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MANAGEMENT OF GRAVES' HYPERTHYROIDISM IN PATIENTS WITH ORBITOPATHY

Bartalena L. **The dilemma of how to manage Graves' hyperthyroidism in patients with associated orbitopathy.** J Clin Endocrinol Metab. doi:10.1210/jc.2010-2329

SUMMARY

BACKGROUND

Some of the thyrotropin (TSH) receptor antibodies that develop in susceptible individuals can promote thyroid growth, vascularity, and hormone secretion and cause Graves' hyperthyroidism. In orbital tissues from patients with active Graves' orbitopathy, the TSH receptor levels may be higher than in controls, but how TSH receptor antibodies may be related to the development of Graves' orbitopathy remains unclear. Orbitopathy remains clinically silent or is mild in most patients with Graves' disease, and the therapy chosen to treat hyperthyroidism rarely seems to affect their orbitopathy. However, controversy exists about the best way to treat hyperthyroidism in the minority of patients with Graves' disease whose orbitopathy becomes clinically problematic.

METHODS

The author reviewed 30 years of literature on how different approaches to treating Graves' hyperthyroidism may affect associated Graves' orbitopathy.

RESULTS

Orbitopathy can appear while patients are euthyroid while taking antithyroid drugs. Hypothyroidism can affect the eyes, too, so patients being treated with antithyroid drugs need to have their thyroid hormone levels monitored frequently. (The TSH level may be misleading, since it can remain low for some time after serum triiodothyronine and thyroxine levels have fallen below normal). Furthermore, when antithyroid drug treatment is discontinued, hyperthyroidism recurs in about half of cases. Although radioiodine is a common and effective treatment for Graves' hyperthyroidism, randomized trials show that it does increase the risk of orbitopathy developing or becoming worse, as compared with antithyroid drug treatment. In one randomized trial, the risk of orbitopathy progressing after thyroidectomy was the same as after antithyroid drug therapy (1). The risk of orbitopathy developing or becoming worse is substantially increased in smokers. Radioiodine treatment, severe or recent onset of hyperthyroidism, persistently high TSH-binding inhibitory antibodies, and preexisting orbitopathy are also factors associated with an

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increased risk of progressive orbitopathy. Although high-dose glucocorticoids can cause serious side effects, they ameliorate the risk of orbitopathy after radioiodine treatment and also reduce the increased risk of orbitopathy in patients who smoke.

There is no consensus as to the best way to treat active inflammatory orbitopathy. Some prescribe low-dose oral glucocorticoids even for mild orbitopathy. For moderate-to-severe orbitopathy, close follow-up by a team of experienced ophthalmologists and endocrinologists is important, but the therapy chosen still remains a matter of "expert opinion." Oral or intravenous glucocorticoids are commonly used as the initial therapy, but surgery or orbital radiotherapy may be needed if florid inflammation shows no response after a few weeks. The concurrent hyperthyroidism

in such cases is often treated with antithyroid drugs initially, while postponing any decision concerning ablative therapy (surgery or radioiodine) until active orbitopathy has been quiescent for 6 months or longer. Once orbitopathy appears to be stable, diplopia or disfiguring proptosis can be treated with reconstructive surgery. Another point of view, however, is that the thyroid should be ablated promptly after euthyroidism is achieved with antithyroid drugs, concomitant with treatment of the orbitopathy, and prompt thyroid ablation is indicated if the hyperthyroidism is not controlled with antithyroid drug therapy.

CONCLUSIONS

Objective randomized, clinical trials are needed for establishing the best way to treat hyperthyroidism in patients with active moderate-to-severe orbitopathy.

COMMENTARY ●●●●●●●●●●●●●●●●●●●●

The natural history of Graves' hyperthyroidism and that of orbitopathy are quite variable, and the term active moderate-to-severe orbitopathy lacks specificity. Objective ways to assess the degree of edema, fibrosis, and the levels of specific

inflammatory cells separately in each of the various orbital structures would be an important advance in determining what antithyroid therapy is best, as would finding epitope-specific antibodies that correlate with specific orbital responses.

— Stephen W. Spaulding, MD

Reference

1. Tallstedt L, Lundell G, Tørring O, et al. Occurrence of ophthalmopathy after treatment for Graves' hyperthyroidism. *N Engl J Med* 1992;326:1738.