
Corticosteroids in polymyalgia rheumatica - A review of different treatment schedules

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ABSTRACT

Low dose oral steroids (prednisolone 10-15 mg daily) are currently advocated for the treatment of uncomplicated PMR and the dose should be carefully adjusted in relation to disease activity. Intramuscular methylprednisolone has been shown to have a similar remission rate to oral steroids and a better side effect profile with respect to fracture rate and weight gain. Prophylaxis for osteoporosis at least with calcium and vitamin D should be initiated at the start of steroid therapy.

Introduction

Polymyalgia rheumatica (PMR) is an inflammatory syndrome presenting with neck, shoulder and hip girdle pains in the elderly. Most epidemiological studies have been done on Caucasian populations, estimating the incidence to be between 20 to 80 per 100,000 per year in the over 50 age-group. A good therapeutic response to corticosteroids has been recognised as a feature of the condition and constitutes part of the Healey diagnostic criteria (1), which is one of the most widely used systems in Europe. Most rheumatologists and physicians agree that the aim of treatment is to suppress symptoms. There is a belief, still held among some Scandinavian groups, that PMR is a manifestation of systemic arteritis and patients are therefore at risk of the potentially devastating complications of giant cell arteritis (GCA) if undertreated. This is contrary to most epidemiological studies which show that the "conversion" from PMR to GCA is rare (2,3). The high perceived risk of adverse events, e.g. blindness, has undoubtedly fueled the tendency to overtreat with corticosteroids, both in terms of the dose and the length of treatment.

Steroid efficacy and side effects

Although some groups still advocate a trial of non-steroidal anti-inflammatory drugs in mild cases, there is no doubt that

the rapid response of systemic corticosteroids is superior in symptom control. Indeed the combined prescription of the two may be associated with more side effects (4).

Side effects attributable to long-term corticosteroid therapy may be more significant than the complications from the disease per se. If sustained weight gain is included, as many as 76% of corticosteroid treated patients will experience associated side effects (5). Female sex, cumulative dose and age at presentation increase the incidence of adverse effects. In particular, cumulative low dose corticosteroid is associated with rapid bone loss and overt fractures. It cannot be over stressed that patients with PMR should be given advice and be assessed for the risk of osteoporosis before beginning therapy, and should as a minimum be placed on calcium and vitamin D supplements.

Oral steroid regimens

Although disease flares can occur secondarily to a rapid dose reduction, it is clear from the Reggio Emilia study (6) that spontaneous disease flares do occur independently of the dose. A starting dose at or below 10 mg daily is associated with fewer adverse effects, but is occasionally insufficient. Delecoueuillerie looked at 132 PMR patients comparing high (15 to 30 mg/day) and low (7 to 12 mg/day) starting doses, and did not find any significant difference in relapse rate (7). Symptom flare during treatment is a difficult entity to study. All clinicians are aware that patients feel less well with a reduction in steroid dose in PMR, as in any other systemic conditions requiring long-term corticosteroid therapy. It is crucial to devise a clear-cut list of endpoints for future prospective studies. Our own experience is that a combination of inflammatory markers, e.g. C reactive protein (CRP) and functional measures, e.g. the Health Assessment Question-

naire, are necessary to guide therapeutic changes where symptoms of disease activity are not straightforward. The erythrocyte sedimentation rate (ESR) and CRP usually normalise within 2 weeks of therapy initiation. In our clinical experience, CRP monitoring alone is sufficient.

There may be individual differences in steroid requirements and studies suggest that there are mild and more severe subsets of the disease that run different courses and require different total cumulative steroid doses and different treatment durations. This suggests that individual cases should be managed with dosages tailored to individual needs. At present, no good predictors of these different subsets exist.

Deflazacort

Krosgaard *et al.* (8) in a randomised double blind study failed to show a significant difference in bone mineral density changes as compared to conventional oral prednisolone (OP). Based on this and other experiences suggesting that the equivalent dose to OP may be nearer 7:5, we do not feel this drug has a first-line role in PMR therapy at present.

Depot methylprednisolone regimes

Methylprednisolone has a 20% greater glucocorticoid potency (and a lower mineralocorticoid effect) compared to OP. It has been shown in a 60 patient multicentre prospective study that intramuscular methylprednisolone (MP) can confer a similar remission rate to OP. The side-effect profile is superior, especially with respect to: (i) the fracture rate: 8 (OP) versus 1 (MP) in patients reporting symptomatic fractures; and (ii) the proportion of weight gain: mean 3.42 kg (OP) versus 0.82 kg (MP) over 96 weeks ($p < 0.005$) (9,10). This is thought to be secondary to a significantly reduced cu-

mulative dose.

We feel this should be the preferred initial treatment in PMR, although some patients with severe disease may require conversion to OP. Our studies excluded patients with arteritic symptoms at the outset: headaches, visual symptoms, temporal tenderness and jaw claudication). Based on the present evidence, we cannot recommend the use of MP in giant cell arteritis.

Disease modifying agents

Anecdotal reports exist of the use of disease modifying agents including methotrexate and azathioprine in patients in whom steroid reduction is difficult. Although promising in principle, no large studies with sufficient power have been published. Feinburg *et al.* (11) looked at 43 patients prospectively, and did not find any benefit with methotrexate at doses of 7.5 to 12.5 mg weekly over 3 months. All of the published therapeutic studies have a relatively small number of patients with a short duration of follow up and high numbers of treatment drop outs.

Conclusion

Among the rheumatic diseases, PMR has been ignored for many years, not the least because of the false impression that its management is "easy" once corticosteroids are initiated. With the advent of increased concerns about corticosteroid-associated osteoporosis (12), one should not forget the other significant side effects which may be even more troublesome and worrying to patients. For the physician managing PMR should be likened to a balancing act, on the one hand reducing the risk and symptoms of disease flare, and on the other minimising the corticosteroid side effects. Large scale, collaborative, prospective studies

are clearly needed to provide reliable data which is currently lacking, especially to determine subsets for different intensities of management.

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