EFFECTS OF CHOLECALCIFEROL AND CALCIIFEDOL IN OSTEOPOROTIC WOMEN WITH SECONDARY HYPERPARATHYREODISM DUE TO SEVERE VITAMIN D DEFICIENCY UNDERGOING ZOLEDRONIC ACID TREATMENT: A RANDOMIZED-CONTROLLED TRIAL

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Background: Secondary hyperparathyroidism (shPTH) due to vitamin D deficiency impairs the bone mineral density (BMD) response to alendronate,1, 2 but the optimal strategy for its correction in postmenopausal osteoporotic women (PMO) about to start zoledronic acid (ZOL) therapy is still unknown.

Objectives: To evaluate the effects of cholecalciferol (D3) and calcifediol (25OHD) on serum 25-OH-vitamin D (25OHD), parathyroid hormone (PTH) and BMD in PMO presenting with shPTH due to vitamin D deficiency.

Methods: PMO with 25OHD <20 ng/ml, shPTH (PTH >66 pg/ml) and BMD T-score at the lumbar spine (LS), femoral neck (FN) or total hip (TH) <−2.5, or between -1.25-2.5 plus one vertebral/femoral fracture, were randomly assigned to receive a therapeutic dose of D3 (300,000 IU bolus) followed by 175 mcg weekly of D3, or 175 mcg/week of ZOL alone, 2 months before receiving a single intravenous infusion of ZOL (5mg). BMD at the LS, FN and TH was assessed at baseline and after one year from ZOL. Serum calcium, PTH and 25OHD were measured at baseline, and 6- and 12-month after ZOL. Adverse and clinical events were ascertained by 3- and 9-month telephone interviews, and by 6- and 12-month clinical evaluation.

Results: 45 PMO (25OHD N=23, D3 N=22) were enrolled over one year and 32 subjects (mean age ±SD 75±10 years, range 51-91) completed the 1-year of treatment/follow-up (25OHD N=17, D3 N=15). Most PMO discontinued for protocol violation, while three deceased before study ending (25OHD N=1, D3 N=2) for reasons not related to the agents investigated. The baseline characteristics were comparable in both groups. At baseline mean 25OHD (±SE) was 8.1±1.1 ng/ml in the 25OHD group and 8.1±1.3 ng/ml in the D3 group. The corresponding figures for PTH were 111±56 pg/ml (25OHD) and 117±55 pg/ml (D3). Mean 25OHD (±SE) increased in both groups at 6- and 12-month, being significantly greater in the 25OHD group (12-month, 56±2 ng/ml and 173±41 ng/ml). BMD at baseline and 12-month from ZOL showed that 25OHD increased in both groups (ΔFemoral neck BMD = 0.046 [0.002; 0.090]), 25OHD was 0.107 [0.029; 0.228]; median BMD variation in total femur was 0.013 [-0.013; 0.043]. We observed a discrete correlation between FRAX-based hip fracture probability (with BMD) at baseline was 16% [10.0; 23], and median hip fracture risk was 7.2% [3.4; 13.8].

Conclusion: Calcifediol 175 mcg weekly appears more potent in improving 25OHD and decreasing PTH concentrations compared to cholecalciferol therapeutic dose (300,000 IU), being more effective in severe vitamin D deficiency when compared to ZOL therapy. Further studies are warranted to clarify implications on BMD improvements on the long-term of PMO secondary cause OP.

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REFERENCES: