EFFECTS OF ETIDRONATE ON BONE FRACTURE RATE AND PARAMETERS OF BONE-TURNOVER AFTER LIVER TRANSPLANTATION (OLT)

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After OLT bone mass rapidly declines and fracture (f) rate is increased. In 44 patients (pts) cyclical etidronate (E) was given pre-OLT (11) yr after OLT in addition to alfacalcidol and calcium. Pre-OLT, at 3, 6, and 12 mo post-OLT, bone density (BD) and biochemical parameters of bone-turnover were measured and X-rays of spine and hips were taken. # rate was compared with a historical control group of OLT pts without E (n=25). New vertebral f# were seen in 25% of pts vs 28% in controls (n=3). Pre-OLT vertebral BD showed a negative z score in 83% of pts and decreased 8% in the first 6 mo. Thereafter it increased. Negative z scores of hip BD were seen in 81% and decreased 7% in the first year. Increased urinary hydroxyproline (mean 36 pre-OLT vs 16 micromol/mmol creatine in 98 normals, p<0.01) normalized in the second half year after OLT. Calcium levels increased in the post-OLT period (p<0.05, 0.5 to 10.5 mmol/mmol creatine, p<0.001). 1.25(OH)2D levels were lowered pre-OLT (33 vs 66 pmol/L, p<0.001) and normalised at 3 mo after OLT (59 pmol/L, p<0.01). Osteoclast and PTH remained unchanged and within normal ranges. Conclusions: E does not prevent accelerated bone loss after OLT. With E vertebral # rate was as high as in a historical group without E.

IMPORTANCE OF VITAMIN D STATUS FOR THE RESPONSE OF UNDERCARBOXYLATED OSTEOCALCIN (ucOC) TO VITAMIN D TREATMENT

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We have previously shown, that in the elderly, increased ucOC level is correlated with the vitamin D status (1) and the hip bone mineral density (BMD). In order to further understand the influence of the vitamin D status on ucOC level, we studied a group of 303 elderly women (80±4.5 yrs) treated with vitamin D 400 UId for one year. Total (T) OC and ucOC correlated with BMD of hip and of distal radius (r=0.26, r=0.18–0.29, p<0.01). After correction for age, age of menopause and body weight, only ucOC (r=0.13–0.22, p<0.05 – 0.01) but not OC correlated with BMD. Vitamin D treatment did not decrease TOC, ucOC or ucOC/OC0 ucOC in comparison with the placebo group. This discrepancy with the data obtained previously in the French group (1) may be due to: 1) a smaller dose of vitamin D, 2) no calcium supplementation, 3) less severe vitamin D deficiency (25OH D) and the correction for different methods: 25OH D vs 1,25OH D (3mgi/d; 0.001) and almost twice higher calcium intake (900 vs 500 mg/d) leading to a lower incidence of secondary hyperparathyroidism (11 vs 33%, p<0.001) accompanied by a lower occurrence of hyperphosphatemia (11 vs 27%, p<0.001). Moreover, initial ucOC concentration correlated withPTH (r=0.12, p<0.05) and with alkaline phosphatase (r=0.33, p<0.001). A decrease in ucOC in the vitamin D treated group correlated with the initial PTH level (r=0.17, p<0.05).

The data above confirm the correlation of ucOC with BMD in the elderly and suggest that the initial vitamin D status may contribute to the ucOC response to the vitamin D treatment.

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PAGET'S DISEASE OF BONE: A 3 YEAR EXPERIENCE OF CLODRONATE THERAPEUTIC

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Diphosphonates are widely used as therapeutic agents in Paget's disease of bone. OBJECTIVE: Assess the clinical, biochemical and endocrine evolution during therapeutic courses with clodronate-nitrocresol administration of 600 mg/day during 3 days and repeated every 6 th week.

POPULATION: Up to this moment we have 20 patients (14F-6M) with clinical disease since the age of 35,9 years (SD=16,5) and diagnosed at 59,4 years (SD=14,3). The disease extension was evaluated from radiographs and bone scintigraphy [x=20,75% (SD=15,8)]. The initial values of alkaline phosphatase (normal range 28-78 U/L) were 366 U/L (SD=365) and of total urinary hydroxyproline (normal range <190 mmol/24 h) were 778 mmol/24 hours (SD=1036). The number of therapeutics per patient is 5,5 (SD=6,7).

RESULTS: All the patients referred a symptomatic and persistent improvement of the bone pains after the second therapeutic course. Normalization of the biochemical parameters was attained in 7 patients after 7 therapies (SD=2,3). Nine patients have still biochemical persistent disease after 15,5 therapies (SD=4,6). Four patients abandoned the protocol. There was no significant difference between the initial and latest values of total serum calcium or phosphorus for all the groups. There was a small but significant increase in serum magnesium and creatinine (p<0.05) but still in the normal range. From the endocrine evaluation there was no difference in serum 1,25(OH)2-vitamin D3 and urinary AMRs but there was an increase in serum PTH [x=36.4 (SD=17.7) to 48 (SD=28.4) pmol/L, p=0.05]. In 12 patients we evaluated ionized and total serum calcium and PTH before and immediately after one therapeutic and we found a significant decrease in ionized calcium ([x=0.99 (SD=0.04) to 0.96 mmol/L, (SD=0.03), p=0.05] with a significant increase in PTH [x=5.8 (SD=21.2) to 73,1 (SD=39.6), p<0.05] with no difference in total calcium. Conclusions: Clodronate causes a decrease in ionized calcium which probably leads to the transient increase in PTH. There were no important biochemical alterations but it is advisable to follow the patients serum creatinine.

SEX HORMONE BINDING GLOBULIN PREDICTS VITAMIN D DEFICIENT HYPERPARATHYROIDISM AND THE BONE MINERAL INCREASE AFTER VITAMIN D SUPPLEMENTATION.

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The effect of vitamin D supplementation on vitamin D status, parathyroid function and bone mineral density (BMD) of the hip was investigated in 264 healthy elderly women (mean age 80.3 ± 3 yrs) for 1 year. Serum levels of sex hormone binding globulin (SHBG) were also studied to estimate remaining estrogen activity. After obtaining baseline values, the patients received vitamin D, 400 IU/day or identical placebo tablets. In 65% of the women, serum 25(OH)D was below 30 nmol/L. Serum PTH was negatively related to serum 25(OH)D when the latter was below 25 nmol/L (p=0.02). This negative relationship was significantly influenced by serum SHBG, i.e. higher SHBG (lower estrogen activity) resulted in higher serum PTH in case of vitamin D deficiency. Vitamin D supplementation led to a significant decrease of serum PTH (P<0.01) and increase of the BMD of the femoral neck (2.2% P<0.01). The latter was significantly modified by serum SHBG with a larger increase of BMD at higher SHBG levels (P<0.05). We conclude that a lower remaining estrogen activity leads to higher serum PTH levels in case of vitamin D deficiency and to a greater increase of BMD following vitamin D supplementation.