

COMBINED MYCOPHENOLATE WITH INTRAVENOUS METHYLPREDNISOLONE THERAPY IS MORE EFFECTIVE THAN INTRAVENOUS METHYLPREDNISOLONE ALONE IN ACTIVE AND MODERATE-TO-SEVERE GRAVES' ORBITOPATHY – A RANDOMIZED, OBSERVER BLIND, MULTICENTER TRIAL

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Background and Objectives: The European Thyroid Association guidelines recommend intravenous methylprednisolone (IVP) as first-line treatment for active & severe Graves' orbitopathy (GO), however lack of response or relapse after discontinuation of treatment are frequent encounters. The efficacy and safety of combination IVP and mycophenolate sodium (M) therapy (P+M) was compared to IVP alone in active/severe GO.

Methods: For this observer-blind, randomized, multicenter, prospective European Group on GO (EUGOGO) trial, 164 patients with active & moderate-to-severe GO randomly received P alone (0.5g/week for 6 weeks followed by 0.25g/week for 6 weeks) or the same P protocol with 0.720g M /day for 24 weeks. Primary endpoints were the response rates at (12 and) 24 weeks defined as reduction of at least two parameters of a composite ophthalmic index without simultaneous deterioration in any parameter.

Results: 37/71 (52.1%) and 52/75 (69.3%) patients receiving P and P+M, respectively responded at week 24 (odds ratio 2.08, 95%CI 1.06-4.09, p = 0.033). Inactivation of GO was noted in 80% and 89% (p<0.0001), respectively. Quality of life, clinical activity (CAS) and severity scores, diplopia score, ocular adduction, down gaze duction, and TSH receptor antibody levels significantly improved within the groups with significant differences of overall ophthalmic improvement, CAS, down gaze duction, eyelid and caruncle swelling between the treatment groups. During the 12 week follow-up, nine (14%) and 13 (20%) patients improved while three (8.6%) and three (5.8%) relapsed in the P and P+M groups, respectively. Overall improvement was noted in 34/65 (52.3%) and 49/66 (74.2%), odds ratio 2.63, 1.26-5.49, p = 0.011, respectively at week 36. Mild/moderate drug-related side effects occurred in 16/81 patients (20%) and 21/83 (25%), p = 0.479 in the P and P+M groups, respectively.

Conclusions: Addition of mycophenolate significantly improves the efficacy of methylprednisolone pulse therapy in patients with active & moderate-to-severe GO.