

Good article
on ↑ Bone density &
↓ Cardiovascular
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Metabolic and Hormonal Effects of 25-mg and 50-mg 17 β -Estradiol Implants in Surgically Menopausal Women

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A prospective study involving 12 surgically menopausal women was undertaken to determine whether 17 β -estradiol pellets could maintain bone mineral content without inducing adverse cardiovascular side effects. Surgically menopausal women were randomly selected to have either 25-mg or 50-mg pellets implanted subcutaneously. The bone mineral content of the midshaft of the nondominant radius in the combined group—measured by single photon absorptiometry—increased by 1.8% over the two-year period of observation ($P < .03$); the distal bone mineral content of the radius was maintained at 0.8% per annum. No adverse effects were noted in the coagulation profiles or in the coagulation inhibition and fibrinolysis assays of both groups. Serum high-density lipoprotein cholesterol and triglycerides were unaltered, but serum cholesterol values decreased during the six-month period of observation by 14 mg/dL ($P < .05$) and 11 mg/dL in the 25- and 50-mg groups, respectively. Carbohydrate and insulin metabolism was unaffected, as was the systolic and diastolic blood pressure. There were no significant intergroup differences in any of the parameters measured. The serum estradiol/estrone ratios of 1.45 and 1.59 reflected a physiologic estrogen milieu at the 25- and 50-mg dosages. Subcutaneous 17 β -estradiol pellets can effectively maintain the bone mineral content of surgically menopausal women without inducing adverse cardiovascular side effects. (*Obstet Gynecol* 70:749, 1987)

Women who experience a premature surgical menopause are at increased risk of developing osteoporosis and atherosclerotic cardiovascular disease. Long-term estrogen replacement therapy has been shown to lessen the risk of menopause-related osteoporosis¹ and, according to some, cardiovascular disease.^{2,3} The beneficial effect on the conservation of bone mass is lost rapidly in surgically menopausal women once estrogen therapy is

stopped.⁴ In addition, orally administered estrogen is associated with alterations in biologic parameters, such as plasma renin substrate and coagulation factors, that may predispose some women to hypertension and other cardiovascular-related complications.⁵ The need for a method to ensure long-term compliance and safety is thus self-evident. Subcutaneous estradiol implants have the potential advantage of achieving patient compliance because they must be administered by a physician, usually at four- to six-month intervals. Irregular hormonal usage or noncompliance can thus be monitored easily. Furthermore, this form of therapy bypasses the enterohepatic circulation, thus avoiding the induction of hepatic factors that may have a negative effect on the cardiovascular system.

Subcutaneous 17 β -estradiol pellets have proved effective in the management of the symptomatic menopause.⁶ However, there are very few data to document that they are as effective for the preservation of bone mass, the most important indication for long-term estrogen therapy in the menopause. The following study posed four questions: 1) Is parenterally administered 17 β -estradiol effective in maintaining the bone mineral content of surgically menopausal women? 2) What effect has this route of administration on cardiovascular-related parameters: blood pressure, lipids and lipoproteins, coagulation and anticoagulation factors, and glucose and insulin metabolism? 3) Do the therapeutic and potential side effects of 25 mg of 17 β -estradiol vary significantly from those associated with a 50-mg dosage? 4) Are the hormonal levels obtained by this method compatible with a "physiologic" approach to estrogen replacement therapy?

Materials and Methods

Twelve women who had each had a total hysterectomy and bilateral salpingo-oophorectomy for benign dis-

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