

Methylprednisolone Pulse Therapy for Graves' Orbitopathy Did Not Cause Hepatotoxicity in 30 Patients

Wichary H, Gasińska T. Methylprednisolone and hepatotoxicity in Graves' ophthalmopathy. *Thyroid* 2012;22:64-9. Epub October 26, 2011.

SUMMARY

Background

Graves' orbitopathy (GO) varies in severity from minimal to severe. Corticosteroids are used as first-line therapy in patients with active moderate to severe orbitopathy. In recent years, intravenous methylprednisolone has become the standard therapy, but the dose schedule has varied among different centers. Severe liver toxicity has been reported as a side effect of this therapy. The aim of the current study was to assess changes in liver function related to this therapy.

Methods

The study enrolled 30 patients with moderate to severe active GO who had been euthyroid for at least 4 months while undergoing methimazole therapy. None of the patients had received radioiodine before the pulse therapy with methylprednisolone (MPRED). The activity of the GO was assessed by a clinical activity score, and the severity was estimated by the modified NOSPECS classification (1). Clinical evaluation of the orbit was performed to assess improvement. The course of MPRED was a cumulative dose

of 8 g given intravenously over a 4-week period, but the specific dosing regimen was not stated. Patients had detailed studies of liver function, lipids, neoplastic markers, and hepatitis serology before and shortly after MPRED therapy.

Results

All patients had improvement in soft-tissue swelling, clinical activity score, and eye movements, but no improvement in proptosis after MPRED therapy. There were small decreases in total serum proteins, gamma globulin, fibrinogen, alkaline phosphatase, and direct bilirubin and no significant changes in liver enzymes after MPRED therapy. Total, LDL, and HDL cholesterol increased with therapy. There were no significant changes in hepatitis serology. Seven patients had evidence of past hepatitis B infection, but there was no new active infection related to the therapy.

Conclusions

In this study of 30 patients treated with high-dose intravenous methylprednisolone, there was no deterioration of hepatic function or reactivation of hepatitis B.

ANALYSIS AND COMMENTARY

Although the evaluation of liver function was performed very carefully and completely, the number of subjects was too small to exclude the possibility of severe liver dysfunction related to the therapy. In a study of 800 patients treated with intravenous pulses of MPRED for GO with cumulative doses ranging from 3 to 24 g, 7 patients had severe liver damage that was fatal in 3 (2). In a recent review (3) of MPRED therapy for GO and its toxicity in 1045 patients (which also included the 800 patients studied by Marino et al. (2) as well as single case reports), severe liver toxicity was reported in 15

(1.4%). The data suggest that it would take a study of several hundred patients to find a few with significant liver toxicity related to the MPRED therapy. Nevertheless, the current thorough study of 30 patients indicates that mild liver-function abnormalities are not a common side effect of this therapy. The results suggest that careful studies of liver function should be performed before using MPRED therapy for GO and that this therapy should be avoided in patients with significant hepatic dysfunction.

— Jerome M. Hershman, MD
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