The relationship between plasma estradiol and the increase in bone density in postmenopausal women after treatment with subcutaneous hormone implants

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Twenty-three postmenopausal women with a median of 2 years past menopause (range, 1 to 12 years) and a median age of 52 years (range, 39 to 62 years) were recruited to participate in a longitudinal study designed to investigate the factors that influence the increase in bone density with subcutaneous estradiol and testosterone implants. All women received 75 mg of estradiol with 100 mg testosterone subcutaneously. Bone density was measured at the spine and hip by dual-photon absorptiometry before therapy and after 1 year of subcutaneous hormonal therapy. The mean pretreatment bone density at the lumber vertebrae and neck of the femur was 0.84 grams of hydroxyapatite per square centimer (SD, 0.11) and 0.73 grams of hydroxyapatite per square centimeter (SD, 0.10), respectively. The bone density at both sites increased with values of 0.91 grams of hydroxyapatite per square centimeter (SD, 0.11) and 0.75 grams of hydroxyapatite per square centimeter (SD, 0.11), respectively. These values represent an increase of 8.3% ($p < 0.0001$) at the spine and 2.8% ($p < 0.01$) at the neck of the femur. The plasma estradiol level increased from a median of 80.5 pmol/L to 453 pmol/L ($p < 0.001$). The percentage increase of vertebral bone density was not related to age, number of years past the menopause, pretreatment bone density, or serum testosterone levels, but a significant correlation was found between the percentage increase in bone density at the spine and the serum estradiol level ($p < 0.02$, $r = 0.45$).
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Key words: Osteoporosis, menopause, estradiol

After Albright's[1] observation that estrogen therapy can reduce urinary calcium excretion in postmenopausal women a number of prospective studies confirmed the values of estrogen replacement therapy in the prevention of postmenopausal osteoporosis.[2-4] Epidemiologic studies[5, 6] also showed a reduction in the incidence of osteoporotic fractures with such therapy.

Most studies used oral estrogen therapy, which although effective in the suppression of climacteric symptoms usually results in plasma estradiol and follicle-stimulating hormone (FSH) levels that are still in the postmenopausal range.[7] Although it has been claimed that the minimum dose of oral estrogen required to prevent postmenopausal osteoporosis is 0.625 mg conjugated equine estrogen[8] the optimal dose and route of estrogen necessary to achieve an increase in bone density is not known.

The percutaneous route of administration avoids the enterohepatic circulation and is associated with physiologic plasma levels of estradiol and estrone. This is in contrast to the low levels of estradiol and high levels of estrone found after oral therapy with both conjugated equine estrogens or estradiol valerate.[9, 10] Subcutaneous implants of estradiol and testosterone are effective in the alleviation of climacteric symptoms,[11] and a cross-sectional study[12] showed an apparent superiority of implant therapy over oral therapy in the therapeutic effect on bone density. The suggestion was made in this study that the greater bone density after implant therapy was a result of the greater plasma estradiol levels achieved with this route when compared with oral estrogen therapy.

We present the results of a prospective study of estradiol and testosterone implants on the bone density and plasma hormone levels in postmenopausal women over 1 year of therapy.

Patients and methods

A total of 23 postmenopausal women with a median age of 52 years (range, 39 to 62) were recruited into

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