Alendronate increased bone mineral density but did not reduce new fractures in glucocorticoid induced osteoporosis


Question
In patients who have osteoporosis that is induced by long term glucocorticoid treatment, is alendronate effective for increasing bone mineral density (BMD) and reducing new fractures?

Design
2 parallel randomised, placebo controlled trials with 48 weeks follow up.

Setting
15 centres in the US and 22 centres in other countries.

Patients
560 patients who were 17–83 years of age and had rheumatological, pulmonary, dermatological, gastrointestinal, or other diseases that required ≥1 year of glucocorticoid treatment (daily dose ≥7.5 mg of prednisone or its equivalent). Exclusion criteria were evidence of metabolic bone disease (other than glucocorticoid induced or postmenopausal osteoporosis), low serum 25-hydroxyvitamin D concentrations, concomitant drug treatments that might affect bone turnover, pregnancy, lactation, renal insufficiency, severe cardiac disease, or major upper gastrointestinal disease. A 2.5 mg dose of alendronate was used in the multinational study only, and patients allocated to this group (n=83) were not analysed. Patients (n=477, 30% men, 22% premenopausal women, 49% postmenopausal women) were stratified according to duration of glucocorticoid treatment: <4 months (34%), 4–12 months (21%), and >12 months (45%).

Intervention
Patients were allocated to 1 of 3 treatments: alendronate, 5 mg/day (n=161) or 10 mg/day (n=157), or a matching placebo (n=159) for 48 weeks. Patients received elemental calcium, 800–1000 mg/day, and vitamin D, 250–500 IU/day.

Main outcome measures
Percentage change in BMD of the lumbar spine measured by dual energy x ray absorptiometry. Secondary outcome measures included percentage changes in BMD of the trochanter, femoral neck, and total body; incidence of fractures; and adverse events.

Main results
Analysis was by intention to treat. Compared with placebo, patients in the alendronate groups had greater percentage changes in BMD of the lumbar spine (2.9% v −0.4%, p≤0.001 for 10 mg alendronate and 2.1% v −0.4%, p≤0.001 for 5 mg alendronate); femoral neck (1.0% v −1.2%, p=0.001 for 10 mg alendronate and 1.2% v −1.2%, p<0.001 for the 5 mg alendronate); and trochanter (2.7% v −0.7%, p=0.001 for 10 mg alendronate and 1.1% v −0.7%, p≤0.01 for 5 mg alendronate) at 48 weeks. BMD of the total body was analysed in <80% of patients. The incidence of vertebral or non-vertebral fractures and overall or severe adverse events did not differ significantly between groups. Upper gastrointestinal adverse events occurred most frequently in the 10 mg alendronate group (25% for 10 mg alendronate, 19% for 5 mg alendronate, and 16% for placebo, p for trend <0.5).

Conclusion
In patients with osteoporosis that is induced by long term glucocorticoid treatment, alendronate increased bone mineral density of the lumbar spine, femoral neck, and trochanter but did not significantly reduce the incidence of fractures.

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In both studies patients were taking glucocorticoids for a variety of disorders and men and women over a wide age range were included.

These results are encouraging, although more data are required on anti-fracture efficacy at both vertebral and non-vertebral sites and it should be emphasised that the studies to date have been relatively short term. In view of its adverse gastrointestinal effects, alendronate should be used with particular caution in patients receiving glucocorticoids, and cyclical etidronate should be advised in those with a history of dyspepsia, reflux or other oesophageal disease. The most important message, however, is that effective prophylaxis against glucocorticoid induced bone loss can be achieved and should be used more widely by the many physicians who prescribe glucocorticoids for their patients.

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