Comparing therapies for postmenopausal osteoporosis prevention and treatment

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CRD summary
This review compared therapies for the prevention and treatment of osteoporosis in postmenopausal women. The authors concluded that several therapeutic options were found to improve bone mineral density and reduce the risk of bone fractures. The review had several methodological weaknesses and was poorly reported. More focused and better-reported reviews are required to verify the conclusions.

Authors' objectives
To evaluate the efficacy of calcium and vitamin D supplementation, hormone replacement therapy (HRT), bisphosphonates, selective oestrogen receptor modulators (SERMs) and calcitonin in the prevention and treatment of osteoporosis in postmenopausal women.

Searching
MEDLINE (from 1966 to July 2002), EMBASE (from 1980 to July 2002) and International Pharmaceutical Abstracts (from 1970 to July 2002) were searched for relevant studies; the search terms were given. The bibliographies of retrieved papers were also checked. No language restrictions were imposed.

Study selection
Study designs of evaluations included in the review
Specific inclusion criteria for the study design were not given. However, both experimental and observational studies were eligible for inclusion. These included meta-analyses, randomised controlled trials (RCTs), prospective and retrospective cohort studies, case-control studies and case series.

Specific interventions included in the review
Studies of agents recommended by the Food and Drug Administration (FDA) for the prevention and/or treatment of osteoporosis in postmenopausal women were eligible for inclusion. These were calcium, HRT, the bisphosphonates alendronate and risedronate, the SERM raloxifene, and calcitonin. Studies of agents that were not recommended by the FDA (including progestin, oral contraceptives, thiazide diuretics, anabolic steroids and tibolone) and biochemical markers were excluded from the review.

Participants included in the review
Inclusion criteria for the participants were not given. By implication, studies of postmenopausal women were eligible for inclusion. Further details of the participants in each of the included studies were not given.

Outcomes assessed in the review
Studies that evaluated bone mineral density (BMD) or fracture efficacy were eligible for inclusion.

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

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

Data extraction
The authors did not state how the data were extracted for the review, or how many reviewers performed the data extraction. Data were extracted on the change in BMD and the relative risk (RR) and 95% confidence intervals of bone
fracture following the intervention, as reported in each individual study.

Methods of synthesis
How were the studies combined?
The results of the studies were presented in a narrative discussion according to treatment group and outcome.

How were differences between studies investigated?
The authors did not systematically investigate differences between the studies. Instead, reasons for potential inconsistencies were briefly discussed when appropriate.

Results of the review
It was not possible to determine how many studies were included in the review, or how many participants were evaluated.

Calcium and vitamin D.
Calcium supplementation was associated with a decrease in BMD loss from the radius (1.82%), femoral shaft (0.7 to 1.3%), femoral neck (0.3%), lumbar spine (2.6 to 3.92%), proximal femur (1.3%) and total body (0.9 to 1.85%). There were significant decreases in the fracture incidence observed in pre- and postmenopausal women (P=0.023 and P<0.05, respectively). However, there was no significant decrease in fracture incidence in peri-menopausal women. There were inconsistent results in the studies that evaluated the use of vitamin D for the prevention of bone fractures (the results were not given). Both calcium and vitamin D supplementation were relatively well tolerated.

HRT.
The results of both the experimental and observational studies suggested that BMD was preserved in women receiving HRT. However, it was not clear if this translated into a reduction in the risk of bone fractures. Four observational studies found a significant decrease in fracture risk associated with HRT (RR ranged from 0.23 to 0.65). However, the reduction in fracture risk was not significantly significant in two RCTs. HRT was associated with serious life-threatening adverse events including an increased risk of endometrial cancer, breast cancer and acute myocardial infarction.

Bisphosphonates.
Alendronate and risedronate were associated with significant increases in BMD (ranging from 1.6% to 8.8%), based on patients in six studies. The increase was sustained for 5 to 7 years following treatment with alendronate, based on patients in two of the included studies. Six studies found that alendronate and risedronate were effective in reducing the risk of vertebral and nonvertebral fractures (range, where reported: 14 to 48%). Bisphosphonates were well tolerated and the most frequently reported adverse events were associated with the upper gastrointestinal tract.

SERMs.
Raloxifene was associated with significant increases in BMD (ranging from 0.6 to 2.2%). One study found that raloxifene was associated with a significant reduction in the risk of fracture of the lumbar spine and femoral neck. The most frequent adverse events were leg cramps and peripheral oedema, while the most serious adverse event was an increased risk of thromboembolism.

Calcitonin.
The results on the effectiveness of calcitonin on BMD were conflicting. Most of the included studies found that calcitonin was associated with a significant increase in BMD (ranging from 0.5 to 5%), whereas some studies found no difference or a slight decrease. However, calcitonin was found to significantly reduce the incidence of new bone fractures compared with placebo. No safety data were provided.
Authors’ conclusions
All of the therapies that were evaluated in the review were effective in the stabilisation and improvement of BMD. However, their use in reducing the risk of bone fractures was inconclusive. The choice of treatment should be patient-specific and should consider concomitant disease, medication and risk factors.

CRD commentary
The review lacked explicit inclusion and exclusion criteria for both the participants and study design. This made it difficult to ascertain whether the included studies were appropriate to the review question. For example, the included studies that evaluated calcium were performed in pre-, peri- and postmenopausal women, but the objective implied that only postmenopausal women were of interest. The authors did not use methods to minimise the introduction of bias and error into the study selection or data extraction processes. Furthermore, the authors did not assess the quality of the included studies, or consider the different study designs in the results or conclusions.

Given the variety of study designs included in the review, the decision to present the results in a narrative discussion was appropriate. However, it was not possible to determine the exact number of participants in each of the included studies, as the study details in the tables and text appear to have been reported selectively. This makes it impossible for the reader to assess the reliability of the conclusions. The authors’ conclusions should therefore be viewed as exploratory, and need to be supported by additional systematic reviews that are more focused and better reported.

Implications of the review for practice and research
Practice: The authors stated that calcium and vitamin D should be administered to all pre- and postmenopausal women. The selection of concomitant additional therapies used for the prevention and treatment of osteoporosis in postmenopausal women should be based on patient-specific characteristics, and should carefully consider the risks versus the benefits.

Research: The authors did not state any implications for further research.

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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.