardisty et al. 1980) it is possible to predict the outcome of stopping antithyroid drugs in many patients. However, neither of these tests is easily adapted to routine clinical work at the present time and therefore most thyrotoxic patients are subjected to repeated courses of antithyroid drugs. These may last up to 18 months or more according to the beliefs of the clinician and longer courses are associated with problems of compliance and regular clinic supervision. Also referral for more definitive therapy (partial thyroidectomy or radioiodine) is often delayed while awaiting the outcome of antithyroid drug therapy.

There are many examples in the literature of patients going into remission after short courses of therapy (Astwood 1947; Frisk 1947; Williams 1946) and it has recently been suggested that such short courses were as effective as more conventional courses of treatment (Greer et al. 1977). This is in contrast to standard textbook advice, that unless therapy is continued for at least one year relapse is inevitable and associated with an exacerbation of thyrotoxicosis (DeGroot & Stanbury 1975). In the present study short courses of treatment continued only until patients were euthyroid, resulting in long-term remission in a third of patients with Graves’ disease. Duration of therapy was at the most 4 months and frequently shorter. The remission rate for patients with a first episode of thyrotoxicosis (40%) is similar to that reported for
conventional periods of treatment (Solomon et al. 1953; Hershman et al. 1966; Greer et al. 1977). Those patients who relapsed did so rapidly after discontinuing antithyroid drugs (≤ 12 weeks) and a subsequent more prolonged course of therapy has only resulted in remission in 2 of 10 patients that have completed such a course. Two patients remained euthyroid immediately after stopping treatment but became thyrotoxic again 12 and 16 months later with several normal biochemical tests in the interval. This contrasts with the majority of patients who relapsed and may therefore represent a further distinct episode of thyrotoxicosis as opposed to a late failure of the initial short course of therapy. Those patients who had a past history of thyrotoxicosis all relapsed after short courses of antithyroid drugs.

Analysis of factors that might influence the outcome including age, sex, initial plasma thyroxine, goitre and thyroid antibodies showed no difference in incidence between those who remitted and those who relapsed, except that thyroid microsomal antibody titres were positive more often in those who remitted.

Until tests are generally available for determining remission in thyrotoxicosis without discontinuing antithyroid drugs, the empirical approach will have to be used. It therefore seems justified, particularly in those patients with a first episode of thyrotoxicosis, to continue antithyroid drugs only to the point when they are euthyroid as outlined in this paper. This will result in a considerable saving in patient and clinic time without significantly altering overall remission rates.

References

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