Soy isoflavone intake increases bone mineral density in the spine of menopausal women: meta-analysis of randomized controlled trials

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CRD summary

The authors concluded that isoflavones significantly reduced spine bone loss in menopausal women; effects were greater when more than 90mg/day of isoflavones was consumed and isoflavone was taken for six months. The evidence appears to support the authors' conclusions, but the non significant results at 12 months were unexplained and may weaken the strength of evidence supporting the reported benefits of isoflavones.

Authors' objectives

To evaluate the effect of isoflavones on spinal bone mass in women.

Searching

MEDLINE (from 1966), EMBASE (from 1985), the Cochrane CENTRAL Register, Science Citation Index and CNKI (from 1979) were searched to January or September 2006. In addition, the reference lists of relevant reviews and papers were screened and experts were contacted for unpublished data.

Study selection

Parallel-group randomised controlled trials (RCTs) that evaluated the effects of soy products or isoflavones, taken for at least 3 months, on spinal bone mass in women were eligible for inclusion. Studies had to measure bone mass as spine bone mineral density (SBMD) or spine bone mineral content (SBMC).

All of the included studies compared isoflavones with placebo. Most of the studies evaluated isolated soy protein that mainly contained isoflavones; other studies evaluated isoflavone tablets. Isoflavone intake ranged from 4.4 to 150 mg/day. Some studies evaluated more than one isoflavone dose. The duration of interventions ranged from 3 to 24 months. The majority of studies were in Caucasian women; others were in Asian women. All studies were of healthy women who were not undergoing other treatments for osteoporosis, and most were of postmenopausal women. The included studies measured bone mass using dual X-ray absorptiometry and reported SBMD as area density (g/cm^2) and SBMC as content (g).

The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.

Assessment of study quality

Validity was assessed using the Jadad criteria (randomisation, blinding and withdrawals). The maximum possible score was 5 points.

Two reviewers independently assessed validity and any disagreements were resolved through discussion.

Data extraction

For each study, SBMD and SBMC values were extracted at baseline and post-treatment for each treatment group and the mean difference was calculated.

Two reviewers independently extracted the data and resolved any discrepancies through discussion.

Methods of synthesis

Pooled weighted mean differences (WMDs) between treatments were calculated using fixed-effect models; studies were weighted by the inverse variance. When an individual study evaluated more than one isoflavone treatment regimen, these were treated as separate comparisons in the meta-analyses. Statistical heterogeneity was assessed using

the χ^2 statistic. Publication bias was assessed using a funnel plot. Subgroup analysis was used to examine the effect on SBMD of isoflavone form and intake, duration of treatment, race and menopausal status.

Results of the review

Ten RCTs (n=608) were included.

Six studies scored 5 out of 5 points on the Jadad quality scale, three scored 4 points and one scored 3 points (the criteria not met were reported).

Isoflavones were associated with a statistically significant increase in SBMD compared with placebo (WMD 20.6 mg/cm^2, 95% confidence interval, CI: 4.5, 36.6, p=0.01), based on 10 studies (16 comparisons). The authors reported that the results were inconsistent among studies but did not report results of formal tests for heterogeneity.

Subgroup analyses showed increases in SBMD to be statistically significant for:

studies of isolated soy protein (WMD 21.3 mg/cm^2, 95% CI: 3, 39.7; 7 studies, n=460), but not isoflavone tablets (3 studies, n=148);

studies using an isoflavone intake of more than 90 mg/day (WMD 28.5 mg/cm^2, 95% CI: 8.4, 48.6; 6 studies, n=352), but not those using a lower dose (7 studies, n=318);

studies lasting 6 months (WMD 27 mg/cm^2, 95% CI: 8.3, 45.8; 5 studies, n=277), but not those lasting more than 12 months (4 studies, n=310);

studies of Caucasian women (WMD 21.3/cm^2, 95% CI: 3, 39.7; 7 studies, n=460), but not Asian women (3 studies, n=148); and

studies of postmenopausal women (WMD 22.4 mg/cm^2, 95% CI: 5.3, 39.5; 8 studies, n=511), but not perimenopausal women (2 studies, n=97).

None of these subgroup analyses showed significant heterogeneity.

Isoflavones were associated with a non statistically significant increase in SBMC compared with placebo (WMD 0.93 g, 95% CI: -0.37, 2.24, p=0.08), based on 6 studies (9 comparisons).

The funnel plot showed no strong evidence of publication bias.

Authors' conclusions

Isoflavones significantly reduce spine bone loss in menopausal women. The effects are greater when more than 90 mg/day of isoflavones is consumed and isoflavone is taken for 6 months.

CRD commentary

The review question was stated clearly and inclusion criteria were specified. Several relevant sources were searched and some attempts were made to minimise publication bias; no strong evidence of publication bias was found. It is not clear whether any language restrictions were applied. Only RCTs were included, and validity was assessed and the results reported. Appropriate methods were used to minimise reviewer error and bias during the validity assessment and data extraction processes, but it was not reported whether similar approaches were used when selecting the studies. The data were pooled using meta-analyses, heterogeneity was assessed, and various subgroup analyses were conducted. However, it is not clear if subgroup analyses were determined a priori. In addition, it may not have been appropriate to pool multiple datasets from the same study where there was more than one treatment arm. Potential reasons for the lack of a significant effect of isoflavones given for 12 months were not discussed, despite the significant benefit at 6 months. The evidence appears to support the authors' conclusions, but the non significant results at 12 months were unexplained and may weaken the strength of evidence supporting the reported benefits of isoflavones.

Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that future RCTs of isoflavones should be larger, evaluate graded doses of isoflavones, and assess the long-term effects on bone mass and fracture risk.

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