Effects of genistein and hormone-replacement therapy on bone loss in early postmenopausal women: a randomized double-blind placebo-controlled study.


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The natural isoflavone phytoestrogen genistein has been shown to stimulate osteoblastic bone formation, inhibit osteoclastic bone resorption, and prevent bone loss in ovariectomized rats. However, no controlled clinical trial has been performed so far to evaluate the effects of the phytoestrogen on bone loss in postmenopausal women. We performed a randomized double-blind placebo-controlled study to evaluate and compare with hormone-replacement therapy (HRT) the effect of the phytoestrogen genistein on bone metabolism and bone mineral density (BMD) in postmenopausal women. Participants were 90 healthy ambulatory women who were 47-57 years of age, with a BMD at the femoral neck of <0.795 g/cm2. After a 4-week stabilization on a standard fat-reduced diet, participants of the study were randomly assigned to receive continuous HRT for 1 year (n = 30; 1 mg of 17beta-estradiol [E2] combined with 0.5 mg of norethisterone acetate), the phytoestrogen genistein (n = 30; 54 mg/day), or placebo (n = 30). Urinary excretion of pyridinoline (PYR) and deoxypyridinoline (DPYR) was not significantly modified by placebo administration either at 6 months or at 12 months. Genistein treatment significantly reduced the excretion of pyridinium cross-links at 6 months (PYR = -54 +/- 10%; DPYR = -55 +/- 13%; p < 0.001) and 12 months (PYR = -42 +/- 12%; DPYR = -44 +/- 16%; p < 0.001). A similar and not statistically different decrease in excretion of pyridinium cross-links was also observed in the postmenopausal women randomized to receive HRT. Placebo administration did not change the serum levels of the bone-specific ALP (B-ALP) and osteocalcin (bone Gla protein [BGP]). In contrast, administration of genistein markedly increased serum B-ALP and BGP either at 6 months (B-ALP = 23 +/- 4%; BGP = 29 +/- 11%; p < 0.005) or at 12 months (B-ALP = 25 +/- 7%; BGP = 37 +/- 16%; p < 0.05). Postmenopausal women treated with HRT had, in contrast, decreased serum B-ALP and BGP levels either at 6 months (B-ALP = -17 +/- 6%; BGP = -20 +/- 9%; p < 0.001) or 12 months (B-ALP = -20 +/- 5%; BGP = -22 +/- 10%; p < 0.001). Furthermore, at the end of the experimental period, genistein and HRT significantly increased BMD in the femur (femoral neck: genistein = 3.6 +/- 3%, HRT = 2.4 +/- 2%, placebo = -0.65 +/- 0.1%, and p < 0.001) and lumbar spine (genistein = 3 +/- 2%, HRT = 3.8 +/- 2.7%, placebo = -1.6 +/- 0.3%, and p < 0.001). This study confirms the genistein-positive effects on bone loss already observed in the experimental models of osteoporosis and indicates that the phytoestrogen reduces bone resorption and increases bone formation in postmenopausal women.