

Review: Etidronate decreases vertebral but not nonvertebral fractures in postmenopausal women

Cranney A, Welch V, Adachi JD, et al. Etidronate for treating and preventing postmenopausal osteoporosis. *Cochrane Database Syst Rev.* 2001;(4):CD003376 (latest version 25 Mar 2001).

QUESTION

In postmenopausal women, is etidronate effective and safe for treating postmenopausal osteoporosis and preventing fractures?

DATA SOURCES

Studies were identified by searching MEDLINE, HealthSTAR, EMBASE/Excerpta Medica, and *Current Contents* (1966 to 1998) with terms that include etidronate, osteoporosis, postmenopausal, diphosphonates, and bisphosphonates. Conference abstracts were hand searched, references of relevant articles were scanned, and experts were contacted.

STUDY SELECTION

Published and unpublished studies were selected if they were randomized controlled trials (RCTs) of ≥ 1 year of duration in postmenopausal women; compared etidronate (using the intermittent cyclic method at 400 mg/d for 14 to 20 d, and then using calcium or vitamin D, or both) with placebo, calcium, vitamin D, or calcium plus vitamin D; and evaluated outcomes of fracture reduction, change in bone mineral density (BMD), or toxicity.

DATA EXTRACTION

Data were extracted on participants, treatment type and duration, outcomes, method of densitometry, and methodologic quality.

MAIN RESULTS

13 RCTs (1267 women), 9 (1010 women) of which reported vertebral fractures, met the selection criteria. 5 trials included women with established osteoporosis, and 8 trials included early postmenopausal women without osteoporosis. All studies ensured allocation concealment, and 12 used an intention-to-treat analysis. 6 trials were blinded, and 7 were unblinded.

At 2 years, etidronate reduced vertebral fractures but had no effect on nonvertebral fractures or hip fractures alone (Table). At 3 years, etidronate was associated with greater

percentage changes in BMD than was placebo at the lumbar spine (risk difference [RD] 4.3%, 95% CI 2.7% to 5.9%), at the femoral neck (RD 2.19%, CI 0.4% to 3.95%), and for the total body (RD 0.97%, CI 0.4% to 1.6%) but not at the distal forearm (RD 0.43%, CI -1.6% to 2.5%). Etidronate and placebo did not differ for the number of overall withdrawals.

CONCLUSION

In postmenopausal women, etidronate safely increases bone mineral density and decreases vertebral fractures but has no effect on nonvertebral or hip fractures.

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Etidronate vs placebo in postmenopausal women at 2 years*

Outcomes	Weighted event rates		RRR (95% CI)	NNT (CI)
	Etidronate	Placebo		
Vertebral fractures	5.9%	10%	40% (12 to 59)	25 (14 to 91)
Nonvertebral fractures	11.1%	11.3%	2% (-42 to 32)	Not significant
			RRI (CI)	NNH
Hip fractures	1.7%	1.4%	20% (-63 to 288)	Not significant

*Abbreviations defined in Glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article using a fixed-effects model.

COMMENTARY

In this well-done meta-analysis, Cranney and colleagues confirmed that postmenopausal women taking etidronate for at least 2 years have higher bone mineral density and a lower risk for vertebral fractures than do those taking placebo. Studies comparing etidronate with hormone replacement therapy, calcitriol, or calcitonin and studies of men and patients with steroid-induced osteoporosis were not included in this review.

The reduction in risk for vertebral fractures with etidronate appears to be slightly less than that with alendronate or risedronate (which have about a 50% risk reduction) and similar to that observed with raloxifene (1-3). However, no head-to-head comparisons of these agents are available.

In RCTs, only alendronate and risedronate reduce the risk for nonspinal and hip fractures, which suggests that etidronate could be used for women in their middle menopausal years (55 to 65 y) who are at high risk for vertebral fracture. Raloxifene would also be appropriate for this population. Among older women (> 65 y) who are at risk for hip fractures, use of alendronate or risedronate should be considered.

Although this meta-analysis has clarified the role of etidronate in the prevention and treatment of postmenopausal osteoporosis, some contentious areas relating to the use of bisphosphonates still exist, including the optimal duration of use and the effect on fracture risk when the bisphosphonate is stopped. How etidronate compares with other antiresorptives and the efficacy of etidronate in men also require further study.

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