Meta-analysis about efficacy of anti-resorptive drugs in post-menopausal osteoporosis

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Authors' objectives
To compare the effect of three groups of anti-resorptive drugs in post-menopausal osteoporosis.

Searching
MEDLINE was searched from 1983 to 1995 (keywords given). Source references of retrieved articles were analysed.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials including a placebo arm, in which treatment and follow-up lasted at least a year.

Specific interventions included in the review
The inclusion criteria stated oestrogens, calcitonins, bisphosphonates and placebo. Estradiol valerate and 17-beta-estradiol were specifically mentioned in the review.

Participants included in the review
Patients with post-menopausal osteoporosis. People with senile osteoporosis or due to use of a medication or having a related disease were excluded.

Outcomes assessed in the review
Spine bone mass based on dual photon or dual-energy densitometry.

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
Six of the criteria specified by Chalmers et al. (1981) were used, related to size and choice of sample, randomisation and observation of patients. Since the inclusion criteria served as qualitative standards to be complied with, other parameters were not taken into account. Each of the quality criteria was scored 0, 1 or 2. The studies with a score under 4 were considered poor quality. No practical details, such as the number of reviewers involved, are presented.

Data extraction
Effect sizes and 95% confidence intervals were calculated from each study using the average and standard deviation or standard error of the results taken from the evaluation of the lumbar densitometry after 1 year's treatment. No practical details, such as the number of reviewers involved, are presented.

Methods of synthesis
How were the studies combined?
Global effect sizes were calculated for each review question. The calculations were performed using the DSTAT programme.

How were differences between studies investigated?
Tests of heterogeneity were performed to give Q values. If these were significant, outliers (studies furthest from average) were excluded and the effect size recalculated. Sensitivity analyses were performed based on quality scores and other variables (eg. mode of administration, dose) which may have effected the results.
**Results of the review**

Oestrogens versus placebo: 11 RCTs (447 participants).

Calcitonins versus placebo: 12 RCTs (687 participants).

Biphosphonates versus placebo: 8 RCTs (453 participants).

Oestrogens versus placebo: Global effect size: 0.60 (95% CI: 0.41, 0.80, p < 0.00001), Q = 38.59 (p < 0.00001). After the removal of one study, recalculated effect size: 0.54 (95% CI: 0.34, 0.73, p < 0.00001), Q = 14.76 (p = 0.10). Sensitivity analyses found only the type of oestrogen and monthly drug dose used significant.

Calcitonins versus placebo: Global effect size: 1.02 (95% CI: 0.84, 1.20, p < 0.00001), Q = 339.26 (p < 0.00001). After removal of 4 outliers, the recalculated effect size: 0.41 (95% CI: 0.21, 0.61, p = 0.00001), Q = 13.19 (p = 0.07). Sensitivity analyses were not significant.

Biphosphonates versus placebo: Global effect size: 0.87 (95% CI: 0.68, 1.07, p < 0.00001), Q = 10.89 (p = 0.14). None of the sensitivity analyses were significant.

**Authors’ conclusions**

The meta-analysis indicates that biphosphonates exert a greater effect on the spinal bone mass in women during the postmenopausal period as compared to oestrogen replacement and calcitonin. The mode of administration of the drug, use of calcium in the control group, type of equipment used to analyse bone mass or the year of publication did not have a significant influence on the results.

**CRD commentary**

This review is based on a clear research question, which specifies the intervention, participants and outcomes of interest. The inclusion and exclusion criteria are presented and the quality of included studies was assessed. However the comprehensiveness of the review may be compromised by the inclusion of only studies published in English or Portuguese and by searching only one database. No details are presented of the review processes, such as the number of reviewers undertaking assessments of relevance, so the rigour of the review cannot be assessed. Only minimal details of individual studies are provided (number of participants, effect sizes and confidence intervals), preventing independent appraisal of factors which may influence heterogeneity or the sensitivity analysis.

This review does not report any direct comparisons between the three drugs so it is not possible to conclude that one is superior to the others but only that all are superior to placebo.

**Implications of the review for practice and research**

Practice: Anti-resorptive drugs are more effective than placebo in preventing loss of bone mass.

Research: Direct comparisons between the groups of anti-resorptive drugs should be sought and subjected to systematic review. If no such comparisons are identified, good-quality randomised controlled trials which directly compare these treatments are required.

**Bibliographic details**


**PubMedID**

9875682

**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Bone Resorption /drug therapy /prevention & control; Calcitonin /therapeutic use; Diphosphonates /therapeutic use; Estrogens /therapeutic use; Female; Humans; Osteoporosis /drug therapy /prevention & control; Placebos; Postmenopause /metabolism; Randomized Controlled Trials as Topic

**AccessionNumber**
11999000166

**Date bibliographic record published**
31/07/2000

**Date abstract record published**
31/07/2000

**Record Status**
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.