ULTRASOUND BONE DENSITOMETRY AND 2-YEAR HORMONAL REPLACEMENT THERAPY EFFICACY IN THE PREVENTION OF EARLY POSTMENOPAUSAL BONE LOSS

R.Giorgino, D.Lorusso, P.Paparella
Dpt.Obstet.Gynaecol., Catholic University, Rome

To our knowledge, few data are available concerning the outcome of a therapeutic regimen on ultrasound bone densitometry parameters. The purpose of this study was to evaluate the effects of a two-year transdermal estrogen replacement therapy on ultrasonic bone parameters. Forty-four healthy postmenopausal women with intact uterus (aged 46-57 years, time since last menstruation 1-4 years) were given continuously 50 µg transdermal estradiol daily together with an oral progestin for 10 to 12 days in each month [group *T*]. Ultrasound bone parameters (ultrasonic velocity, SOS; attenuation slope, BUA; Stiffness Index, STF) were measured at the right calcaneus in each patient at 6-month intervals for 2 years. At the same time, a group of 47 healthy chronological and menopausal age-matched women were evaluated as controls [group *C*]. Results are shown below:

Month		0	6	12	18	24
BUA	T	109.9	110.9	111.8$	112.2$ †	112.4$ †
	C	111.8	111.3	110.5	109.5**	108.2$ † ¶
SOS	T	1531.5	1534.0$	1535.9$ †	1536.9$ †	1537.4$ † ¶
	C	1526.0	1525.1	1523.7	1523.0*	1521.2$ †
STF	T	82.5	83.8$	85.0$ †	85.5$ †	85.8$ † ¶
	C	82.2	81.6	80.7*	79.8$ †	78.5$ † ¶

Scheffe test: * p<0.05 ** p<0.01 $ p<0.001 vs baseline; † p<0.01 ¶ p<0.001 vs month 6; ¶ p<0.01 vs month 12.

In conclusion, HRT determined significant and progressive increases in calcaneus ultrasound parameters over 2 years in normal early postmenopausal women. Thus, estrogens likely produce a positive effect both on bone mass and quality.

PTu569

A RANDOMIZED STUDY OF THE EFFECT ON BONE MASS OF THERAPY WITH EITHER GESTRINONE, TRIPTORELIN OR COMBINED THERAPY IN ENDOMETRIOSIS.

Devogelaer JP, Donnez J, Nagant de Deuxchaisnes C. Department of Rheumatology and Gynecology, St-Luc University Hospital, Brussels, Belgium.

LHRH agonists induce an acute bone loss. Alternative therapies are therefore needed.In a 16-week randomized study of 65 premenopausal women (A 29.7 ± 0.6) with endometriosis, we have compared the effect on bone of decapeptyl (D)(3.75 mg IM every 4 weeks; n = 22), gestrinone (G), an anti-estrogen antigonadotropin (G 2.5 mg orally thrice weekly; n = 23), or a combined therapy (D+G; n = 23). Most of them were reseen after 16 weeks, and a therapy-free 6-month period. The bone mass of the lumbar spine (L-BMD), of the upper extremity of the femur (total hip), and of the total body (head excluded) and the body composition were measured with a QDR-1000 W (Hologic, Inc)(see Table).

Bone changes (%) after 16 weeks of therapy, and after 6 months off therapy

		L-BMD	Total hip	Total body	Lean tissue
D	+ 16 weeks	- 4.2	- 3.3	- 2.8	- 2.3
	p :	< 0.05	< 0.05	< 0.05	< 0.05
	+ 6 mo.	- 3.1	- 2.6	- 2.3	+ 0.4
D	+ 16 weeks	- 3.8	- 1.0	- 0.8	+ 5.7
+	p :	< 0.05	NS	NS	< 0.05
G	+ 6 mo.	- 1.3	- 1.5	+ 1.1	+ 3.6
G	+ 16 weeks	- 1.2	- 0.3	- 0.3	+ 11.0
	p :	< 0.05	< 0.05	< 0.05	< 0.05
	+ 6 mo.	- 0.7	- 0.3	+ 1.5	+ 3.5

Fasting urinary Ca and hydroxyproline/creat ratios increased while on D but decreased while on G or D + G therapy. In conclusion, like other LH-RH agonists, D provoked not only a dramatic bone loss at the lumbar spine, but also at the hip as well as at the total body, implying that cortical bone could also be threatened by such therapy. With G, a marginal bone loss was observed only at the spine, the bone mass of the hip and total body was respected. Moreover, the effect of G on body composition demonstrated an anabolic effect, i.e., a decrease in fat content and an increase in lean tissue. Combined therapy behaved intermediately. In conclusion, G, whether alone or combined with D, could constitute an alternative in the treatment of endometriosis, as far as bone preservation is concerned.

PTu570

THE EFFECT OF PERCUTANEOUS ESTRADIOL ON POSTMENOPAUSAL BONE LOSS.

LP. Devogelaer, C. Lecart, C. Nagant de Deuxchaisnes. Departments of Rheumatology and Gynecology, St-Luc University Hospital, B-1200 Brussels, Belgium.

Percutaneous estradiol (PE2) at a dose of 3 mg/d abolishes postmenopausal (PM) bone loss. The effect of the usually recommended dose of 1.5 mg/d PE2 was assessed in hysterectomized (H) patients, to avoid progestogens which can interfere with bone metabolism. 39 PMH women were treated for 2 years in a double-blind study either by PE2 (1.5 mg/d) + estriol (E3) placebo (P) (n = 19) or by PE2 P + E3 (2 mg/d) orally (n = 20). Patients' characteristics were similar in both groups. Lumbar (L)-BMD and proximal femur-BMD were measured every 3 months by DXA on a QDR-1000 from Hologic, Inc. During PE2 therapy, E2 and E1 increased significantly up to 86 ± 16 and 85±11 pg/ml, respectively($p < 0.001$). In the E3 group, these values did not change. L-BMD increased significantly ($p < 0.05$) by 1.2 ± 0.5 %/year in the PE2 group versus a loss of 1.2 ± 0.4 %/year ($p < 0.01$) in the E3 group. The difference between both groups was significant ($p < 0.001$). At the total hip, no significant change was observed in the PE2 group, versus a significant loss of 1.3 ± 0.3 %/year ($p < 0.001$) in the E3 group (PE2 vs E3 group; $p < 0.05$). The urinary excretion of pyridinium crosslinks decreased significantly in the PE2 group but did not change in the E3 group. There was a positive correlation between serum E1 and E2 and the slopes of L-BMD ($r = 0.42$; $p < 0.01$ and $r = 0.46$; $p < 0.01$, respectively). In conclusion, E3 (2 mg/d) cannot counteract bone loss as it is well-known. PE2 (1.5 mg/d) administered as a gel protects against PM bone loss both at the lumbar spine and at the hip. This convenient and well-tolerated way of E2 administration constitutes an alternative to transdermal E2.

PTu571

FACTORS INFLUENCING RESPONSE TO HORMONE REPLACEMENT THERAPY (HRT).

J. Symons, J. Rowan, Parke-Davis Pharmaceutical Research/Division of Warner-Lambert Co., Ann Arbor, MI, and H. Genant, University of California-San Francisco, San Francisco, CA

We have demonstrated that continuous daily administration of ethinyl estradiol (EE) and norethindrone acetate (NA) in various dose combinations (0.5 mg NA/ 2.5 µg EE, 1/5, and 1/10) maintained or increased lumbar spine bone mineral density (BMD) compared to placebo or dose matched unopposed EE. The NA/EE combinations prevented endometrial proliferation and hyperplasia, while having no deleterious lipid effects. The purpose of this analysis was to determine whether there were differences in baseline characteristics that could affect the response to HRT. A total of 1265 women at 65 study sites enrolled in this double-blind, placebo-controlled, randomized clinical trial. Lumbar spine BMD was measured at baseline and after 12 and 24 months of treatment using quantitative computed tomography (QCT). At enrollment each woman reported the date of her LMP, level of physical activity, and cigarette smoking history. At the end of the study the treatment groups were stratified for each of the measures to determine if there were differences in treatment response. Results indicated that women $\geq$ 2.5 years since menopause had lower baseline BMD and responded to lower doses of HRT compared to women < 2.5 years postmenopause. No association was found between baseline physical activity level and baseline BMD or response to treatment. While there were no consistent baseline BMD differences between smoking categories, women who had never smoked responded to NA/EE at lower doses compared to past or present smokers. Considering the prevention and treatment of osteoporosis, these results have implications for treatment and lifestyle change recommendations.

PTu572