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Treatment of polymyalgia rheumatica and giant cell arteritis. I. Steroid regimens in the first two months

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SUMMARY Thirty nine patients with polymyalgia rheumatica (PMR) and 35 with giant cell arteritis (GCA) were treated with high or low dose steroid regimens in a prospective study of the first two months of treatment. Patients with PMR needed 15–20 mg prednisolone initially; 13/20 (65%) relapsed on an initial dose of 10 mg/day. All but two patients with GCA were successfully treated with 40 mg/day prednisolone initially but relapsed on a reduction to 20 mg/day. One patient with GCA receiving 30 mg/day relapsed after four weeks. Six patients with PMR developed GCA during the first two months and required an increased prednisolone dose to control symptoms. The erythrocyte sedimentation rate or C reactive protein did not predict relapse.

Most clinicians have firm views on the steroid dose required to treat polymyalgia rheumatica/giant cell arteritis (PMR/GCA), but these are generally based on tradition and anecdote. Recommendations vary widely and there are no trials comparing differing treatment regimens. Occasional retrospective comparisons have been carried out. As steroid treatment is associated with serious side effects it is important to determine the lowest optimal prednisolone dose.

Polymyalgia rheumatica has traditionally been treated with a low steroid dose or even non-steroidal anti-inflammatory drugs.[1 2] Several groups advise an initial prednisolone dose of 10 mg/day.[3–6] Behn *et al* found 10 mg satisfactory in many cases but noted that patients taking less were significantly more likely to need an increase in dose.[7] Others suggest 10–20 mg as a starting range.[8–10] One retrospective review found a mean initial dose of 22·8 mg/day.[11] It has been proposed that patients with PMR should be treated with higher doses because of the risk of developing arteritis,[12 13] and Bengtsson and Malmvall treated both patients with PMR and those with GCA with a mean of 33 mg/day.[14] No papers give specific information on reducing the initial dose of prednisolone. Steroid reduction once patients are 'almost symptom free and the erythrocyte sedimentation rate (ESR) less than 20 mm/h' has been proposed,[3] but the authors state that these patients did not experience the rapid response to corticosteroid treatment considered by many to be of diagnostic importance in PMR. This might have been because prednisolone doses used were too low (10 mg or less). Another study advised steroid reduction when the patient was 'virtually free of symptoms'[15]; the ESR was felt to be less important.

The recommended steroid dosage for treatment of GCA ranges from 20 to 80 mg/day.[4 9 10 13 16–20] Huston and Hunder reported that 10–20 mg/day relieved symptoms but 40–60 mg was needed to prevent blindness.[9] Graham *et al* used 80 mg prednisolone/day plus intravenous hydrocortisone[21]; many of their patients had visual or neurological symptoms. The prednisolone dose was reduced to 40 mg by nine days then by 5 mg/week until 10 mg was reached. An initial dose of 45–60 mg for one month, then weekly decrements of not more than 10% has been proposed.[22] There is no other information on the rate of steroid reduction in the early phase of the condition, though a rate of 1 mg/month once the prednisolone dose is stable has been suggested.[23] The aim of this study was to compare the efficacy of different steroid regimens for both PMR and GCA over the first two months of treatment.

Patients and methods

Seventy four patients with active untreated PMR/GCA diagnosed between 1982 and 1985 on the criteria of Jones and Hazleman[24] were included in the study. Thirty nine presented with PMR and 35 with GCA, 17 of whom also had symptoms of PMR. PMR and GCA were treated with high or low dose

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Table 1 *Steroid regimens for the first two months of treatment. Values are the prednisolone dose in mg/day for patients with PMR or GCA*

	PMR			*GCA*			
	4 weeks	*2 weeks*	*2 weeks*	*5 days*	*4 weeks*	*2 weeks*	*2 weeks*
High	20	15	10	40	40	30	20
Low	10	7·5	5	40	20	15	10

regimens during the first two months of treatment (Table 1).

Nineteen patients with PMR were randomly allocated to the high dose regimen and 20 to the low. Fifteen patients with GCA were allocated to the low dose and 20 to the high dose regimen. A detailed clinical assessment was made during patient visits every one to two weeks and disease activity was then classified as (*a*) active disease, either no improvement from previous visit or a relapse; (*b*) symptoms/signs of activity still present but definite improvement from previous visit; (*c*) well, symptoms and signs resolved.

If the disease process did not appear to be controlled or if new symptoms developed the prednisolone dose was altered to achieve adequate control. Failure with a particular regimen was therefore defined as an increase from the planned prednisolone dose or inability to reduce the prednisolone dose as planned.

Laboratory investigations included measurement of full blood count, ESR (Westergren), serum C reactive protein (CRP) (nephelometer), orosomucoid, α_1-antitrypsin, haptoglobin, immunoglobulins, immune complexes, and complement at each clinic visit. Liver function tests, urea, and electrolytes were measured on the first visit and every fortnight thereafter.

The ESR was abnormal (>30 mm/h, Westergren) in all patients before treatment and the CRP was abnormal (>6 mg/l) in 49/55 patients.

STATISTICS

χ^2 Tests were used to analyse results.

Results

PMR—HIGH REGIMEN

Two of 19 patients were unable to continue with the high dose regimen. Both experienced a flare up of PMR symptoms at six weeks when they tried to reduce from 15 to 10 mg of prednisolone/day but were clinically asymptomatic over the final 2 weeks taking 15 mg/day. In both, the ESR and CRP had fallen in the first month but rose in the second month when symptoms recurred on steroid reduction. Three further patients developed symptoms of GCA, one within one week of starting treatment when the ESR remained abnormal, two between three and five weeks when the ESR or CRP was normal and did not alter.

PMR—LOW REGIMEN

Thirteen of 20 patients relapsed with the low dose regimen. Six had severe pain and stiffness one to three weeks after starting treatment but responded to an increase in prednisolone to 15–20 mg/day. The other seven patients relapsed in the second month, two when the dose was reduced to 7·5 mg and five on reduction to 5 mg/day. All responded when reverting to the previous dose. The ESR or CRP, or both, remained raised or rose after an initial fall, in three of the six cases who flared in the first month. In two other cases the dose of prednisolone was increased a few days before blood tests were taken, and ESR or CRP did not rise.

Three patients developed GCA during the first two months of treatment. All developed headache and scalp tenderness and one had visual blurring. Two had already required an increase in steroid dose because of a relapse in symptoms of PMR during the first three weeks. Symptoms and signs of GCA responded in all cases to an increase in prednisolone. The ESR became raised in two cases when GCA developed.

GCA—HIGH REGIMEN

Four of the 20 patients relapsed with the high dose regimen. One woman who presented with loss of vision developed reduced visual acuity in the other eye with ischaemic changes on fundoscopy after one week of treatment. Severity of headache became more prominent in one patient, with blurring of vision on attempted reduction to 30 mg prednisolone/day after one month; another woman experienced a recurrence of temporal headache on attempted reduction of prednisolone to 20 mg/day at six weeks. The fourth patient had GCA of the myometrial and axillary arteries and required 60 mg prednisolone to relieve her arm claudication. All patients responded to higher doses of prednisolone. Only one patient with a flare had an associated increase in ESR and CRP.

Table 2 *Early relapses. Patients requiring prednisolone dose increased within the first two months of treatment*

Regimen	*Dose increased*	*Total number of patients*
PMR low	13	20
PMR high	2	19
GCA low	6	15
GCA high	4	20

GCA—LOW REGIMEN

Six of the 15 patients with GCA following the low dose regimen deviated from the planned treatment. Two developed visual blurring, one with temporal artery tenderness, and four had increasing headache, two with muscle symptoms. Three relapsed in the first month and three in the second; all improved when the prednisolone dose was increased. Two of the patients who relapsed in the second month had a concomitant increase in ESR or CRP. Eight of the 10 patients with GCA who relapsed had both GCA and PMR.

The results show that 13/20 (65%) of patients with PMR were not controlled by the 'low' dose regimen, compared with only 2/19 patients (11%) not controlled by the PMR 'high' dose regimen (Table 2). The relapse incidence was significantly different (χ^2= 12·22, p<0·001). The GCA low dose regimen was inadequate for 6/15 patients (40%) and 4/20 patients (20%) were not adequately controlled by the high dose regimen, although one of these had an extremely rare presentation. The relapse incidence with each regimen was not significantly different. Only two of the 35 patients with GCA did not achieve symptomatic control with an initial dose of 40 mg prednisolone. About half the relapses in both patients with PMR and in those with GCA were associated with attempted reduction in steroid dose during the second month of treatment. Four of the six patients with PMR who developed GCA did so within three weeks of starting treatment. The ESR or CRP, or both, became abnormal in 11 of 30 patients when an alteration of steroid dose was required. An increase of ESR or CRP to abnormal levels occurred in both patients with PMR and in those with GCA. Dose was altered according to clinical symptoms and did not depend on laboratory values.

Discussion

There are few prospective studies of treatment in PMR/GCA, and this is the first to compare differing treatment regimens and to examine both the initial prednisolone dose and the rate of reduction. In particular, we wished to see if high steroid dose could be avoided, and it does seem that GCA can be adequately controlled on a lower dose of steroid than is commonly advocated. Disease activity was well controlled in all but two of the patients with GCA taking 40 mg prednisolone/day initially. Threatened visual loss may require more than 40 mg prednisolone, but this occurred in only one patient. If patients are reviewed frequently, prophylactic high dose steroids are not necessary in GCA. Dose reduction to 20 mg prednisolone/day in the first month or to 20 mg or less in the second month accounted for 70% of the relapses in patients with GCA; the rate of reduction was the problem rather than the initial dose.

There was a high relapse rate in patients with PMR treated with an initial dose of 10 mg prednisolone/day; in contrast, almost all patients with PMR were controlled by the high dose regimen of 20 mg/day initially, and this difference was highly significant. This is contrary to previous studies, which showed that 10 mg prednisolone/day was adequate.[3–6] Two patients who relapsed developed symptoms of GCA shortly afterwards and therefore may have had more severe disease. If these two are excluded, 64% of relapses in the patients with PMR following the low dose regimen occurred in association with attempted steroid reduction to 7·5 or 5 mg prednisolone/day during the second month. In retrospect, the steroid reduction rate was probably too rapid.

Six of the 39 patients who presented with PMR (15%) developed symptoms of GCA within two months, but control of disease activity was achieved rapidly by increasing the steroid dose. This was feasible because patients were being reviewed frequently; in routine practice complications might have developed. The incidence of the early development of arteritis is lower than reported previously, however.[24] The relapse rate in the first two months is higher than is implied in other studies, where the initial prednisolone dose selected appears to have achieved symptomatic control. There are several reasons for this possible discrepancy with our study. Firstly, none of the studies discusses in detail how rapidly symptoms were controlled. Definitions of adequate symptomatic control may vary. Patients may have been reviewed less frequently than in our study, and most studies were retrospective. All these factors may have contributed to under-recording of symptoms.

In the companion paper, we have examined complications of steroid treatment and shown a clear relation between initial and cumulative prednisolone doses and side effects.[25] So there is evidence

that one should avoid high doses of steroids where possible. This study suggests that 15–20 mg prednisolone can be used for the initial treatment of PMR and that 40 mg prednisolone is sufficient for most patients with GCA. In the second month of treatment 10 mg of prednisolone controlled PMR; less was associated with an unacceptable relapse rate. Patients with GCA probably need 20–30 mg in the second month. A rise in the ESR or CRP did not invariably predict relapse, and alteration in steroid dose should be based predominantly on the clinical symptoms and signs.

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