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

Campbell IA, Douglas JG, Francis RM, et al. 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.

Clinical impact ratings GP/FP/Primary care ★★★★★☆ IM/Ambulatory care ★★★★★☆ Rheumatology ★★★★★☆ Respirology ★★★★★☆

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

METHODS

Design: randomised controlled trial.

Allocation: concealed.*

Blinding: blinded [data analysts]†.*

Follow-up period: 5 years.

Setting: 40 chest clinics in the UK.

Patients: 352 men and women 50–70 years of age (mean age 60 yrs, 58% men) who were outpatients; randomisation was violated in 349 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.

Interventions: patients were stratified by level of glucocorticoid exposure and allocated to oral etidronate, 400 mg/day for 2 weeks every 3 months (n = 81); calcium carbonate, given as 500 mg/day 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 = 93).

Outcomes: new vertebral and non-vertebral fractures.

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

*See glossary. †Information provided by author.

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, semi quantitative 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.

For correspondence: Dr I A Campbell, Llandough Hospital, Penarth, UK. ian.campbell@cardiffandvale.wales.nhs.uk

Sources of funding: Allen and Hanburys, and Glaxo.

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

<table>
<thead>
<tr>
<th>Comparisons</th>
<th>Event rates</th>
<th>RRR (95% CI)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Et and Et+Ca v Ca and no treatment</td>
<td>16% v</td>
<td>15% (~33 to 46)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Ca and Et+Ca v Et and no treatment</td>
<td>17% v</td>
<td>8% (~45 to 41)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; RRR, NNT, and CI calculated from data in article.

Commentary

Campbell et al 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 randomised to etidronate had a 5% increase in lumbar spine BMD. No difference between groups existed in hip BMD or fractures. Calcium, 500 mg/day, 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. 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.

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. Men and women taking oral or inhaled steroids at doses of >1000 µg/day 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 US. In Canada and Europe, etidronate is also available. However, findings from this study by Campbell et al, and the lack of studies showing that etidronate decreases hip and non-spiral fractures in patients treated with steroids and in postmenopausal women, suggest that etidronate is not the best choice.

Sophie A Jamal, MD, PhD
St Michael’s Hospital, University of Toronto
Toronto, Ontario, Canada

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

_Evid Based Med_ 2005 10: 53
doi: 10.1136/ebm.10.2.53

Updated information and services can be found at:
http://ebm.bmj.com/content/10/2/53

References
This article cites 1 articles, 1 of which you can access for free at:
http://ebm.bmj.com/content/10/2/53#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

- Asthma (154)
- Immunology (including allergy) (571)
- Musculoskeletal syndromes (219)
- Osteoporosis (55)
- Clinical trials (epidemiology) (1594)
- Injury (154)
- Menopause (including HRT) (85)
- Epidemiologic studies (1092)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/