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Characteristics of Non-responders to 5-years of Hormone Replacement Therapy. The Danish Osteoporosis Prevention Study (DOPS). L. Rejnmark[1], P. Vestergaard[1], C. L. Tofteng*[2], N. Kolthoff*[3], L. S. Stilgren[4], K. Brixen[4], L. Mosekilde[1]. [1]Dept. of Endocrinology and Metabolism, Aarhus Amtssygehus, Aarhus, Denmark, [2]The Osteoporosis Research Centre, Hvidovre Hospital, Hvidovre, Denmark, [3]Dept. of Clinical Physiology and Nuclear Medicine, Hilleroed Hospital, Hilleroed, Denmark, [4]Dept. of Endocrinology, Odense University Hospital, Odense, Denmark.

A nested case control study was performed to characterize perimenopausal women not responding to hormone replacement therapy (HRT) with an increase in bone mineral density (BMD). In the Danish Osteoporosis Prevention Study (DOPS), 2016 women three months to two years after menopause were allocated to a HRT- (n=723) or to a control-group (n=1293). After 5-years, 543 women had been treated continuously with HRT. Among these, paired DEXA-scans had been performed at baseline and after five years in 466 women receiving HRT. We defined densitometric non-responders as women on HRT, who had a decrease in BMD over 5-years similar to or grater than the mean bone loss in the control group. Baseline characteristics were used as exposures. In the control group, femoral-neck and lumbar spine BMD decreased by 6.3±0.2% (mean±SD) and 6.4±0.2%, respectively. In the HRT group, 10.7% and 6.0% were classified as non-responders according to their changes in femoral-neck and lumbar spine BMD, respectively. 2.6% were classified as non-responders at both measurement sites. Baseline measures of body weight, age, BMD, daily calcium- and vitamin D intake, smoking status, and biochemistry (urinary hydroxyproline, bone-specific alkaline phosphatase, 25-hydroxyvitamin D) did not differ between responders and non-responders to HRT at the femoral-neck, lumbar spine, or at both sites. Thus, only a small proportion of perimenopausal women who begin HRT do not benefit from the treatment as assessed by DEXA. However, non-responders are difficult (impossible?) to identify at the time of initiation of treatment.

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51. **Osteoporosis Fracture Tracking Study: Medical Care Is Often Delayed for Patients of Orthopaedic Surgeons.** J. G. Skedros. Utah Bone and Joint Center; Dept of Orthop Surg, U of UT, Salt Lake City, UT, USA.

Patients with osteoporotic fractures typically do not receive subsequent medical treatment for osteoporosis. We hypothesized that even if patients with osteoporotic fractures were specifically referred to their primary care providers (PCPs), the majority would not be treated within 84 days (12 weeks) of fracture. We evaluated the effectiveness of 14 surgeons in facilitating a timely PCP visit for their patients. Participating orthopaedic surgeons received remuneration for each patient completing the study. Patients who qualified were >50 years old, had an apparent osteoporotic (low-energy) fracture, and had no prior treatment for osteoporosis. Two letters requesting a PCP appointment were sent: the first letter within 10 days of fracture, and the second letter 3-10 weeks after fracture. Patients were also: 1) informed that they may have osteoporosis and may be at risk for subsequent fracture, and 2) instructed to make a PCP appointment for possible further work-up and treatment. Results showed that of 55 patients (48 females, 7 males: avg. age 70.8, range 51-90), 23 (42%) were not seen by a PCP within 84 days. 32 (58%) patients saw a PCP within 84 days, but osteoporosis was not addressed in 4 patients (avg. days to PCP, 38: range 7-71days). Of patients seen within 84 days, pharmacologic treatment (e.g., estrogen, bisphosphonate, etc.) was started in 19 (59 %), but typically not within 37 days of fracture. Of the 14 participating orthopaedic surgeons, five were non-compliant and six were inconsistent in their participation, forgetting to send the letters and to inform their patients to make a PCP appointment. These results indicate that standing discharge hospital orders (for medications, PCP follow up, bone density scanning, etc.) may be more effective in achieving timely medical treatment for patients with osteoporotic fractures.

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Subsidizing Medications Does Not Ensure the Use of Potent Osteoporosis Drugs Following Low-Impact Fractures. Y. Liel*[1], H. Castel*[2], D. Y. Bonneh*[3]. [1]Endocrinology, Soroka Medical Center, Beer Sheva, Israel, [2]Medicine, Soroka Medical Center, Beer Sheva, Israel, [3]Southern District, Clalit Health Services, Beer Sheva, Israel.

Recently, potent anti-resorptive drugs (a bisphosphonate, and a SERM) were introduced into the National Health Basket in Israel for treatment of all osteoporotic women and for men with glucocorticoid-related osteoporosis. We carried out the present study to evaluate the effect of subsidizing osteoporosis drugs on the use of osteoporosis drugs in patients following low-impact fractures. Hospital charts of women and men age 50 and older with new fractures due to low or moderate impact treated in the emergency room (mostly peripheral bone fractures), orthopedic surgery and rehabilitation departments (mostly proximal-hip fractures), were reviewed. Notation of osteoporosis as contributing cause for the fracture, and treatment recommendations were abstracted from the records. In addition, we took advantage of the centralized pharmacy database of the largest health maintenance organization (HMO) in the area to follow dispensation of osteoporosis drugs in the community following fracture incidents. The cumulative data from the period of January and February of 2000 and 2001 ("post-basket") was compared with the cumulative data from January and February of 1998 and 1999 ("pre-basket"). Our results revealed a significant, approximately 2-fold increase in the baseline rate of dispensation of osteoporosis drugs between the pre- and post-basket periods. The rate of patients treated after a fracture incident also increased significantly 1.6 fold in the post-basket period. However, even in the post-basket period two-thirds of the patients remained untreated following a fracture incident and most of those treated received only calcium and vitamin D. Only about 15% received any of the potent osteoporosis drugs. Men were considerably less likely to be treated than women. In a univariate analysis, younger age, female gender, being treated in the emergency room, incident of fracture in the post-basket period and being treated for osteoporosis before the fracture incident, were significantly correlated with treatment following the fracture. In a multivariate model, age lost its effect and treatment before the fracture incident emerged as the far most influential variable. Subsidizing has a significant positive effect on osteoporosis drugs utilization. However, other factors are important. There is an ongoing need to increase awareness and encourage the use of potent pharmacological means for primary and secondary prevention of osteoporotic fractures.

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Phytoestrogen-Rich Herbal Formula For Prevention Of OVX Induced Bone Loss In Rats. L. Qin*[1], G. Zhang*[2], W. Y. Hung*[3], M. A. Dambacher[4], P. C. Leung*[5]. [1]Orthopaedics & Traumatology, Chinese University of Hong Kong, Hong Kong, Hong Kong Special Administrative Region of China, [2]Suguang Hospital, Shanghai University of Chinese Medicine, Shanghai, China, [3]Dept. of Orthopaedics and Traumatology, The Chinese University of Hong Kong, Hong Kong, Hong Kong Special Administrative Region of China, [4]University Clinic of Balgrist, Zurich, Switzerland, [5]Institute of Chinese Medicine, The Chinese University of Hong Kong, Hong Kong, Hong Kong Special Administrative Region of China.

The purpose of this animal experimental study was to investigate a phytoestrogen-rich herbal formula (genistein and daidzein at 250mAU) and calcium supplementation for prevention of OVX induced bone loss. In this study, tis phytoestrogen-rich herbal formula Xianlingubao (XLGB) with Epimedium Leptorhizum as the main component was developed and studied in 45 eleven-months old female Wistar rats, that were randomly grouped according to their body weight. These included one sham-operated (Sham) and four OVX subgroups, i.e. OVX along, OVX with XLGB, OVX with calcium, and OVX with HLGB and calcium (Table 1). Daily oral administration of XLGB (250 mg/kg) and/or element calcium (25 mg/kg) started immediately after OVX for 12 weeks before scarifying the animals. Left femur was prepared for BMD measurements at both proximal femur and femoral diaphysis using DXA. (XR36) for data comparison. BMD measurement results showed that osteoporosis was established in trabecular bone rich proximal femur but not in cortical bone dominant disphysis in the OVX rats as compared with Sham group. XLGB, calcium, and XLGB with calcium intervention all showed preventive effects against OVX induced bone loss in proximal femur. The mean BMD of proximal femur in OVX rats treated with both XLGB and calcium administration was higher than that of treated with XLGB along or with calcium along, however, without statistical significance (Table 1: *: $p<0.05$; **: $p<0.01$, as compared with OVX group). In conclusion, the phytoestrogen rich herbal formula HLGB was effective for prevention of OVX induced bone loss in the high turnover trabecular bone rich proximal femur. The additional calcium supplementation did not reveal additive effects in prevention of bone loss or in increase of BMD.

Table 1: Phytoestrogen-rich herbal formula and/or dietary calcium in prevention of OVX induced bone

Groups (n=9, each)	BMD measured by DXA (mg/cm2)	
	Proximal femur	Femoral diaphysis
Sham	191±10**	179±6
OVX	166±7	177±6
OVX+XLGB	184±11**	177±8
OVX+Calcium	176±11*	177±4
OVX+XLGB+Calcium	185±4**	178±5

Disclosures: L. Qin, Hong Kong RGC grant 2001 2.

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PremPro vs. FemHRT in Cynomolgus Monkeys. C. J. Lees. Pathology, Wake Forest University School of Medicine, Winston-Salen, NC, USA.

Women use FemHRT® (ethinyl estradiol and norethindrone) and PremPro® (conjugated equine estrogens and medroxyprogesterone) for the prevention of postmenopausal osteoporosis. The effects of these two treatment modalities on bone were examined in ovariectomized cynomolgus monkeys (*Macaca fasicularis*). Sixty female cynomolgus monkeys were imported from Indonesia, ovariectomized and randomized into 3 groups: 1) placebo (OVX), 2) FemHRT® (human equivalent of 1 mg norethindrone and 5 micrograms ethinyl estradiol) and 3) PremPro® (human equivalent of 2.5 mg medroxyprogesterone and 0.625 mg conjugated equine estrogens). Treatment lasted 1 year. Serum alkaline phosphatase (ALP) levels and fibular bone mineral density and cortical thickness (determined by pQCT) were measured at 12 months. Both PremPro® and FemHRT® groups had significantly lower ALP levels compared to OVX (OVX - 181 ± 9, FemHRT® - 117 ± 9, PremPro® - 97 ± 10, $p < 0.0001$). PremPro® treated monkeys had greater fibular cortical density (CRTDEN 1080 ± 12) and cortical thickness (CRTTHKC 1.54 ± 0.03) compared to OVX CRTDEN 1029 ± 12 ($p < 0.02$) and OVX CRTTHKC 1.44 ± 0.02 ($p < 0.02$). FemHRT® treated animals did not differ from either OVX or PremPro® treated animals in CRTDEN (1060 ± 12) or CRTTHKC (1.49 ± 0.02). PremPro® had a positive effect on bone mass in monkeys. Although, FemHRT® treatment suppressed ALP levels, FemHRT® did not induce significant changes in bone mass.

Disclosures: C.J. Lees, Pfizer 2.