Calcium for prevention of osteoporotic fractures in postmenopausal women

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Authors' objectives
To assess the effectiveness of calcium supplements and/or dietary calcium for the prevention of osteoporotic fractures in postmenopausal women.

Searching
The authors searched MEDLINE (1966 to March 1997) using the textwords 'fracture' and 'calcium'. All publications known to the authors and the reference lists of identified articles were also reviewed for additional relevant studies.

Study selection

Study designs of evaluations included in the review
Randomised trials (RCTs) of calcium supplements; nonrandomised trials of calcium supplements; observational epidemiologic studies (cohort studies and case-control studies) of calcium supplements; and observational epidemiological studies (cohort studies and case-control studies) of dietary calcium. Ecologic studies were excluded.

Specific interventions included in the review
Calcium supplements in doses of 800, 1000, 12000, 1200-2000, or 1500-2500 mg per day (giving a mean dietary calcium 372-734 mg) or dietary calcium (mean dietary calcium 168-992 mg).

Participants included in the review
Men and women whose mean age ranged from 57 to 84 years taken either from the general population (18 studies), hospital populations (8 studies), retirement or nursing home communities (5 studies), vertebral fracture patients (3 studies), or healthy volunteers (3 studies).

Outcomes assessed in the review
Fractures (or a particular type of fracture), including non-spine fractures, vertebral fractures, symptomatic fractures, hip fractures, wrist fractures, forearm fractures, and proximal humerus fractures.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not state that they assessed quality.

Data extraction
The authors do not state who, or how many of the reviewers, performed the data extraction. Data were extracted for the categories of study design, country where study was conducted, calendar years of baseline data collection, mean age of study subjects, dose of calcium supplement (when relevant), method used to collect dietary calcium data (when relevant) and mean dietary calcium intake.

Most studies grouped studies into two to five calcium intake categories and then calculated relative risk for hip fracture with 95% confidence intervals (CIs) relative to some common reference category.

The authors calculated estimates of the size of the effect on hip fracture risk of an increase in dietary calcium intake of 300 mg/day and 1000 mg/day for each of the included studies.
Methods of synthesis

How were the studies combined?
The odds ratios (ORs) were pooled using a fixed-effect model with 95% confidence intervals (CIs).

How were differences between studies investigated?
Heterogeneity among studies was investigated using a meta-regression analysis. Study-specific calcium-hip fracture regression coefficients were regressed against study level characteristics: study type, mean age of study subjects, mean calcium intake, calendar years of baseline data collection, dietary assessment method, and setting of study.

Results of the review

Fourteen studies of calcium supplements (including 4 RCTs with 3,638 participants, and 3 non-randomised trials with 141 participants), 18 studies of dietary calcium and hip fracture (no RCTs), and 5 studies of dietary calcium and other fracture sites (no RCTs).

A further sixteen observational hip fracture studies were included in this analysis. Eleven were case-control studies with 12,465 participants (4,131 cases and 8,334 controls) and 5 cohort studies with 28,511 participants who experienced 915 fractures.

For calcium supplements, the 4 RCTs reported RRs between 0.3 and 0.7, a reduced fracture risk among women randomised to receive calcium supplements. The 3 non-randomised trials found a lower risk of new vertebral fractures in women given calcium supplements than in untreated women. The observational studies had inconsistent findings: the RRs varied between 0.3 and 2.0, with only one of the studies (with calcium given for 3 or more years) statistically significant.

Pooling the results of all 16 studies of dietary calcium gave an OR for hip fracture of 0.96 (95% CI: 0.93, 0.99) per 300 mg/day increase in dietary calcium which was statistically significant.

The pooled OR in the subgroup of 5 cohort studies was 0.96 (95% CI: 0.91, 1.02), p for heterogeneity = 0.44 which was not statistically significant.

The pooled OR for all 16 studies for 1000 mg of calcium/day was 0.88 (95% CI: 0.80-0.97).

Authors’ conclusions

The authors conclude that calcium supplements and dietary calcium probably reduce the risk of osteoporotic fractures in older women.

CRD commentary

The authors have clearly stated their research question and inclusion criteria. The literature search is good although the exclusion of non-English language publications could have resulted in relevant studies being missed. Data extraction is reported in tables and summarised in the text. In two cases, the dates of studies listed in the table do not match those reported in the text. The quality of the included studies was not assessed and the authors have not reported on how the articles were selected, or how many of the reviewers were involved in the data extraction.

The studies were combined using appropriate statistics using the best available data from a subset of the included studies. The authors tested for heterogeneity and investigated and discussed the results from those tests. The authors acknowledge several drawbacks about the quality and design of the individual studies and the conduct of their review. Their conclusions appear to follow from their results.

Implications of the review for practice and research

Practice: The authors state that this review supports the current clinical and public health policy of recommending increased calcium intake among older women for fracture prevention.
Research: The authors state that larger RCTs are needed with symptomatic fractures, particularly hip fractures, as the outcome.

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