

What is the best approach to prevention and treatment of osteoporosis?

Kendra Schwartz, MD, MSPH

Wayne State University, Detroit, Michigan

■ EVIDENCE-BASED ANSWER

Randomized controlled trials (RCTs) have demonstrated decreased vertebral and nonvertebral fracture rates in postmenopausal osteoporotic women taking a bisphosphonate (alendronate or risedronate). Hormone replacement therapy (HRT) also has some evidence for osteoporotic fracture prevention. Concurrent calcium and vitamin D may also prevent fractures. Physical exercise and smoking cessation have been associated with increased bone density, but fracture prevention has not been reported (Grade of Recommendation: B, some extrapolation from individual trials needed).

■ EVIDENCE SUMMARY

Many trials report bone mineral density (BMD) as their primary outcome, which may or may not be associated with fracture rates. Relatively few studies have reported patient-oriented outcomes, such as vertebral or nonvertebral fracture.

Alendronate and risedronate have both reduced vertebral and nonvertebral fractures and increased BMD in clinical trials. The pooled risk estimates for alendronate's antifracture effect are 48% to 53% vertebral and hip fracture reduction and 30% reduction of all clinical fractures (relative risk [RR] = 0.70; 95% confidence interval [CI], 0.59-0.82).¹ Risedronate reduced hip fractures in osteoporotic women aged 70 to 79 years (RR = 0.6; 95% CI, 0.4-0.9), but women 80 years and older with nonskeletal risk factors did not benefit.² One alendronate trial in 241 osteoporotic men demonstrated increased spine and hip BMD and a decreased incidence of vertebral fractures.³

HRT has been associated with increased BMD in RCTs, fewer fractures in observational studies, and fewer fractures in a recent meta-analysis of RCTs. HRT had the greatest benefit among women younger than 60 years (RR = 0.67; 95% CI, 0.56-0.94).⁴ For women older than 60 years, a nonsignificant trend toward benefit was found (RR = 0.88, 95% CI, 0.71-1.08). However, in a large RCT of postmenopausal women, 85% without osteoporotic BMD, 4 years of HRT did not reduce fracture incidence.⁵ Testosterone replacement in men is less studied; some small studies demonstrate increased BMD, but long-term benefits are unknown.⁶

Raloxifene and calcitonin have some supporting evidence as well. In a large 4-year placebo-controlled trial, raloxifene decreased vertebral fracture risk (RR = 0.7; 95% CI, 0.5-0.8) but had no effect on hip fracture and a threefold increase in thromboembolic risk (RR = 3.1; 95% CI, 1.5-6.2).⁷ Regarding calcitonin, one RCT compared 3 doses of intranasal calcitonin and placebo in osteoporotic women and showed an increase in

lumbar spine BMD in treated groups.⁸ Over the 5-year study (59% of participants were lost to follow-up), there was a 39% reduction in risk of radiologic deformities ($P=.03$) only for women taking 200 IU.

Many subjects also used vitamin D and calcium, but effective doses of both agents are still in question. Combined calcium and vitamin D supplements have decreased fracture risk using 700 to 800 IU of vitamin D and 500 to 1200 mg of calcium daily,⁹ but a systematic review of vitamin D without calcium found no clear benefit.¹⁰ A meta-analysis showed that exercise training programs may play a preventive role, potentially preventing or reversing 1% of bone loss annually among women.¹¹ Smoking cessation may also increase bone density.¹²

■ RECOMMENDATIONS FROM OTHERS

The Royal College of Physician Guidelines on Osteoporosis Prevention and Treatment gives HRT an A grade of recommendation for preventing spinal fractures and a B grade for nonvertebral fracture prevention, while alendronate and risedronate received an A grade for both vertebral and nonvertebral fracture prevention. The American Association of Clinical Endocrinologists (AACE) states that HRT is the standard of care for preventing and treating postmenopausal bone loss but supports the use of bisphosphonates as an alternative. The US Preventive Services Task Force emphasizes smoking cessation, regular exercise, and adequate calcium intake, and recommends discussion with patients of the risks and benefits of HRT.

CLINICAL COMMENTARY

Sang-Ick Chang, MD

University of California San Francisco

It is very helpful to have bisphosphonates as a proven alternative to HRT, in cases where HRT is declined or not indicated. This review confirms what most of us have been doing in clinical practice: relying on HRT and bisphosphonates as the 2 preferred prescription medications for osteoporosis, relegating calcitonin to rare situations. Two difficult issues remain in the approach to osteoporosis, which are the dilemmas of who to screen and when to add a second agent.

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