

Mixing modalities: exploring the options for Graves' ophthalmopathy

Graves' ophthalmopathy (GO) can be a difficult clinical problem. While most patients do not require specific treatment, a minority with severe, vision-threatening disease presents tough therapeutic challenges and choices. In these patients with severe manifestations, treatment outcome is frequently unsatisfactory¹; relapses may occur and residual problems, such as proptosis and diplopia, cause continuing distress to many patients. Even the milder forms of GO can profoundly impair quality of life.²

The three major treatment modalities, which have all been in use for many years, include high-dose glucocorticoids, orbital irradiation, and surgical approaches including orbital decompression, eyelid surgery, and correction of strabismus. As may be expected of a disorder that is difficult to treat effectively, numerous other medical treatments have been described in the literature, either as single agents or in combinations. These include immunosuppressive agents, cytokine antagonists, somatostatin analogues, plasmapheresis, and antioxidants. None have been shown to be consistently effective, and many have significant side-effects or potential risks that limit their therapeutic use in GO. Thus, most specialists continue to rely on the three traditional modalities despite controversies as to the best method of deployment and frequently unsatisfactory results.

In the case of orbital radiotherapy, many previously published studies have been retrospective in nature, and even carefully conducted prospective trials³ have been criticised, for, for example, recruiting stable (burnt-out) or previously treated patients, thereby generating results that are difficult to interpret.⁴ This again reflects the general difficulty in conducting clinical trials for a disorder with heterogeneous manifestations and different methods of treatment application, patient selection, or dosology. Nevertheless, some available prospective studies do indicate both the effectiveness and long-term safety of orbital radiotherapy, although not all patients respond to treatment.⁵⁻⁹

Glucocorticoid therapy is generally accepted as an effective means of treatment, and it has been suggested that the effectiveness of orbital radiotherapy can be increased by synergistic interaction with glucocorticoid therapy.^{4,10} However, the long-term efficacy of glucocorticoid therapy is uncertain.

This issue presents the results of a prospective trial¹¹ assessing the efficacy and safety of combined orbital irradiation and systemic steroids compared with steroids alone in moderate-to-severe GO. This report by Ng et al¹¹ is a valuable addition to the literature, since it combines radiotherapy with glucocorticoid therapy, as opposed to the addition of glucocorticoid therapy to radiotherapy. Their results indicate that more rapid improvement of most ocular parameters was obtained with the combination treatment, that the improvement was maintained up to 1 year, and that extra-ocular muscle thickness was reduced only in the group receiving combined therapy. Interestingly, proptosis remained unchanged in both groups.

The authors report this as a preliminary study; the longer term outcomes will be eagerly anticipated. Meanwhile, this study provides further support for the general concept of the combined approach to treatment of this difficult condition.

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