Natural Estrogen Helps Build Bone Mass As Well As Reduce Bone Turnover!

Prestwood KM, Kenny AM, Kleppinger A, Kulldorff M. *Ultralow-dose micronized 17beta-estradiol and bone density and bone metabolism in older women: a randomized controlled trial.* JAMA 2003 Aug 27;290(8):1042-8

Center on Aging, University of Connecticut Health Center, Farmington 06030, USA. Prestwood@nso1.uchc.edu

CONTEXT: Estrogen therapy is known to prevent osteoporosis, but studies have shown that conventional doses increase adverse events. Whether lower doses, one quarter of standard treatment, prevent bone loss is not known. OBJECTIVE: To examine the effect of 3 years of treatment with 0.25 mg/d of micronized 17beta-estradiol on bone mineral density (BMD) and bone turnover in healthy older postmenopausal women.

DESIGN, SETTING, AND PARTICIPANTS: Randomized,double-blind, placebo-controlled trial conducted from July 24, 1998, through June 14, 2002, at a university general clinical research center in the United States. Healthy, community-dwelling women (N = 167) who were older than 65 years at enrollment.

INTERVENTION: Dosage of 0.25 mg/d of micronized 17beta-estradiol (n = 83) or placebo (n = 84); all women who had not had a hysterectomy received 100 mg/d of oral micronized progesterone for 2-week periods every 6 months.

MAIN OUTCOME MEASURES: The BMD of the hip, spine, wrist, and total body measured annually for 3 years. Serum and urine biochemical markers of bone resorption and formation and sex hormones were measured at baseline, 3 months, and during years 1 and 3 of treatment.

RESULTS: Mean BMD increased at all sites for participants taking low-dose estrogen (17beta-estradiol) compared with placebo (P<.001). Compared with participants receiving placebo, participants taking low-dose estrogen had BMD increases of 2.6% for the femoral neck; 3.6%, total hip; 2.8%, spine; and 1.2%, total body. Markers of bone turnover, N-telopeptides of type 1 collagen, and bone alkaline phosphatase decreased significantly (P<.001) in participants taking low-dose estrogen compared with placebo. Estradiol, estrone, and sex hormone-binding globulin levels increased in the estrogen-treated group compared with placebo. The adverse effect profile was similar; specifically, there were no statistically significant differences in breast tenderness, changes in endometrial thickness or pathological effects, or annual mammographic results between the 2 groups. The number of abnormal mammograms over 3 years was 15 for the low-dose estrogen group and 10 for the placebo group (8 occurred at baseline) (P =.26). There were no reports of breast cancer during the study.

CONCLUSIONS: In older women, a dosage of 0.25 mg/d of 17beta-estradiol increased bone density of the hip, spine, and total body, and reduced bone turnover, with minimal adverse effects. Future studies evaluating the effect of low-dose estrogen on fractures are indicated.