Optimal Management of Graves' Disease in Childhood and Adolescence

Graves' disease is the most common cause of thyrotoxicosis in children and adolescents. According to Zimmerman et al, Graves' disease has a profound impact on the physical development, learning, school performance, and quality of life in children. Ideally, the treatment should be effective and safe, with minimal immediate and long-term adverse effects. The options for the treatment of Graves' disease in children and adolescents have remained constant over many decades. These treatment options include antithyroid drugs (ATDs), radioactive iodine (RAI) therapy, and thyroidectomy.

Antithyroid drugs continue to be the first-line of therapy for most patients with pediatric Graves' disease. Unfortunately, antithyroid drugs are associated with low remission and high relapse rates in children (80%), drug toxicity, and issues centering around patient compliance. More recent studies documenting fatal hepatic failure with propylthiouracil in children has raised further concerns about the safety and efficacy of antithyroid drugs in kids.

Definitive therapy, therefore, depends on the use of either radioactive iodine or surgery. In many countries, like the United States, radioiodine ablation is the treatment of choice in adults. At the Mayo Clinic, over 95% of adults with Graves' disease are treated with radioactive iodine. Many large studies have demonstrated both the safety and efficacy of radioactive iodine in the adult population. Today, the goal of radioactive iodine therapy is to completely ablate the gland and render the patient hypothyroid, thus requiring thyroid hormone replacement therapy. Indications for thyroidectomy in adults include large gland Graves' disease (glands weighing greater than 60 grams), failure of antithyroid drugs during the second trimester of pregnancy, a suspicious or biopsy-proven associated malignant thyroid nodule, or severe associated Graves' ophthalmopathy.

Unfortunately, we have a paucity of data on children and adolescents; in particular, prepubertal children. Much of what is claimed about the safety of radioactive iodine in children is extrapolated from studies in adults. As pointed out by Reddy, the high susceptibility of young children to the carcinogenic effects of radiation to the thyroid contrasts with the very low susceptibility in adults. This is indeed consistent with experimental studies on animals that suggest greater radiation effects during periods of rapid cell proliferation, such as is observed during the development of the thyroid gland. Previous studies in children and adults have demonstrated an increased risk of both and malignant thyroid nodules in thyroid glands treated with lower doses of radioactive iodine. As pointed out by Gambhir et al in this month's journal, in children treated with more than 200 to 250 Gy (approximately 220 to 275 μCi/gm), hypothyroidism is achieved in nearly 95% of patients. With these complete ablations, an increased rate of thyroid cancer has not been observed and should not be observed in the future. Of concern, however, is the risk of second non-thyroid malignancies developing in children treated with radioactive iodine during a period of time when their cells are particularly susceptible to the carcinogenic effects of radiation. In our recent study, looking at long-term outcomes of children treated with surgery and radiation for papillary thyroid carcinoma, we saw only two papillary thyroid cancer deaths in 215 patients observed over 60 years. However, mortality from all causes was double from what would have been expected for age- and sex-
Eighty-five percent of the patients with Graves’ ophthalmopathy noted improvement, while only one patient experienced worsening of their eye symptoms following surgery. There were no permanent complications and no major concerns regarding the neck incision. Several other major referral centers around the world have also demonstrated the safety and efficacy of thyroidectomy when performed in high volume centers with experienced thyroid surgeons.³

The biggest concern in operative management of Graves’ disease in children centers around the avoidance of hypoparathyroidism. Although total thyroidectomy is the preferred operation, near-total thyroidectomy, leaving a tiny remnant of thyroid tissue associated with one superior parathyroid gland, ensuring its viability, has diminished significantly the risk of permanent hypoparathyroidism in children undergoing surgery for malignancy and Graves’ disease without altering long-term outcomes.

In conclusion, more recent concerns regarding the safety of antithyroid drugs and the paucity of data on the long-term outcomes of radioactive iodine with regard to a second malignancy, in my opinion, favor a surgical approach, when the patient can be treated at a high volume center by an experienced thyroid surgeon. Although thyroidectomies in children are relatively uncommon, surgeons who perform large numbers of adult thyroidectomies are in the best position to perform the safest pediatric thyroid operations.

REFERENCES


