

THERAPEUTICS

Etidronate, calcium, or both did not reduce fracture rates in patients with asthma receiving glucocorticoid treatment

Campbell IA, Douglas JG, Francis RM, Prescott RJ, Reid DM. Five year study of etidronate and/or calcium as prevention and treatment for osteoporosis and fractures in patients with asthma receiving long term oral and/or inhaled glucocorticoids. *Thorax*. 2004;59:761-8.

QUESTION

In patients with asthma receiving long-term glucocorticoid treatment, does etidronate, calcium, or both reduce fracture rates?

METHODS

Design: Randomized controlled trial.
Allocation: Concealed.*
Blinding: Blinded {data analysts}†.*
Follow-up period: 5 years.
Setting: 40 chest clinics in the United Kingdom.
Patients: 352 men and women 50 to 70 years of age (mean age 60 y, 58% men) who were outpatients; randomization was violated in 3 patients. Patients had asthma and had been taking regular oral or inhaled glucocorticoids, or both, for ≥ 1 year. Only postmenopausal women were included. Women with a hysterectomy were excluded.
Intervention: Patients were stratified by level of glucocorticoid exposure and allocated to oral etidronate, 400 mg/d for 2 weeks every 3 months (*n* = 81); calcium carbonate, given as 500 mg/d of elemental calcium (*n* = 85); etidronate plus calcium, given in the same doses except when calcium was omitted for the 2-week etidronate-treatment period (*n* = 88); or no treatment (*n* = 95).

Outcomes: New vertebral and nonvertebral fractures.

Patient follow-up: 99% (intention-to-treat analysis).

MAIN RESULTS

The groups did not differ for mortality (10%, 24%, 16%, and 16% in the etidronate-only, calcium-only, etidronate-plus-calcium, and no-treatment groups, respectively); symptomatic fractures (6%, 8%, 10%, and 7%, respectively); or symptomatic fractures, semiquantitative vertebral fractures, or both (16% 18%, 16%, and 20%, respectively). Groups receiving etidronate compared with groups not receiving etidronate, and groups receiving calcium compared with groups not receiving calcium, did not differ for rates of any fractures, respectively (Table).

CONCLUSION

In patients with asthma receiving long-term glucocorticoid treatment, etidronate and calcium used alone or combined did not reduce fracture rates.

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*See Glossary.

†Information provided by author.

Etidronate (Et)-containing regimens or calcium (Ca)-containing regimens to prevent any fracture in patients with asthma receiving long-term glucocorticoid treatment‡

Comparisons	Event rates	RRR (95% CI)	NNT
Et and Et + Ca vs Ca and no treatment	16% vs 19%	15% (-33 to 46)	Not significant
Ca and Et + Ca vs Et and no treatment	17% vs 18%	8% (-45 to 41)	Not significant

‡Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

Campbell and colleagues studied the effects of etidronate (with and without calcium), calcium, or placebo on bone mineral density (BMD) and fractures in patients taking oral or inhaled glucocorticoids or both for asthma. Patients randomized to etidronate had a 5% increase in lumbar spine BMD. No difference between groups existed in hip BMD or fractures. Calcium, 500 mg/d, did not have any additional benefit.

How does one interpret these results? Lack of statistical power may explain the negative findings because the study achieved only 50% of its recruitment target. Previous studies show that etidronate is effective at preventing bone loss in patients treated with glucocorticoids, and 1 trial of shorter duration showed a reduction in height loss and vertebral fracture (1). Perhaps the effect of etidronate was diminished because patients had other risk factors for fractures that were not assessed or treated, although levels of exercise did not differ between treatment groups. Alternatively, etidronate may not be potent enough for long-term fracture prevention. The lack of an additional effect of calcium is not surprising; the dose was low, and the data for calcium and vitamin D in glucocorticoid-induced osteoporosis are not compelling (1).

How can we apply findings from this study to the management of glucocorticoid-induced osteoporosis? Until further long-term studies of

the newer bisphosphonates are completed, patients with low-trauma fractures should be prescribed a bisphosphonate, risedronate or alendronate, regardless of BMD (1). Men and women taking oral or inhaled steroids at doses ≥ 1000 µg/d should have BMD testing. For patients with T scores < -2.0 to -1.5, prescription of bisphosphonates should be considered.

What bisphosphonate should one use? Alendronate and risedronate are the only approved bisphosphonates in the United States. In Canada and Europe, etidronate is also available. However, findings from this study by Campbell and colleagues, and the lack of studies showing that etidronate decreases hip and nonspinal fractures in patients treated with steroids and in postmenopausal women, suggest that etidronate is not the best choice.

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Reference

1. Reid IR, Wu F. Glucocorticoid-induced osteoporosis. In: Cummings SR, Cosman F, Jamal SA, eds. *Osteoporosis: An Evidence-based Guide to Prevention and Management*. Philadelphia: American College of Physicians; 2002:223-38.