

Alendronate reduced clinical and radiographic vertebral fractures in postmenopausal women with osteopenia

Quandt SA, Thompson DE, Schneider DL, Nevitt MC, Black DM. Effect of alendronate on vertebral fracture risk in women with bone mineral density T scores of -1.6 to -2.5 at the femoral neck: the Fracture Intervention Trial. *Mayo Clin Proc.* 2005;80:343-9.

Clinical impact ratings: GIM/FP/GP ★★★★★☆ Geriatrics ★★★★★☆ Rheumatology ★★★★★☆

QUESTION

In postmenopausal women with osteopenia, is alendronate more effective than placebo for reducing vertebral fracture (VF) risk?

METHODS

Design: Randomized placebo-controlled trial (Fracture Intervention Trial [FIT]).

Allocation: {Concealed}†.*

Blinding: Blinded {patients, clinicians, and outcome assessors}†.*

Follow-up period: Mean 3.8 years.

Setting: 11 clinical centers in the United States.

Patients: 3737 women 55 to 80 years of age (mean age 68 y) who had been postmenopausal for ≥ 2 years, had a diagnosis of World Health Organization–defined osteopenia (a femoral neck bone mineral density [BMD] ≤ 0.68 g/cm² that corresponds with a BMD T-score between -1.6 and -2.5) with or without baseline radiographic VF.

Intervention: Alendronate, 5 mg/d for 2 years and 10 mg/d thereafter ($n = 1878$), or placebo ($n = 1859$). Women with existing baseline VF received alendronate for 3 years, and women without baseline VF took it for 4 to 4.5 years. 82% of patients with baseline dietary calcium intake < 1000 mg/d were given a daily supplement of 500 mg of calcium and 250 IU of vitamin D.

Outcomes: Clinical VFs (fracture reported by patients, diagnosed by a community physician, and confirmed by written reports; radiographs [compared with the baseline radiograph by the study radiologist]; or other tests) and radiographic VFs (lateral spine radiographs obtained at baseline and 2 and 3 y in women with existing VF and 4 y in women without existing VF). A new VF was defined as a decrease of 20% and a decrease of ≥ 4 mm in height of any vertebral body from baseline to the end of the study.

Patient follow-up: 100% (intention-to-treat analysis).

Main results: Fewer women who received alendronate had clinical or radiographic VFs than did those who received placebo (Table). Alendronate reduced the risk for clinical or

radiographic VFs in patients with baseline VF but not in those without VF (Table).

CONCLUSIONS

In postmenopausal women with osteopenia, alendronate reduced the risk for clinical and radiographic vertebral fractures more than placebo. Women without baseline fracture had less risk reduction, and it was not statistically significant.

Source of funding: Merck Research Laboratories.

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*See Glossary.

†Black DM, Cummings SR, Karpf DB, et al. *Lancet.* 1996;348:1535-41.

Alendronate vs placebo for postmenopausal women with osteopenia at mean 3.8 years†

Outcomes	Alendronate	Placebo	RRR (95% CI)	NNT (CI)
Clinical VF overall	0.6%	1.6%	59% (21 to 79)	109 (61 to 378)
Clinical VF with baseline VF	0.3%	0.9%	63% (8 to 85)	185 (91 to 1810)
Clinical VF without baseline VF	0.3%	0.7%	54% (-16 to 82)	Not significant
Radiographic VF overall	2.7%	4.6%	41% (17 to 59)	53 (32 to 148)
Radiographic VF with baseline VF	1.5%	2.7%	44% (12 to 65)	83 (46 to 376)
Radiographic VF without baseline VF	1.2%	1.9%	27% (-8 to 63)	Not significant

‡VF = vertebral fracture. Other abbreviations defined in Glossary; RRR, NNT, and CI calculated from data in article.

COMMENTARY

One of the more controversial issues that clinicians have to address today is the treatment of patients with osteopenia based on a BMD measurement (i.e., patients with a BMD T-score between -1.0 and -2.5) (1). A need absolutely exists to treat patients with a definite fracture who have osteoporosis based on BMD measures. The study by Quandt and colleagues showed a reduction in fracture rate in high-risk patients who received alendronate. However, the treatment of patients with osteopenia alone is less certain. Questions are often raised about the need for treatment in patients with less risk. In fact, the evidence for treatments that prevent fractures in this population is very limited (2).

Quandt and colleagues examined the effect of alendronate on VF risk in postmenopausal women who had evidence of osteopenia in their hips. It is important to note that femoral neck BMD ranged from -1.6 to -2.5 , and therefore did not include the full range of osteopenia.

This study provides evidence that treatment with alendronate in this defined range of osteopenic patients prevents incident fractures in those

who have prevalent VFs. In these patients, the relative risk reduction is 63% for clinical VF and 44% for radiographic VF, corresponding to a number needed to treat of 185 and 83, respectively; this is also in keeping with what one might expect in a population at lower risk. The risk reductions were similar in women without prevalent VFs, but the baseline risk for fracture was lower in this group and the risk reduction was not statistically significant.

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References

1. McClung MR. Osteopenia: to treat or not to treat? *Ann Intern Med.* 2005;142:796-7.
2. Schousboe JT, Nyman JA, Kane RL, Ensrud KE. Cost-effectiveness of alendronate therapy for osteopenic postmenopausal women. *Ann Intern Med.* 2005;142:734-41.