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CLINICAL UPDATE

Should methotrexate be added to prednisone therapy for temporal arteritis?

Jover JA, Hernandez-Garcia C, Morado IC, Vargas E, Banares A, Fernandez-Gutierrez B. Combined treatment of giant-cell arteritis with methotrexate and prednisone. A randomized, double-blind, placebo-controlled trial. ***Ann Intern Med*** **2001;134(2):106-14.**

Background: Giant-cell (temporal) arteritis is a systemic vasculitis affecting elderly people that can lead to blindness. Current treatment involves at least 1 year of corticosteroid therapy, which is associated with many potential adverse effects. The role of corticosteroid-sparing agents such as methotrexate in the treatment of temporal arteritis has remained unclear.

Question: Does combined therapy with prednisone and methotrexate in the management of temporal arteritis reduce the rate of relapses and side effects, compared with therapy with prednisone alone?

Design: This randomized, double-blind, placebo-controlled trial was conducted at a university-based clinic in Spain. Patients with biopsy-proven temporal arteritis and less than 2 weeks of high-dose corticosteroid treatment (prednisone > 10 mg/d or equivalent) were enrolled. Exclusion criteria included liver disease, renal failure, alcohol abuse, chronic infection, history of neoplasm and use of other immunosuppressive drugs. Patients were randomly assigned to receive prednisone plus either methotrexate or placebo; follow-up was 24 months. Prednisone was initiated at 60 mg/d for the first 2 weeks and then tapered over the next 24 weeks. Methotrexate was given as a single weekly oral dose of 10 mg for 24 months. If a relapse occurred, the doses of both drugs were increased according to a protocol, followed by another attempt to taper the prednisone. The primary outcome measures were the number of disease relapses and the cumulative dose of prednisone during treatment. Secondary outcome measures included the number of adverse effects from the treatment drugs.

Results: Twenty-one patients received prednisone and methotrexate and 21 received prednisone and placebo. The 2 groups were similar at baseline, with a mean age of 78 years, a mean erythrocyte sedimentation rate of 91 and 100 mm/h respectively, and a polymyalgia rheumatica prevalence of 57% and 52% respectively. One patient in the methotrexate group and 2 in the placebo group were lost to follow-up. All patients responded to initial treatment. Disease relapse occurred in 9 patients (45%) in the methotrexate group, compared with 16 patients (84%) in the placebo group ($p = 0.018$). Moreover, fewer relapses involving cranial symptoms occurred among patients in the methotrexate group than among the control subjects (2 v. 7 patients, $p = 0.06$). The median duration of prednisone treatment was significantly shorter in the methotrexate group than in the placebo group (29 v. 94 weeks, $p = 0.0016$), resulting in a lower mean cumulative dose of prednisone (4187 v. 5489 mg, $p = 0.009$). There was a trend toward a lower incidence of diabetes mellitus (3 v. 7 patients), arterial hypertension (12 v. 16 patients) and cushingoid appearance (3 v. 6 patients) in the methotrexate group. Three patients receiving methotrexate experienced myelosuppression or mucositis that necessitated withdrawal of the drug. Of these, 1 patient was not taking folic acid supplementation and 2 had mild renal impairment.

Commentary: This well-designed study showed that methotrexate was efficacious in preventing relapses of temporal arteritis while reducing the duration, cumulative dose and toxicity of prednisone. Although the adverse effects associated with methotrexate in this study underline the need for due caution, the larger experience with it in the treatment of rheumatoid arthritis suggests that adverse effects can be kept to a minimum with careful patient selection, folic acid supplementation and close monitoring.[1] Further studies will reveal whether a different regimen of methotrexate or another corticosteroid-sparing agent can provide similar effectiveness, with fewer side effects.[2]

Practice implications: Biopsy-proven temporal arteritis should continue to be treated initially with high-dose prednisone therapy. Concurrent treatment with methotrexate can reduce the duration and toxicity of corticosteroid therapy and should be considered. Referral to a specialist in internal medicine or rheumatology can help with patient selection, assessment and subsequent follow-up. — *Benjamin H. Chen*

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References

1. Guidelines for the management of rheumatoid arthritis. American College of Rheumatology Ad Hoc Committee on Clinical Guidelines. *Arthritis Rheum* 1996;39:713-22.
2. DeSilva M, Hazleman BL. Azathioprine in giant cell arteritis/polymyalgia rheumatica: a double-blind study. *Ann Rheum Dis* 1986;45:136-8.