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Cyclic medroxyprogesterone treatment increases bone density: A controlled trial in active women with menstrual cycle disturbances

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Abstract

OBJECTIVE: Bone loss occurs in young women who experience amenorrhea or ovulatory disturbances. The purpose of this study was to determine whether bone loss could be prevented by stimulating a more normal hormonal pattern, using treatment with cyclic medroxyprogesterone, with or without calcium supplementation, in physically active women with disturbed menstruation.

DESIGN: This study was a 1-year randomized, double-blind, placebo-controlled trial. Women who were stratified by menstrual cycle disturbance were randomized into four groups. The outcome variable was the change in spinal bone density measured by dual

g. paper. The outcome variable was the change in spinal bone density, measured by dual-energy techniques.

SETTING: A large metropolitan area.

PARTICIPANTS: Sixty-one healthy, normal-weight physically active premenopausal women aged 21 to 45 years who experienced amenorrhea, oligomenorrhea, anovulation, or short luteal phase cycles completed the study.

INTERVENTION: Therapies were cyclic medroxyprogesterone (10 mg/day for 10 days per month) and calcium carbonate (1,000 mg/day of calcium) in four groups: (A) (n = 16) cyclic medroxyprogesterone plus calcium carbonate; (B) (n = 16) cyclic medroxyprogesterone with calcium placebo; (C) (n = 15) placebo medroxyprogesterone with active calcium; or (D) (n = 14) both medroxyprogesterone and calcium placebos.

RESULTS: The initial bone density (mean = 1.12 g/cm²) did not differ by group ($P = 0.85$). The 1-year bone density change was strongly related to treatment with medroxyprogesterone ($P = 0.0001$) and weakly to calcium ($P = 0.072$) treatment. Bone density increased significantly (+1.7% $\hat{\pm}$ 0.5%, $\hat{\pm}$ SEM, $P = 0.004$) in the medroxyprogesterone-treated groups (A and B), did not change in the calcium-treated group (C) ($\hat{\pm}$ 0.7% $\hat{\pm}$ 0.6%, $P = 0.28$), and decreased on both placebos (D) ($\hat{\pm}$ 2.0% $\hat{\pm}$ 0.6%, $P = 0.005$).

CONCLUSIONS: Cyclic medroxyprogesterone increased spinal bone density in physically active women experiencing amenorrhea or ovulatory disturbances.

POTENTIAL CLINICAL SIGNIFICANCE: Amenorrhea, oligomenorrhea, anovulation, and short luteal phase cycles are common in premenopausal women and associated with spinal bone loss occurring at a stage of life when bone density would normally be stable or increasing. This controlled trial shows a significant gain in bone in women in the cyclic medroxyprogesterone intervention group, whereas those subjects in the placebo group lost bone. Calcium supplementation appeared to be helpful but did not reach statistical significance. The implications of these findings for the prevention of osteoporosis warrant further investigation.



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