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THE EFFECTS OF SHORT-TERM ERT ON COGNITIVE PERFORMANCE IN NATURALLY POSTMENOPAUSAL WOMEN

W J Woodruff, S L Thomas, B A Karlan, A J Rapkin,
UCLA School of Medicine, Department of Gynecology, Center for the Health Sciences, Rm 22-188, 10833 Le Conte Avenue, Los Angeles, CA 90095-1740

The short-term use of transdermal estrogen was examined in 12 naturally postmenopausal women in a crossover design to test the hypothesis that ERT use enhances cognitive performance in memory efficiency and executive function. Plasma samples (x3) were collected at baseline (with assessments of mood, personality, cognitive difficulties) as well as after 14-days of ERT or placebo (with cognitive testing) followed by 14-days of placebo or ERT (with cognitive retesting). To qualify Ss were: 1) 12-mos into natural menopause (serum FSH >40mIU/ml, estradiol (E2 <20 pg/ml), 2) no ERT use within past 12-mos, 3) no severe vasomotors (hot flashes, HA, night sweats, sleep/mood disorders), 4) nonsmoker on no meds, 5) no major medical problems (CVD, diabetes, renal/liver disease, thyroid or clotting disorders, obesity, CA or abnormal uterine bleeding). The groups differed on trait anxiety $t(5,5)=2.94$, $p<.01$ and age $t(5,5)=-2.69$, $p<.02$. The AB group was more anxious at the time of testing and younger. No overall treatment effect was found for ERT use on verbal learning & memory (CVLT) and cognitive flexibility (seriation judgment-reasoning tasks contained in the timed Color Trails and Stroop Color-Word Interference Test). Practice effects were seen in the CVLT, Color Trails 2, & Digit Span retests. +ERT impact may be suggested by periodicity analyses (treatment+practice) wherein the majority (86.5%) of significant effects in 2 sample *t*-tests were seen in the placebo-ERT (BA) Ss as compared to 13.5% in ERT-placebo Ss (AB) group.

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BONE MINERAL DENSITY (BMD) AT LUMBAR SPINE AND FEMORAL NECK IN HYSTERECTOMISED WOMEN TREATED WITH CHRONIC OESTRADIOL IMPLANTATION.

D W Purdie, P A Ballard, M Wahab, A Cooper,
J C Willson, Centre for Metabolic Bone Disease, Royal Hull Hospitals Trust and University of Hull, UK.

The provision of hormone replacement therapy (hrt) by subcutaneous oestradiol implant is a recognised treatment of the hysterectomised and oophorectomised patient. The chronic effects of implanted estrogen upon bone mass are poorly understood. We report the bone mineral density (BMD) findings on a precisely defined group of 12 hysterectomised/ ophorectomised women who had received 100 mg Estradiol s.c., on demand, for 15-21 years. None had received Testosterone or any other agent known to influence bone or mineral metabolism. The mean delivered dose of E2 was 135 mg/year and group mean plasma E2 at the time of densitometric assessment was 1355 pmol/L. At the spine, the T score (T=No. of SD from young normal mean) was +2.03, (95% CI 0.76-3.29). This value is +17.8% above the young adult mean and the mean BMD difference is significant ($P<0.001$). At the femoral neck, the group exhibited a T score of +1.08 (95% CI 0.44-1.72) which was 13.3% above young adult mean ($P<0.01$). Corresponding Z scores where the patients were compared with age-matched controls were, at spine and hip, Z = +2.23 and +3.39 respectively. We conclude that bone gain in implanted women is substantial and progressive and results in BMD values comparable to Peak Density in young adults.

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3 YEARS PREVENTION OF POSTMENOPAUSAL BONE LOSS: CONJUGATED ESTROGEN-MEDROXYPROGESTERONE VS TIBOLONE

D.Thiébaud, JM Bigler, Th. Pache, H.J. Welti, P. Burckhardt.
Department of Internal Medicine. Department of Obstetric and Gynecology, University Hospital, CHUV, 1 01 1 Lausanne, Switzerland.

Introduction: Postmenopausal bone loss can be prevented by combined estrogen-progestagen replacement therapy (HRT). Tibolone (Livial^{R}) is a synthetic steroid related to norethynodrel and norethisterone with mixed estrogenic, progestogenic and mild androgenic activity, which does not stimulate endometrial proliferation and causes no bleedings.

Aim of the study: to investigate the efficacy of Tibolone on the prevention of post menopausal bone loss and to compare its efficacy with conventional sequential HRT over 3 yrs. 40 early postmenopausal women were randomly assigned to 0.625mg CEE (Premarin^{R}) plus 10mg MPA (Prodafem^{R}) in a 21/10 regimen : **group PP** (52±1 yrs; BMI ±25 kg/m^2; n=20 at 0m and n=12 at 36m) or 2.5 mg Tibolone daily : **group Tib** (53±1 yrs; BMI ±25, n=20 at 0m and n=11 at 36m). Bone mineral density (BMD) and biochemistry were measured at 0, 6, 12, 24 and 36 months, using DXA (Hologic QDR 2000) at the lumbar spine and the proximal femur. BMD results: g/cm^2 (mean ± SEM):

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F134 (cont)

Months	0	12	24	36	% (0-36)
Group PP					
BMD spine	0.95±0.03	0.96±0.03	0.96±0.03	0.95±0.04	**+ 1.9**
fem. neck	0.76±0.02	0.76±0.02	0.76±0.02	0.74±0.02	**+ 0.4**
total hip	0.87±0.02	0.87±0.02	0.88±0.02	0.86±0.02	**+ 0.4**
trochanter	0.65±0.02	0.67±0.02	0.67±0.02	0.66±0.02	**+ 2.6**
Group Tib					
BMD spine	0.88±0.03	0.90*±0.03	0.91**±0.02	0.91**±0.03	**+ 4.6**
fem. neck	0.74±0.02	0.74 ±0.02	0.75* ±0.02	0.75 ±0.03	**+ 1.6**
total hip	0.84±0.03	0.85 ±0.03	0.86**±0.03	0.87**±0.03	**+ 3.2**
trochanter	0.64±0.03	0.66*±0.03	0.66* ±0.02	0.68**±0.03	**+ 4.5**

* p<0,05,** p<0,01 in comparison with day 0 (Wilcoxon test)

Results: In both groups bone loss was prevented. However, contrary to PP treatment, Tibolone increased bone density significantly at the spine and the hip after 24 and 36 months. Between group differences was significant (Mann-Whitney test) at the trochanter and total hip.

IGF-1 and IGF-BP3 did not change over time in both groups. Osteocalcin decreased significantly in both groups from 21±2 µg/l to 12-15µg/l between 6 to 36 months. Urinary hydroxyproline and calcium decreased only in the Tib group. Reasons for drop out were non compliance in 11 patients (missing visits, moving, concurrent medications) and minor side effects in 5 patients.

In conclusion, Premarin-Prodafem prevented cortical and trabecular bone loss with no additional significant effect. Tibolone not only prevented bone loss but increased BMD over 3 years at both, the lumbar spine and the hip, which suggests a sustained positive effect on bone mass.