

Commentary

Anti-thyroid drug treatment before radioiodine in patients with Graves' disease: soother or menace?

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Anti-thyroid drugs are used extensively to treat patients with Graves' disease. The remission rate after a 6–24 month course of treatment is approximately 50% (Leech & Dayan, 1998), but declines with the duration of follow-up (Hedley *et al.*, 1989). No reliable long-term follow-up data are available, but the proportion of patients in remission after 20 years may be as little as 20% (Sugrue *et al.*, 1980), a figure close to the natural remission rate of this disease (Irvine *et al.*, 1977). Radioiodine is highly effective in ablating the thyroid gland, albeit at the expense of life-long thyroxine replacement therapy. The safety of radioiodine has recently been confirmed by a large retrospective survey which included over 35 000 patients followed up for 750 000 patient-years (Ron *et al.*, 1998). Concerns about the risk of radioiodine inducing or exacerbating ophthalmopathy were highlighted by a prospective study, which showed a small but significant association (Bartalena *et al.*, 1998). However, hypothyroidism (an independent risk-factor for the development of ophthalmopathy) was far more frequent in the radioiodine group and probably confounded the results. A more recent prospective study, which eliminated hypothyroidism by frequent blood testing and prompt action with thyroxine replacement, found no differences in the incidence of ophthalmopathy between patients treated with radioiodine or antithyroid drugs (Manso *et al.*, 1998).

Anti-thyroid drugs are often used prior to radioiodine ablation, based on the belief that euthyroidism will be restored more rapidly, and that exacerbation of the thyrotoxic state by radioiodine-induced thyroiditis may be prevented. The impression that radioiodine can cause deterioration of the hyperthyroid state, or indeed precipitate a thyroid storm, has been based on anecdotes. A recent prospective study addressed this very question (Andrade *et al.*, 1999). Fifty-one patients with untreated Graves' disease were randomly allocated to receive methimazole or no drug treatment before radioiodine therapy. The groups were well matched for important clinical and biochemical parameters. Patients receiving antithyroid drugs discontinued treatment four days before radioiodine. Serum thyroid

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hormone concentrations were measured at frequent intervals before and after radioiodine. The group of patients treated with radioiodine alone showed a decrease in serum free T4 and T3 concentrations 5 days after radioiodine. In contrast, patients pretreated with antithyroid drugs experienced a rise in serum thyroid hormone concentrations 1–2 weeks after radioiodine therapy. In both groups serum T3 concentration declined slowly over the remainder of the 30-day follow-up period. Two of the 28 patients treated with radioiodine alone showed a progressive rise in serum T3 and T4. The authors concluded that radioiodine therapy *per se* does not cause exacerbation of thyrotoxicosis. The rise in thyroid hormone concentrations observed in the antithyroid drug pretreated patients was probably caused by discontinuation of their oral medication. This study confirms an earlier less rigorous retrospective report (Burch *et al.*, 1994), as well as the clinical impression of many thyroidologists. The question remains whether these findings are applicable to patients with very severe thyrotoxicosis complicated by cardiac failure, for whom pretreatment with antithyroid drugs seems sensible.

Does it matter, whether patients are pretreated or not? Antithyroid drugs are generally safe, but allergic reactions are not uncommon. Agranulocytosis is fortunately rare, but unpredictable, and all patients exposed to these agents must be educated to discontinue their treatment and have a blood count urgently, should they develop infective symptoms. There is therefore a small but significant risk of adverse drug effects. Furthermore, antithyroid drug pretreatment may reduce the efficacy of radioiodine and increase the probability of recurrence of hyperthyroidism (Leech & Dayan, 1998). Pre-treatment with antithyroid drugs does seem to reduce the incidence of postablation hypothyroidism, but eventually many of these patients succumb to hypothyroidism or thyrotoxicosis (Clerc *et al.*, 1993).

Current evidence favours the use of radioiodine as the treatment of choice for the majority of patients with Graves' disease. Pre-treatment with antithyroid drugs is of doubtful benefit with the possible exception of severely thyrotoxic patients, particularly those with cardiac complications.

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