Calcium did not prevent fractures in elderly women

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Q In ambulatory elderly women unselected for low bone mass, does calcium supplementation reduce the risk of fractures?

**METHODS**

Design: randomised, placebo controlled trial.  
Allocation: concealed. *  
Blinding: blinded (patients, healthcare providers, data collectors, and outcome assessors)]*  
Follow up period: 5 years.  
Setting: population-based study in Western Australia.  
Participants: 1460 ambulatory women >70 years of age (mean age 75 y) who were not taking any medication affecting bone mass and were expected to survive >5 years.  
Intervention: calcium carbonate, 600 mg twice daily with meals (n = 730), or placebo (n = 730).  
Outcomes: incident atraumatic clinical fractures and symptomatic vertebral fractures (self reported and confirmed by radiographic reports), and adverse events requiring medical attention.  
Patient follow up: 84% completed the study (100% included in the intention to treat analysis).  
*See glossary.  
†Information provided by author.

**MAIN RESULTS**

A total of 236 women sustained 297 new osteoporotic fractures. Calcium did not reduce the incidence of fractures overall or at any individual site (table). In the 57% of women who were compliant (>80% of tablets taken) throughout the study, calcium reduced fractures overall and at appendicular sites, in particular the upper limbs, but did not reduce vertebral fractures (table). Calcium supplementation showed a reduction in the loss of bone content at 5 years. Compliance with the treatment was good. The trial was conducted in a population with relatively low vitamin D status. Calcium did not reduce the risk of fractures overall or at any bone site (table). 

**CONCLUSIONS**

In ambulatory elderly women unselected for low bone mass, calcium supplementation at 1200 mg/day did not reduce the risk of fractures. Calcium was effective in compliant women, although compliance was poor.

Calcium v placebo to prevent fractures in elderly women at 5 years*

<table>
<thead>
<tr>
<th>Site of fracture</th>
<th>Calcium</th>
<th>Placebo</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>Any</td>
<td>15%</td>
<td>17%</td>
<td>12%</td>
</tr>
<tr>
<td>Appendicular</td>
<td>11%</td>
<td>13%</td>
<td>11%</td>
<td>12%</td>
</tr>
<tr>
<td>Vertebral</td>
<td>5.2%</td>
<td>5.3%</td>
<td>2%</td>
<td>1%</td>
</tr>
<tr>
<td>Compliant</td>
<td>Any</td>
<td>10%</td>
<td>15%</td>
<td>15%</td>
</tr>
<tr>
<td>Appendicular</td>
<td>9.3%</td>
<td>14%</td>
<td>33%</td>
<td>15%</td>
</tr>
<tr>
<td>Upper limb</td>
<td>2.4%</td>
<td>5.4%</td>
<td>55%</td>
<td>91%</td>
</tr>
</tbody>
</table>

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

**Commentary**

This well designed trial showed that, among healthy women 70 years and older, calcium carbonate 1200 mg daily reduced the risk of clinical fractures, but only among women who were compliant. Prince et al did not show a reduced risk of fracture with the intention to treat (ITT) analysis, the preferred method by which to report data from a placebo controlled trial, using data from all subjects regardless of compliance. The non-ITT analysis is problematic. It undermines the purpose of randomisation—that is, to reduce prognostic differences between groups. The applicability of the results may be threatened by the differences between compliant and non-compliant women, with the latter being older, weaker, and slower.

While lack of compliance with calcium may be a likely explanation for the negative results of the ITT analysis, compliance itself may only be a marker for good outcomes. An alternative explanation for the overall negative results may be that the vitamin D concentration in these Australian women, while higher than in other studies conducted in more northern latitudes, still might not have been high enough to ensure optimal skeletal calcium handling. It has been estimated that a serum 25-hydroxyvitamin D concentration >75 nmol/l is needed to lower the risk of fracture. 2

While this study is unable to provide a definitive answer, clinicians who wish to apply the secondary analysis results of this trial to their practice will need to inquire about calcium supplement use at clinic visits and encourage women to adhere closely to the daily use of 1200 mg of calcium.

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