**Effect of Sequential and Daily Continuous Hormone Replacement Therapy on Indexes of Mineral Metabolism**

Ghada El-Hajj Fuleihan, MD; Edward M. Brown, MD; Kate Curtis; Merle J. Berger, MD; Barry M. Berger, MD; Ray Gleason, PhD; Meryl S. LeBoff, MD


**Abstract**

Background
Continuous regimens of estrogen-progesterone have recently been favored over sequential regimens because of a lower incidence of withdrawal bleeding. To determine whether the beneficial effects of sequential hormonal therapy on bone metabolism are preserved with the newer continuous regimens, we studied indexes of skeletal metabolism and changes in bone mineral density during a 1-year prospective trial.

Methods

Our subjects were randomized to one of three treatment groups: those in group C-2.5 were treated with 0.625 mg of conjugated estrogen with 2.5 mg of micronized medroxyprogesterone acetate daily continuously; group C-5 received 0.625 mg of conjugated estrogen and 5.0 mg of micronized medroxyprogesterone acetate daily continuously; and group S-5 received 0.625 mg of conjugated estrogen on days 1 through 25 and 5 mg of micronized medroxyprogesterone acetate on days 14 through 25.

Results.—
At 1 year, all groups demonstrated a significant decrease in indexes of bone formation turnover, including decrements in alkaline phosphatase levels of 11% to 30% and in osteocalcin levels of 45% to 60%. Intact parathyroid hormone levels rose 10% to 20%, with a concomitant near-significant decrement in ionized calcium levels at 12 months. In addition, there were significant decrements in the 24-hour urinary calcium-creatinine ratios and hydroxyproline-creatinine ratios of 13% to 28%, measures of bone resorption. Linear regression analyses showed that the subjects with the high bone resorption achieved the greatest increment in bone mineral density in response to hormone therapy.

Conclusion

The daily continuous estrogen-progesterone regimens are as efficacious as sequential hormonal therapy in decreasing indexes of bone turnover and stabilizing bone mineral density of the spine and proximal femur.

*(Arch Intern Med. 1992;152:1904-1909)*
Author Affiliations

From the Endocrine-Hypertension Division (Drs El-Hajj Fuleihan, Brown, Gleason, and LeBoff and Ms Curtis), the Department of Pathology (Dr B. Berger), and the Department of Obstetrics and Gynecology (Dr M. Berger), Brigham and Women's Hospital, Boston, Mass.

Footnotes

Accepted for publication January 24, 1992.


Reprint requests to Endocrine-Hypertension Division, Brigham and Women's Hospital, 221 Longwood Ave, Boston, MA 02115 (Dr El-Hajj Fuleihan).