

Raloxifene reduced vertebral fractures in postmenopausal women

Erttinger B, Black DM, Mitlak BH, et al., for the Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene. Results from a 3-year randomized clinical trial. JAMA. 1999 Aug 18;282:637-45.

QUESTION

In postmenopausal women with osteoporosis, does raloxifene reduce the rate of vertebral and nonvertebral fractures?

DESIGN

Randomized (allocation concealed*), blinded (patients, clinicians, and outcome assessors),* placebo-controlled trial.

SETTING

180 clinical centers in 25 countries.

PARTICIPANTS

7705 postmenopausal women (mean age 67 y, 96% white) with osteoporosis. Exclusion criteria included other bone diseases, postmenopausal symptoms, abnormal uterine bleeding, history of breast or endometrial cancer or thromboembolic disorders, other cancers, treated endocrine disorders except type 2 diabetes or hypothyroidism, renal lithiasis, abnormal hepatic or renal function, untreated malabsorption, and consumption of > 4 drinks of alcohol/d. Follow-up was 89%.

INTERVENTION

Women received calcium, 500 mg/d, and cholecalciferol, 400 to 600 IU/d, and

were allocated to raloxifene, 120 mg/d ($n = 2572$); raloxifene, 60 mg/d ($n = 2557$); or placebo ($n = 2576$) after stratification for previous vertebral fractures.

MAIN OUTCOME MEASURE

Confirmed new vertebral fractures.

MAIN RESULTS

Fewer women in the raloxifene groups had ≥ 1 vertebral fracture than did women in the placebo group for all women and for subgroup analysis using previous fracture data (Table). The groups did not differ for nonvertebral fractures (9.3% for placebo vs 8.5% for raloxifene groups), but bone mineral density was higher in the raloxifene groups than in the placebo group ($P < 0.001$). Women in the raloxifene

groups withdrew from the study more often because of adverse events and developed more thrombosis (1% vs 0.3%); breast cancer incidence was decreased.

CONCLUSIONS

Raloxifene prevented vertebral fractures but not nonvertebral fractures in postmenopausal women with osteoporosis. Results were more dramatic for women with previous fractures.

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*See Glossary.

≥ 1 vertebral fracture with raloxifene vs placebo in postmenopausal osteoporosis at 3 years†

Women	Raloxifene dose	Raloxifene	Placebo	RRR (95%)	NNT
All	60 mg/d	6.6%	10.1%	35% (21 to 47)	29 (20 to 52)
	120 mg/d	5.4%	10.1%	46% (33 to 56)	22 (17 to 33)
With previous fractures	60 mg/d	14.7%	21.2%	35% (19 to 48)	16 (10 to 38)
	120 mg/d	10.7%	21.2%	53% (40 to 63)	10 (7 to 15)
With no previous fractures	60 mg/d	2.3%	4.5%	47% (22 to 65)	47 (29 to 120)
	120 mg/d	2.8%	4.5%	38% (9 to 57)	59 (33 to 274)

†Abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

The MORE trial shows that treatment of postmenopausal osteoporosis with raloxifene, a selective estrogen-receptor modulator (SERM), reduced 3-year fracture risk at the spine but not at the hip or most other appendicular sites. In women with a previous vertebral fracture, the magnitude of this reduction was dose-dependent and at least 4 times greater than in women with no previous fracture.

The results are consistent with evidence that estrogen preserves bone even when introduced many years after menopause (1); the control data illustrate the immense effect of a history of osteoporotic fracture on the risk for subsequent fracture (2). In addition to modifying that risk, raloxifene reduced the incidence of breast cancer and increased the risk for thrombosis. Each of these events occurred once in women without previous fractures for every 3 fractures prevented.

Women who value the vasomotor and urogenital effects of estrogen will reject SERMs, but many others will wish to choose between a SERM and a bisphosphonate. In the Fracture Intervention Trial (3, 4), alendronate reduced fracture risk at the spine

and hip in women with previous vertebral fractures, and it reduced the risk for vertebral fractures in women without previous fractures. Alendronate also produced greater increases in bone mineral density than raloxifene did in the MORE study, and it was not more toxic than placebo. Because alendronate is available, effective, and relatively benign, prescription of raloxifene for the sole purpose of treating osteoporosis will be difficult to justify. However, for women who conclude that the combined benefits of fracture reduction and breast cancer prevention outweigh the risk for thrombosis, raloxifene may be the best choice.

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