

Editorial

The EUGOGO Consensus Statement on the Management of Graves' Orbitopathy: Equally Applicable to North American Clinicians and Patients

THE EUROPEAN GROUP ON GRAVES' ORBITOPATHY (EUGOGO; www.eugogo.org) is a multidisciplinary consortium of clinicians committed to improving the management of patients with the ocular complications of Graves' disease. The group developed a consensus statement on the management of Graves' orbitopathy (GO) that was unveiled at the annual meeting of the European Thyroid Association in Leipzig, Germany, in September 2007, and simultaneously appears in this issue of *Thyroid* and in the *European Journal of Endocrinology* (1). EUGOGO is to be commended for their efforts that reflect a remarkable degree of international cooperation by academic endocrinologists and ophthalmologists.

The authors refer to the document as a "consensus statement" by experts in the field, rather than a practice guideline. This seems appropriate, because while the EUGOGO group can be credited with having performed the majority of randomized controlled trials (RCTs) in this area, they are not of sufficient scope to support formal practice guidelines. Despite this, the document is timely and should prove useful to clinicians who manage GO patients. The authors rightly anticipate that the document will "provide a focus for audit and research" and aid in the identification of topics for future RCTs.

The consensus statement is scholarly and concise, and the recommendations are generally applicable to North American, as well as European, clinicians and patients. The graded recommendations are appended in the document, and the evidence supporting each is discussed in detail in the body of the text. The application of the recommendations requires that clinicians must first segregate their GO patients into "mild," "moderate to severe," or "sight-threatening" categories, and determine whether or not the disease is active. Sufficient details are provided within the text regarding the assessment of disease severity and activity to allow classification into these broad categories. EUGOGO does not advocate using any detailed grading or scoring system other than the relatively simple "clinical activity score" and specific ocular measurements to assess the severity of the disease. While this approach may not ideally capture all features of the disease, it has been validated by the group in numerous clinical studies and should serve as the gold standard against which other GO classification systems are measured.

The document will serve as an especially useful tool for clinicians who already have some expertise in managing GO patients. Others not so experienced but encounter GO patients in their practice are advised to "refer patients with GO, except for the mildest cases, to combined thyroid-eye clinics for further assessment and management." Which referrals should be made urgently and which are nonurgent is carefully outlined in the text. The problematic aspect of this recommendation for clinicians in North America, however, is that regional GO consultants are frequently ophthalmologists who do not work in combined thyroid-eye clinics. One of the many positive results stemming from the inception of EUGOGO has been the mandatory establishment of a combined thyroid-eye clinic within each of the European medical center wishing to participate in the consortium. Only through this type of cooperation can GO patients benefit from the full range of expertise needed to understand and manage all aspects of this perplexing disease.

While the vast majority of the recommendations seem to me to be quite reasonable and based to the extent possible on pertinent literature, I do take issue with the statement that "the treatment of choice for moderate to severe and active GO is pulses of intravenous glucocorticoids (GCs)." While severe GO may warrant this approach, I remain reluctant to recommend iv GCs to patients with only moderate disease (i.e., those having only a single feature that would place them in the "moderate to severe" category, or a few features measuring just above mild). My concern stems both from reports of fatal acute liver failure in four GO patients during or following completion of iv GC treatment (2,3), and from the natural history of the disease showing improvement in the majority of (albeit unselected) patients within a year's time. Fortunately, the frequency of hepatotoxicity appears to be very low; 7 of approximately 800 GO patients treated in Italy with iv GCs suffered severe liver damage, of whom 3 died (3). Because no case of liver failure has been reported in GO patients receiving < 8 g methylprednisolone, the consensus statement indicates that the cumulative dose in one course should be less than this amount and specifies that iv GCs should only be administered in centers experienced in this therapy. Despite this, the risk-benefit ratio for iv GCs in patients with active disease of only moderate severity who might do equally well with oral steroids or even careful

observation and frequent reassessment seems to me to be weighted toward the side of unacceptable risk.

In summary, the consensus statement by EUGOGO is a timely and useful document that can be updated as additional evidence from future RCTs becomes available. The European group is proceeding with multicenter trials that will allow recruitment of large numbers of patients into these studies. This consensus statement brings to the fore a shortcoming in the care of GO patients in the United States, namely, that many patients are not cared for in joint thyroid-eye clinics. In addition, endocrinologists, ophthalmologists, and others who see GO patients in this country are not yet organized to perform multicenter RCTs. There is, however, activity underway to increase cooperation between these groups and to establish the important infrastructure needed to perform large multicenter GO trials in North America.

Finally, while evidence-based guidelines or consensus statements can facilitate decision making, management must be ultimately individualized and focused on the needs and desires of the patient. This requires the application of both the art and science of medicine, and demands that the clinician actively listens to GO patients, many of whom are

understandably apprehensive and frightened. Compassionate counseling of patient should include wide ranging discussions on the nature of the condition and its natural history, as well as customized treatment options. Such an approach is likely to improve outcomes of what is often a highly distressing disease.

References

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2. Weissel M, Hauff W 2000 Acute and fatal liver failure after high-dose glucocorticoid pulse therapy in a patients with severe eye disease. *Thyroid* **10**:521.
3. Marino M, Morabito Brunette MR, Bartalena L, Pinchera A, Marcocci C 2004 Acute and severe liver damage associated with intravenous glucocorticoid pulse therapy in patients with Graves' ophthalmopathy. *Thyroid* **14**:403–406.

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