Therapy Prevents Bone Loss Over Long Term

Ravn P, Bidstrup M, Wasnich RD, Davis JW, McClung MR, Balske A, et al. Alendronate and estrogen-progestin in the long-term prevention of bone loss: four-year results from the early postmenopausal intervention cohort study. A randomized, controlled trial. Ann Intern Med 1999;131:935–42.

Study Overview

Objective. To determine if the effect of alendronate on bone loss is sustained at 4 years of treatment and persists after treatment is discontinued.

Design. Randomized controlled trial.

Setting and participants. 1609 healthy women aged 45 to 59 years and at least 6 months past menopause. Participants were seen at 2 centers in the United States (Portland, Oregon, and Honolulu, Hawaii) and 2 centers in Europe (Nottingham, England, and Copenhagen, Denmark).

Intervention. Subjects were randomized to receive oral alendronate, 5 mg/day or 2.5 mg/day; placebo; or open-label estrogen-progestin. Women in the placebo and estrogen-progestin groups followed the same regimen throughout the 4-year study. Women in the alendronate groups received alendronate for the first 2 years and then either continued without change or received placebo for the last 2 years of the study.

Main outcome measures. Annual measurement of bone mineral density, assessed on an intention-to-treat basis.

Main results. By year 4, the bone density of participants in the placebo group had decreased by 1% to 6% ($P < 0.001$). Four years of treatment with 5 mg of alendronate per day increased bone mineral density at the spine (mean change, 3.8% ± 0.3%), hip (mean, 2.9% ± 0.2%), and total body (mean, 0.9% ± 0.2%) ($P < 0.001$ overall). By year 4, bone mineral density at most skeletal sites was greater in participants who switched from alendronate to placebo than in those who continuously received placebo. In years 3 and 4, bone loss in participants who switched from alendronate to placebo was similar to that seen during years 1 and 2 in those who continuously received placebo. Compared with 5 mg of alendronate per day, estrogen-medroxyprogesterone acetate produced similar increases in bone mineral density, whereas estradiol-norethisterone acetate produced substantially greater increases.

Conclusion

A 4-year regimen with alendronate or estrogen-progestin prevented postmenopausal bone loss. Four years of continuous alendronate treatment was more effective than 2 years of alendronate followed by 2 years of placebo, although a positive residual effect was observed 2 years after alendronate therapy was stopped.

Commentary

Osteoporosis leads to substantial morbidity and disability, increased health care utilization and costs, and reduced patient quality of life [1]. Alendronate has been shown to be an effective alternative to estrogen-progestin in preventing postmenopausal osteoporosis [2,3]. However, the optimal regimens (including length of treatment) for these preventive agents have yet to be established.

The current study illustrates the potential value of bone loss treatment, specifically that involving alendronate. Alendronate regimens of 2 and 4 years both achieved the objective of maintaining bone mass in postmenopausal women who were neither osteoporotic nor osteopenic. In addition, drug safety and patient tolerability were not a problem in women who persisted with a 4-year alendronate regimen, and bone mineral density increased significantly compared with participants who switched to placebo after 2 years.

Applications for Clinical Practice

Because bone mineral density is associated with susceptibility to fractures, effective treatments to maintain bone mass can provide protection against disabling injuries that lead to poor clinical, economic, and quality-of-life outcomes. Physicians should emphasize to patients that persisting with long-term bone loss therapy will result in long-term health benefits.

"Outcomes Research in Review" is edited by Chris L. Pashos, PhD, Vice President and Executive Director of Pharmacoeconomics and Outcomes Research, Abt Associates Clinical Trials, Cambridge, MA, and Associate Editor, Health Policy, Journal of Clinical Outcomes Management. *Dr. Pashos selects, summarizes, and provides the commentary on the studies that appear in this section.*

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