

## **Steroid withdrawal in polymyalgia rheumatica: the theory versus the practice**

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Polymyalgia Rheumatica (PMR) was a term first used by Barber in 1957, to describe a sudden onset inflammatory condition typified by pain and stiffness of the shoulder and pelvic girdles associated with constitutional effects. The condition previously carried numerous other names, with the first being described by Bruce in 1888 as senile rheumatic gout. Initially, treatment with salicylates was suggested, with glucocorticoids (steroids) being reserved for more severe cases. Since the 1960s steroids have become the treatment of choice.

In common with many conditions the ideal oral steroid regimen has not been formally tested using a placebo controlled, double-blind randomised trial. National guidance has been produced, with BSR and EULAR recommending an initial starting dose of prednisolone between 12.5 mg to 25 mg daily continued for two to four weeks. Following this, in patients who respond to treatment, the guidance recommends reducing the dose to 10 mg once daily after four to eight weeks (1, 2), with further reductions by 1 mg daily each month until steroids are fully withdrawn (1). This slow withdrawal from 10 mg daily is supported by more recent observational data and a systematic review (3). Using these regimens the earliest steroids are recommended to be stopped is after 44 to 50 weeks after commencement (1, 2).

Despite current guidance, many patients with PMR are unable to stop their steroids within this time-frame. Observational data from the US in 1980s showed that around 40% of patients with PMR were able to stop their steroids in a mean time of 95 weeks, yet it was estimated that another 40% would continue steroids for longer than 4 years (4). The median duration of steroid therapy has also been increasing year on year within the UK. The Health Improvement Network (THIN) includes data from UK adult patients registered with contributing general practices between January 1989 and December 2008 (5). In 1991 the median duration of steroid therapy for men with PMR/GCA was men was 53 weeks (28.4, 126.1) and 58 weeks (CI 95% 28.4, 122.9) for women; by 2005 it had reached 56.7 weeks in men (33.6, 101) and 63.7 weeks (32.3, 128.3) in women (5).

These data suggest that there is a reluctance to discontinue steroids in patients with PMR. This high prevalence of long-term steroid use in this group of patients is a particular concern because of the increasing awareness of the risks associated with steroids even at what might have hitherto been regarded as safe 'physiological' doses.

Cumulative steroid exposure is strongly related to the well-recognised adverse effects including: eye related morbidity (cataracts, glaucoma), cardiovascular risk factors (hypertension, diabetes), increased risk for infections and fragility fractures (6). A Task Force endorsed by the European League Against Rheumatism (EULAR) produced recommendations for steroid therapy in rheumatic diseases. The systematic review of 18 studies revealed the following adverse event rate per 100 patient years of follow-up: eye morbidity (cataracts, glaucoma) 4/100, cardiovascular morbidity (dyslipidaemia, oedema and electrolyte imbalance, renal and heart dysfunction, hypertension) 15/100, endocrine morbidity (glucose intolerance and diabetes, fat redistribution, hormone dysregulation) 7/100, infections (viral, bacterial, skin) 15/100 and musculoskeletal morbidity (osteoporosis, osteonecrosis, myopathy) 4/100 (6).

Oral steroids remain the leading cause of hypothalamic-pituitary-adrenal (HPA) dysfunction (7). No study has investigated the burden of HPA dysfunction in patients with PMR, however a study was performed in those with the related condition of Giant Cell Arteritis. Nevertheless, in a study of 150 patients with GCA, 49% of patients were considered non-responders to a Short-Synacthen test (ACTH) (8). Of these 85% recovered normal adrenal function within 36 months, however 5% never recovered their adrenal function (8). The main predictive factors were total dose and duration of steroid therapy (> 8.5 g steroid and > 76 weeks treatment course). It is likely that patients with GCA receive higher initial starting doses, and have greater cumulative steroid dosages than patients with PMR.

Knowledge of HPA dysfunction is important not least so as the patient can be appropriately managed. In 1952 a patient developed circulatory shock following withdrawal of their steroids prior

to surgery (9). Since then guidelines have been produced, with patients receiving greater than 10 mg of steroid needing perioperative cover with additional steroids (10). Perhaps this pragmatic-focus based purely on the dose of steroids has led to the disinterest in ascertaining the prevalence of HPA dysfunction in patients with PMR on long-term, low-dose steroids. However it is plausible that patients with PMR, even on doses lower than 10 mg daily, have HPA dysfunction.

Currently there is insufficient evidence to inform clinicians on how best to manage the withdrawal of steroids in patients with PMR that are in remission on treatment. The slow withdrawal of steroids at a rate of 1 mg daily each month that has become enshrined in clinical practice and national guidelines has an empirical basis. The guidance for PMR needs to be refined, and should take into account an assessment of adrenal function in all patients on long-term steroids.

In summary, prescriptions for long-term steroids in patients with PMR are increasing, suggesting that there are important barriers to the implementation of current guidance in clinical practice and raising significant concerns over harm. Advice on steroid withdrawal in PMR needs to be backed by much more sound evidence on the true risk of flare, together with sound knowledge of the rate of hypoadrenalinism in this patient group. Rheumatologists and general practitioners need to be wary of the patients who are in remission and yet maintained on long-term steroids.

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