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BRIEF QUESTIONS AND ANSWERS ON CURRENT CLINICAL CONTROVERSIES

CME CREDIT

Q: What is the appropriate initial dose of corticosteroids to treat giant cell arteritis?

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Corticosteroids are given mainly to prevent blindness and stroke

A: CORTICOSTEROIDS PROVIDE very rapid control of the common signs and symptoms of giant cell arteritis—headache, stiffness, and musculoskeletal pains. Although both doctor and patient welcome swift control of these symptoms, the compelling reason for treating giant cell arteritis with corticosteroids is to prevent blindness and stroke. Traditional teaching suggests an initial dose of 1 mg/kg per day of prednisone or an equivalent drug, often around 60 mg per day.

Unfortunately, treatment with corticosteroids is not innocuous, especially in elderly patients most prone to giant cell arteritis. Adverse effects include vertebral fractures, diabetes mellitus, infection, and atherosclerotic disease. Morbidity has been demonstrated to rise with the mean daily dose of corticosteroids and the cumulative dose of corticosteroids, both of which directly correlate with the initial dose.[1,2]

Thus, the question becomes: What initial dose of corticosteroids is high enough to control symptoms and prevent blindness, yet low enough to minimize potential complications? There is no definite answer at this time, although there is some evidence that less than 60 mg per day may be better for some patients.

HOW COMMON ARE COMPLICATIONS OF STEROID THERAPY?

Excess mortality in giant cell arteritis, while not reported in all series, has been shown to be 112% higher than in the age-matched population in one series and is related in part to corticosteroid therapy.[1,3] Although mortality and morbidity early in corticosteroid treatment are usually related to vascular complications associated with the disease itself,[4,5] later in the course of treatment morbidity and mortality due to infection, diabetes mellitus, and atherosclerotic disease are more frequent and are presumably related to corticosteroid therapy.[1,2,4,6] These adverse effects occur in as many as 88% of patients.[2]

WHAT DOSAGE OF STEROIDS CONTROLS THE DISEASE?

Although one review suggested that only 5% to 10% of patients have "resistant" giant cell arteritis (defined as a daily corticosteroid dose requirement of 15–20 mg of prednisone equivalent per day 2 months after initiation[7]), this estimate may be low. For instance, in one study, 25 (58%) of 43 consecutive patients were still receiving a mean of 22 mg of prednisone per day 6 months after initiation of therapy.[1]

Even a daily dose as low as 15 mg of prednisone equivalent may be too high a threshold below which morbidity and mortality may be reduced. For instance, in a 1981 retrospective series, excess mortality, usually due to infection, was associated with a daily maintenance dose of more than 10 mg of prednisone equivalent per day.[4] These data suggest that morbidity is best controlled by timely tapering to a maintenance dose of less than 10 mg of prednisone equivalent per day. Therefore, the initial dose of corticosteroids must be high enough to immediately control disease activity but low enough to allow rapid establishment of an acceptable daily dose.

WHAT IS THE OPTIMAL INITIAL DOSE?

Only a few well-designed prospective series have studied the initial dose of corticosteroids. In two series,[8,9] a starting dose of 11 to 20 mg of prednisolone per day controlled symptoms in 95% to 97% of patients. Patients given an

initial dose less than 20 mg per day of prednisolone had a much lower rate of remission and experienced a significantly higher frequency of disease flare than did patients given 20 mg per day or more of prednisolone.[9] Another study found that 12 (80%) of 15 patients were well controlled on 20 mg of prednisolone per day after being given an initial dose of 40 mg of prednisolone per day for the first 5 days.[10]

If these three series are combined, 128 patients were treated initially with 20 mg per day of prednisolone or less, and none experienced cerebrovascular morbidity or blindness. Of the entire cohort of 196 patients, only 1 patient experienced blindness, which occurred after 4 weeks of prednisolone at the higher dose (60 mg per day).

A contemporary series provides further evidence that a dose of prednisone of 20 mg per day may be sufficient initial treatment for most patients with giant cell arteritis. In a subset of 35 patients with both polymyalgia rheumatica and giant cell arteritis who were initially treated with 40 to 60 mg of prednisone per day, the 10 patients who relapsed did so only after the daily dose of prednisone had been reduced to 17.5 mg or less.[11]

As expected, other studies show that adverse effects increase with the dosage. A recent retrospective follow-up of 77 patients who were given varying initial doses of prednisone (30–40 mg per day, 41–60 mg per day, or > 60 mg per day) demonstrated statistically and clinically significant increases in adverse effects for patients taking more than 40 mg per day.[2] The lowest-dose group experienced a 36% frequency of adverse effects vs 80% in the two higher-dose groups. In addition, life-threatening adverse effects occurred in 14% of the lower-dose group vs 34% of the two higher-dose groups. The frequency of relapse and adverse outcomes due to giant cell arteritis was not significantly different among the groups.

THE AUTHOR'S RECOMMENDATIONS

Unfortunately, a conclusive study to answer the question has not been performed. It would require very long-term follow-up of patients who were randomized to various initial doses of corticosteroids beginning at 20 mg per day and including a range up to 60 mg per day. However, the data to date suggest that rigorous adherence to a dose of 1 mg/kg per day of prednisone equivalent as initial treatment for giant cell arteritis may be excessive, especially for subsets of patients who are at high risk from corticosteroid treatment, such as those with documented osteopenia, diabetes, and atherosclerotic disease—all common in the elderly.

However, in patients already experiencing central nervous systems signs or symptoms or blindness, physicians may prefer to use a higher initial dose of corticosteroids. While there are no studies that have stratified treatment protocols for these patients, and while the visual and central nervous system adverse effects of giant cell arteritis were no more likely to occur in low-dose than in high-dose corticosteroid-treated patients in two comparative series,[2,9] a short initial course of higher-dose corticosteroids is unlikely to result in serious adverse effects.

This analysis allows flexible, evidence-based clinical judgment to replace dogma in choosing the initial dose of corticosteroid for giant cell arteritis.

My own practice is to treat uncomplicated giant cell arteritis with a starting dose of prednisone of 20 mg per day. I instruct patients to call on the telephone in 3 days to report their response. If symptoms are entirely controlled, I continue 20 mg per day for 2 to 4 weeks and then taper to 5 to 7.5 mg per day during the next 1 to 3 months. If symptoms are not controlled, I raise the dose to 40 mg per day and provide a facilitated visit within the next 2 or 3 days. I reserve initial treatment with 1 mg/kg/day (60 mg) of prednisone for patients who present with ocular or central nervous system involvement.

Rigorous adherence to an initial dose of 1 mg/kg per day may be excessive

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