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CLINICAL

Iodine-131 therapy for hyperthyroidism may have long-term consequences other than thyroid failure

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TITLE Increased long-term cardiovascular morbidity among patients treated with radioactive iodine for hyperthyroidism

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SUMMARY

In this population-based cohort study from a single centre in Finland, the rate and causes of hospitalisation of patients with hyperthyroidism treated with iodine-131 between 1969 and 2002 and followed up for a median period of nine years were compared with those of an age- and gender-matched control group. The median age at treatment with iodine-131 was 62 years in a total of 2,611 patients.

The rate of hospitalisation due to cardiovascular or cerebrovascular disease was higher among the radioactive iodine-treated patients than among the reference population (RR range 1.20–1.48). Importantly, the risk remained elevated for up to 35 years. The most frequent cardiovascular disorder leading to hospitalisation was dysrhythmia, principally atrial fibrillation. There was also a significantly increased risk of hospitalisation as a result of embolic and ischaemic, but not haemorrhagic, stroke.

The authors calculated that the magnitude of the vascular morbidity in the patient group was comparable to an increase in systolic blood pressure of 10 mm Hg, or in low density lipoprotein cholesterol of 1 mmol/l, although they could not distinguish between the effects of iodine-131 treatment and those of hyperthyroidism. They concluded that patients treated for hyperthyroidism with iodine-131 constituted a high-risk group for vascular disease and may benefit from preventive interventions.

OPINION

These findings by Metso et al. add to the growing body of evidence that patients treated with iodine-131 for hyperthyroidism may be at increased risk of cardiovascular and cerebrovascular disease.[1–3] The mechanisms that mediate this increased vascular risk remain unclear. Thyroid hormone excess is important, particularly in the first two to three months before iodine-131 is effective and in those elderly patients with multinodular goitre in whom relatively mild hyperthyroidism may be of many years' duration before presentation with atrial fibrillation and cardiac failure. But the increased risk persists long after thyroid hormone concentrations have been restored to normal.

It has been suggested from studies in our own department that the damage induced by iodine-131 within the thyroid may act as a remote focus of chronic inflammation, producing pro-inflammatory cytokines whose systemic effects include endothelial injury and, ultimately, atherosclerosis.[3] There is, as yet, insufficient evidence about vascular risk to modify attitudes to iodine-131 therapy. However, patients are increasingly wary about irradiation in general and, of all the therapies, iodine-131 is the most likely to induce or worsen thyroid eye disease. The greatest problem is that it is almost inevitable that patients with Graves' disease treated with iodine-131 will develop hypothyroidism and there is simply no consensus about what constitutes an acceptable biochemical profile in patients taking thyroxine replacement. The same problem arises following surgery for Graves' disease as the current illogical fashion is for near total thyroidectomy. There is also anxiety about the bioequivalence of the increasing number of generic preparations of levothyroxine.

If I had Graves' disease I would not wish to be made hypothyroid and would wish to avoid any possibility of increased vascular risk. I would therefore opt for relatively long-term treatment with carbimazole, which is shown to be cheap, effective and safe for periods of at least ten years.[4] By that time my disease may have entered remission spontaneously.

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