Bone turnover and bone mass in polymyalgia rheumatica

Sir, Polymyalgia rheumatica (PMR) is now often treated with low-dose corticosteroids in general practice, as well as in rheumatology clinics. It is important that we offer general practitioners clear advice on the prevention of osteoporosis in these patients. Pearce et al. [1] report significant loss of bone density by 6 months in 19 patients with PMR. However, the small number of patients followed beyond 1 yr makes it difficult to give clear information about the subsequent effects of treatment on bone density. In our recent study of 50 patients with PMR followed over 2 yr [2], we reported similar bone loss with a percentage change in bone mineral density (BMD) at the spine of −1.3% at 6 months, −2.8% at 12 months and −2.3% at 24 months. The change in hip BMD was −2.6% at 3 months, −3.1% at 12 months and −3% at 24 months with respect to baseline. As steroid was weaned by 2 yr, the bone loss did not continue and there was a trend towards improvement of BMD. However, only 27 out of 50 patients were off treatment at 2 yr, so that ~50% of elderly patients are exposed to further prednisolone therapy.

Pearce comments that the CTX bone resorption marker was raised prior to treatment and suggests that this may be related to a disease effect. We observed a similar finding using the bone markers pyridinoline (PYR) and deoxypyridinoline (DPR), which were both significantly raised with respect to controls in PMR prior to treatment [PYR 74.9 ± 30 nmol/mmol creatinine, DPR 14.6 ± 6.4 nmol/mmol creatinine (mean ± s.d., P = 0.01]. Bone resorption (PYR) correlated with untreated disease activity (ESR) (r = 0.48, P = 0.003) and interleukin-6 (IL-6) levels (r = 0.48, P = 0.05). IL-6 is recognized to be the major inflammatory cytokine in PMR. The initial ESR influenced the percentage change in BMD at 1 yr (r = 0.35, P = 0.01), while cumulative steroid dose, mean ESR and type of steroid used did not.

Our study would suggest that the inflammatory disease itself has important consequences on bone in PMR. Our sequential studies of bone markers showed that these fell once steroids were started, suggesting an important role of steroids in reducing the inflammatory effect of the disease on bone. Since PMR can affect bone, it is important not to encourage practitioners to skimp on steroid treatment leaving the disease itself to have a detrimental effect on bone. There is a need for a clear message to primary care physicians who care for the majority of cases of PMR. Although bone loss does
occur at the 6 month–1 yr point, our study suggests that there is scope for recovery. We would advise that patients with PMR should receive adequate steroids to suppress the ESR and inflammatory process, and so limit the detrimental effect on bone. In patients with active PMR at presentation and in those remaining on steroids for longer than 6 months, we would suggest some form of osteoporosis prophylaxis. There are data from rheumatoid arthritis that calcium and vitamin D can inhibit the effect of low-dose steroid on bone loss. We would propose that patients starting on treatment for PMR receive a calcium and vitamin D supplement, particularly if the ESR is >50 at baseline, and they remain on this during steroid treatment.

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Reply

Drs Dolan and Panayi raise important and difficult issues. High rates of bone loss and the increased incidence of fractures in patients receiving corticosteroid therapy (CST) are commonly attributed to the CST, but may also be partly due to the disease. Bone resorption markers were elevated before CST was started [1, 2]. One resorption marker correlated with disease activity, and the initial ESR correlated with change in bone mineral density (BMD) at 1 yr [1]. Resorption markers decreased on commencement of CST [1, 2]. Thus, increased bone resorption is the result of the disease, and CST may reduce bone loss and fracture risk below the (raised) level that would be observed had the disease been untreated. Apportioning bone loss to disease or CST, and determining whether bone loss is greater with or without CST, would require randomizing of patients with comparable disease severity to placebo or CST and comparing changes with a group of age- and gender-matched controls. This trial is not feasible or ethical. Physicians should actively treat the disease with the minimum dose of CST and consider prophylaxis against bone loss in patients requiring long-term CST—but what prophylaxis?

Although neither study addressed the question of prophylaxis, the issue should be discussed. Clear guidelines for prophylaxis are not available because well-designed studies forming their basis have not been carried out. Many patient-, disease- and CST-related factors influence bone loss and fracture risk. These must be equally distributed in the treatment and placebo arms in randomized double-blind placebo-controlled trials before inferences can be made about the efficacy of a drug. If this is not done, less severe disease or disease of shorter duration, lower doses of CST, and less immobilization in the treatment arm will lead to lower rates of bone loss and fewer fractures in the treated group being erroneously attributed to the treatment.

The aim of treatment is not to prevent bone loss, it is to reduce fracture risk safely. The decision to initiate treatment depends on the individual’s overall fracture risk, conferred by the patient’s age, menopausal status, lifespan, the effect of the disease, the reversibility of the changes induced by the disease and the CST, and the safety and efficacy of the intervention. Why recommend calcium and vitamin D if there is no evidence that this treatment reduces fracture rates, if the changes are reversible, if fracture risk is low even when bone loss occurs? The bisphosphonate etidronate has been reported to reduce fracture rates in patients receiving CST [3]. However, patients with rheumatoid arthritis were over-represented in the placebo arm. Prevention of bone loss or improvement in BMD has been reported using several agents [4–8]. The comparative anti-fracture efficacy of these drugs will not be defined until properly designed trials are published and replicated. Until then, clear guidelines will remain unavailable and the choice of prophylaxis will be a matter of clinical judgement.

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