Ultralow-Dose Estrogen and its effects on Bone Density and Bone Metabolism in Older Women  Karen M. Prestwood, MD; Anne M. Kenny, MD; Alison Kleppinger, MS; Martin Kulldorff, PhD

Introduction  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.

Purpose  To examine the effect of 3 years of treatment with low dosage of estrogen on bone mineral density (BMD) and bone turnover in healthy older postmenopausal women.

Methods  A group of 167 healthy, community-dwelling women over 65 years old were randomly divided into two groups. The first group (n = 83) was given a low dose of estrogen daily for three years (conducted from July 24, 1998, through June 14, 2002); the second group (n = 84) was given a sugar pill daily for the same time period. Neither patients, nor researchers knew the content of pre-packaged, numbered medication until the end of the third year.

The bone density (calcium phosphate content) of the hip, spine, wrist, and total body was 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 bone density increased at all sites for participants taking low-dose estrogen (17β-estradiol) compared with placebo. The probability that this result occurred due to chance alone (coincidence) is less than one tenth of one percent (or < 0.1%). Compared with participants receiving placebo, participants taking low-dose estrogen had increased bone density of 2.6% in the femoral neck (narrowest portion of hip joint); 3.6% higher bone density in the total hip; 2.8% higher in the spine; and 1.2% higher in the total body.

Markers of bone turnover decreased significantly (P< .001) in participants taking low-dose estrogen compared with placebo. Estrogen derivatives and sex hormone–binding protein levels increased in the estrogen-treated group compared with placebo. There were no statistically significant differences in breast tenderness, changes in endometrial thickness or pathological (disease) effects. There were no reports of breast cancer during the study.

Conclusions  In older women, a dosage of 0.25 mg/d of 17β-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 recommended.

Write a hypothesis that can be tested with this experiment by filling in the blanks below:

A. There is a significant difference in the ________________________________
   (dependent variable)

B. in older ____________________________________________________________
   (experimental subjects)

C. treated with ________________________________________________________
   (independent variable)
   compared to older women without treatment.

2. What was the control group?

3. What was the sample size?

4. What random variables may have affected the results?

5. How could you improve this experiment?

6. Was the hypothesis supported or falsified by the data?