IMPACT OF VITAMIN D DEFICIENCY ON THE EFFICACY OF PTH 1-84 TREATMENT IN MALE PATIENTS WITH SEVERE OSTEOPOROSIS

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Objectives:

PTH (1-84) is approved for the treatment of postmenopausal osteoporosis with fractures. Vitamin D deficiency is very common in patients with osteoporosis and low circulating 25(OH) levels have been linked to lower BMD and smaller or even lacking response to osteotropic medication The aim of this prospective open label study was the evaluation of efficacy and tolerability of PTH (1-84) in males with osteoporotic fractures in relation to VitD metabolism.

Material & Methods:

A total of 15 males with osteoporotic fractures with a mean age of 60.6 ± 16.2 years were prospectively assigned to PTH (1-84) 100 µg sc daily for 24 months. Risk factors among the patients were prior glucocorticoid use, celic disease, diabetes type II, lactose intolerance, androgen deprivation therapy and low trabecular connectivity in transiliac bone biopsy specimen. 13 men had received prior bisphosphonates with a mean duration of 7.6 ± 3.8 years, 9 of them had major osteoporotic fractures and 4 had significant bone loss during previous antiresorptive medication. 12/15 patients had prior vertebral fractures (mean 3 fractures) and 3 patients had prior fracture of femoral neck.
We investigated DXA of spine and hip, bone turnover markers, fracture status and improvement of daily activities and reduction of pain during the first 12 months of therapy. Fractured vertebrae were excluded from BMD evaluation. All patients received 1000mg calcium and 800IE vitamin D supplementation daily.

Results

In a preliminary analysis baseline and 12 months results were compared. Mean levels of PTH decreased from 49.6 ± 16.7 to 36.3 ± 21.0 ng/ml (P=0.030); P1NP increased from 26.38 ± 9.64 to 148.13 ± 35.45 µg/l (P=0.005) and S-CTX increased from 0.29 ± 0.16 to 0.75 ± 0.44 ng(ml (P=0.002) [Fig 1-3].

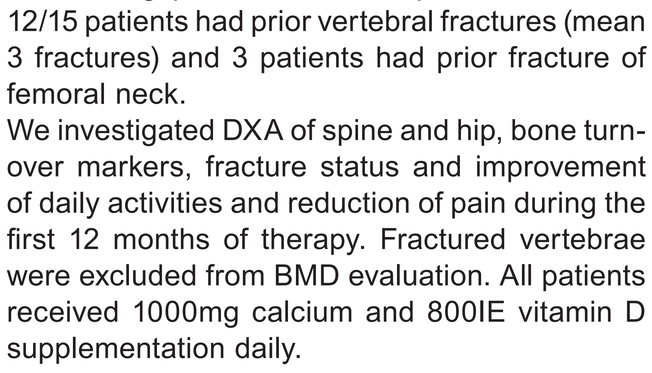

Fig. 1: Biochemical Markers II

Fig. 2: Biochemical Markers III

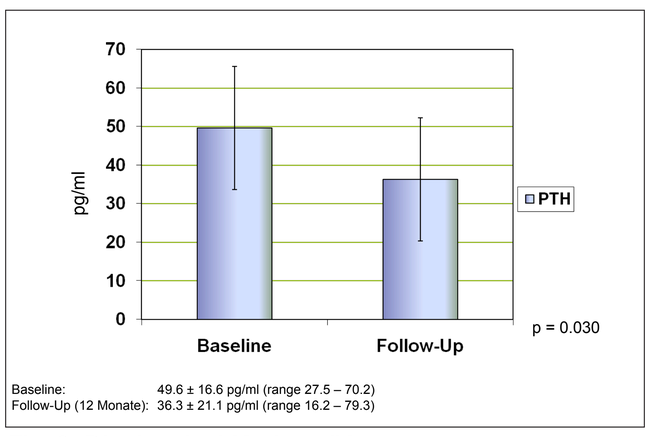

Fig. 3: Biochemical Markers IV

BMD L1-L4 increased only moderately from a mean of 0.84 ± 0.14 to 0.87 ±0.11 g/cm2 (P=0.097) while BMD at hip did not change at all [Fig 4].

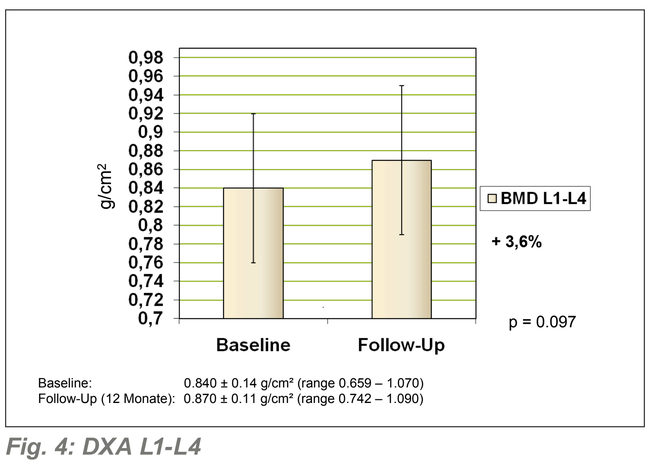

Fig. 4: DXA L1-L4

In view of only minor changes of BMD the patients were divided into two groups according to initial vitamin D levels. A cut off point was set at 30 ng/ml. According to this threshold value 7 out of 15 subjects (48%) had low vitamin D levels and only 4 of them reached levels above 30 ng/ml during therapy. Furthermore in this group there was no change in the BMD of the lumbar spine or the hip after 12 months PTH medication. While vitamin D levels increased in the group <30 during Ca/VitD supplementation there was a mean decrease of vitamin D in the group >30 of 12.8 ng/ml (P=0.032) notable [Fig 5,6].

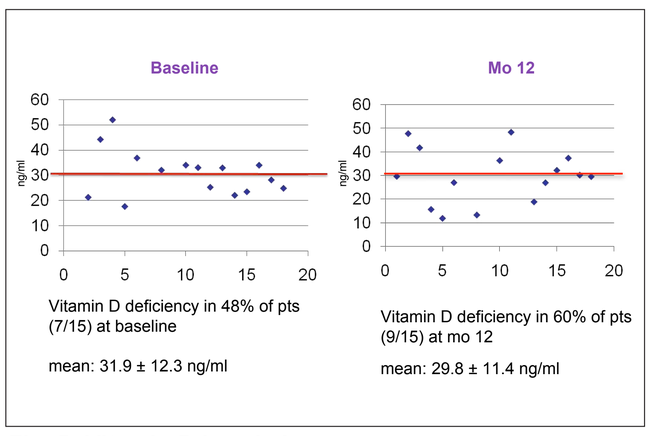

Fig. 5: Vitamin D Levels I

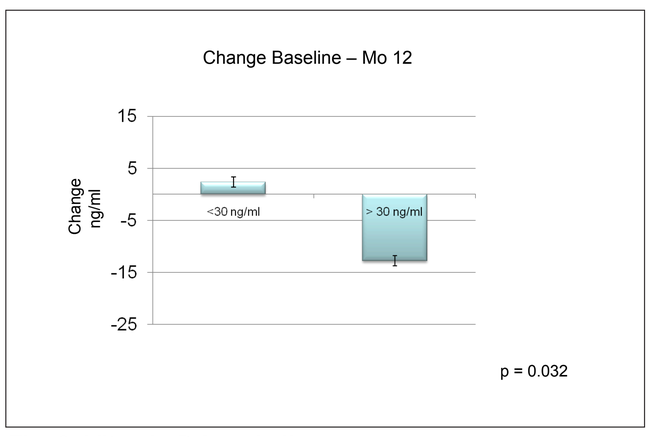

Fig. 6: Vitamin D Levels II

No hypercalcaemia was observed after 12 months compared to baseline (2.23 and 2.30 mm/l, respectively). No new vertebral fracture occurred in the 15 patients, but one new hip fracture occurred after a major trauma. Two thirds of the patients reported a significant reduction of back pain resulting in an improvement of daily activities (P<0.05).

Conclusion:

During 12 months therapy with PTH 1-84 biochemical markers of bone turnover increased sginificantly indicating the anabolic effect of osteoinductive PTH 1-84 medication, however spine and hip BMD did not increase as one would have excpected. In view of the missing gain in BMD further analysis revealed that 48% of the male patients had an initial vitamin D deficiency and gave a possible explanation for the lacking increase in BMD. Our results implicate that Vitamin D is as important as anabolic PTH therapy for an increase of bone mineralsation. Therfore an initial correction of decreased Vi D levels with proper vitamin D supplementation is essential prior to PTH therapy.
We conclude PTH 1-84 is generally well tolerated and has effectiveness in preventing vertebral fractures in men, but vitamin D levels must sustain clearly above the upper limit of normal.

Keywords: Male osteoporosis, PTH (1-84), vitamin D levels, bone mineral density, bone turnover markers, vertebral fractures

Disclosure: The authors state that they have no conflict of interest