INVITED COMMENTARY

Thyrotoxicosis in childhood

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Thyrotoxicosis during the first two decades of life is rare compared to that in adults, with an incidence of 0.8 per 100,000 children per year (1). This limits the experience in the paediatric clinics, and adult treatment strategies are often applied to the thyrotoxic child.

About 95% of thyrotoxic children have Graves' disease (1, 2), in contrast to findings in adults where a significant number of toxic adenomas and multinodular toxic goitres are seen, especially in areas with a relatively low iodine intake (3). It is suggested that Graves' disease in childhood is a self-limiting disorder with a remission rate of 25% every 2 years (4). These observations have to be considered in the choice of therapy.

There are three principal treatments today: antithyroid drugs (ATD), surgery or radioiodine. It is well known that the primary management of thyrotoxicosis in adults is different in Europe, Japan and the USA (5). In a recent European questionnaire study on juvenile thyrotoxicosis, ATD therapy was the treatment of choice and most favoured a fixed treatment period of 1–2 years. Antithyroid drugs were also the most frequent choice for patients with recurrent thyrotoxicosis (6).

Long-term ATD treatment has to be used in order to await remission of juvenile thyrotoxicosis (2, 4). Antithyroid drugs can be given in combination with T4 or the ATD dose can be adapted according to the clinical response. Favouring the adaption strategy in children is the finding in adults that a low dose of methimazole has a similar clinical effect as the higher dose but with less side effects (7). Whether T4 addition has a beneficial effect on the risk of recurrence still needs to be proven in adults outside Japan (8), and no data exist on the recurrence rate in children after T4 supplementation. Toxic side effects and compliance are major problems in long-term ATD treatment. But compliance is also a potential problem in patients on lifelong T4 treatment after surgery or on radioiodine therapy.

Subtotal or total thyroidectomy is the second choice of therapy in Europe in young patients relapsing following ATD therapy, but only in adolescent patients with large goitres (6). Postsurgical recurrences, and probably also hypothyroidism, depend upon the experience and skills of the surgical team. This is also true for the early side effects (hypocalcaemia, palsy of the recurrence nerve). The frequency of these early surgical side effects is relatively low (1–3%) but cannot be neglected. The incidence of hypothyroidism progressively increases in the decades following surgery to 30–75% (9, 10).

The third approach to treatment is the radioiodine ablative therapy, which has become the definite therapy of choice in older children and adults in USA (2, 11). Radioiodine is an effective treatment with a low relapse rate if an "ablative" dose is employed. This renders a significant number of patients hypothyroid (up to 60–90% in long-term follow-up studies) and in many studies the doses of 131I are chosen to induce an early onset of hypothyroidism (11). The cancer risk until now has been a major concern to the European paediatric endocrinologist, and radioiodine therapy has therefore only been chosen in patients with recurrent thyrotoxicosis after surgery (6). In adults, however, long-term follow-up has shown no evidence of an increased risk to leukaemia, whereas there is some evidence of a slightly increased risk of gastric cancer after 10 years or more, even though the irradiation of extrathyroidal tissue is minimal (12, 13). The long-term post-radioiodine risk in children for developing cancer, osteoporosis after irradiation of calcitonin-producing cells or late hypoparathyroidism remains to be seen. In adults, radioiodine treatment is followed by progression in ophthalmopathy in some patients (14). Whether this is a concern in children, where significant ophthalmopathy is rare, is not known. There is no evidence of congenital abnormalities amongst children of women treated with radioiodine (12, 15).

An effort is still needed to identify prognostic factors for recurrence rates and long-term remission of thyrotoxicosis. In adults, initial goitre size seems to correlate with final outcome, but many other criteria have not given satisfactory results, e.g. serum T3 level, TSH-R, Tg and TPO antibody titres, initial severity of the disease, HLA types (16). Long-term prospective follow-up studies are needed, to clarify the natural and clinical course of the childhood thyrotoxicosis, before a more differentiated rational strategy can differentiate between those patients who need destructive therapy early on, from those that might go into remission on short-term or long-term ATD. The future will show if therapies directed at alternately the autoimmune abnormalities will ultimately offer the best therapeutic alternative.
References


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