Effects of Cholecalciferol and Calcifediol in Osteoporotic Women with Secondary Hyperparathyroidism Due to Severe Vitamin D Deficiency Undergoing Zoledronic Acid Treatment: A Randomized-Controlled Trial

G. Botticella1, M. Pizzonia2, B. Cosso3, R. Bruno3, D. Camellino1, G. Girasole1, A. Giusti2, M. Pedrazzoni1, S. Alexovits1, F. Pietravino2, F. Santolini2, A. Nencioni2, G. Bianchi1,1
1Local Health Trust 3, Division of Rheumatology, Department of Medical Specialties, Genoa, Italy, 2University of Genoa, Geriatric Clinic, Department of Internal Medicine and Medical Specialties, Genoa, Italy, 3University of Genoa, Geriatric Clinic, San Martino Hospital, Orthopaedic and Trauma Unit, Department of Emergency, Genoa, Italy

Background: Secondary hyperparathyroidism (shPTH) due to vitamin D deficiency impairs the bone mineral density (BMD) response to alendronate, although 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-OHD 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 >65 pg/ml) and BMD T-score at the lumbar spine (LS), femoral neck (FN) or total hip (TH) < -2.5, or between -1.5 and -2.5 plus one vertebral/forearm 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/weekly of 25OHD 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 ±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 protocols’ 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 ng/ml in the 25OHD group and 8±1 ng/ml in the D3 group. The corresponding figures for PTH were 111±6 pg/ml (25OHD) and 117±5 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 [0.767, 0.964] g/cm², median T-score of -2.50 [-3.20, -1.85]. Regarding fracture risk, median FRAX-based 10-year major fracture risk with BMD at baseline was 16% [10.0; 23], and median hip fracture risk was 7.2% [3.4; 13.8].

Conclusion: Cholecalciferol 175 mcg weekly appears more potent in improving 25OHD and decreasing PTH concentrations compared to cholecalciferol therapy in postmenopausal osteoporotic women undergoing ZOL treatment. A randomized, controlled, double-blind, double-blind, parallel-group trial is therefore warranted.

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References:

Figure 1. Mean (95% confidence interval) value of 25-hydroxyvitamin D (25OHD, ng/ml) and parathyroid hormone (PTH; pg/ml) at baseline, and 6- and 12-month (Time) after zoledronic acid infusion, in patients receiving a therapeutic dose of D3 (n=17, 300,000 IU bolus followed by 175 mcg/weekly of cholecalciferol (D3), yellow line), or 175 mcg/weekly of calcifediol (25OHD, blue line).

Frax and the Effect of Teriparatide on Bone Mineral Density in Secondary Osteoporosis

S. Garcia1, B. M. Fernandes1, M. Rato1, F. Oliveira Pinheiro1, D. Fonseca2, D. Santos Oliveira3, A. Martins3, F. R. Martins3, G. Terroso3, M. Bernardes4, L. Costa5, S. João University Hospital Center, Rheumatology, Porto, Portugal; 6Centro Hospitalar Vila Nova de Gaia/Espinho - Unit 1, Rheumatology, Vila Nova de Gaia, Portugal; 7Center for Health Technology and Services Research (CINTESIS), Faculty of Medicine, University of Porto, Porto, Portugal; 8University Hospital Center of Algarve, Faro, Rheumatology, Faro, Portugal; 9Faculdade de Medicina da Universidade do Porto - FMUP, Rheumatology, Porto, Portugal

Background: Teriparatide has been shown to increase spine and hip bone mineral density (BMD) and to reduce vertebral and non-vertebral fractures. (1) It is currently not clear whether the effect of teriparatide is dependent on the baseline etiology of osteoporosis (OP) type, a finding that could have an impact on our therapeutic decision.

Objectives: To evaluate the effects of teriparatide on bone mineral density in secondary OP and baseline 10-year fracture probability, assessed using FRAX®, in primary and secondary OP patients.

Methods: This is a longitudinal, retrospective study including consecutive patients with the diagnosis of OP treated with teriparatide for 24 months, with a ten-year follow-up period, at our rheumatology department. Demographic, clinical, laboratory, BMD and occurrence of fracture data were collected. The 10-year risk of osteoporotic fracture was estimated using the fracture risk assessment tool (FRAX) v.4.1 with the Portuguese population reference. Statistical analysis was performed using the software SPSS 23.0. Correlations between continuous variables were evaluated with spearman coefficient. p<0.05 was considered statistically significant.

Results: Eighty patients (88.6% female, median age 65.00 (59; 75)) were included. Forty-nine patients (61.3%) had secondary OP, mainly of cortisone etiology (61.2%, n=30). Before treatment, median lumbar spine BMD was 0.870 [0.767, 0.964] g/cm², median T-score of -2.60 [-3.30, -1.90]; median total femoral BMD was 0.742 [0.667, 0.863] g/cm², median T-score of -2.10 [-2.80, -1.30]; median femoral neck BMD was 0.671 [0.611, 0.787] g/cm², median T-score of -2.50 [-3.20, -1.85]. Regarding fracture risk, median FRAX-based 10-year major fracture risk with BMD at baseline was 16% [10.0; 23], and median hip fracture risk was 7.2% [3.4; 13.8].

The median variation of BMD, after finishing teriparatide treatment, in the spine was 0.107 [0.029; 0.228]; median BMD variation in total femur was 0.013 [-0.013; 0.069] g/cm², median T-score of 0.046 [-0.002; 0.109]. We observed a numerically superior effect, albeit without any statistical significance, of teriparatide on bone mineral density gain in secondary OP (versus primary OP) at lumbar spine, total femur and femoral neck.

Most patients continued anti-osteoporotic treatment with a bisphosphonate (81.2%, n=65) and, during follow-up, 17 patients had an incident fracture (8 hip fractures and 6 vertebral fractures), median of 5 [1.75, 8.25] years after ending teriparatide.

We found a discrete correlation between FRAX-based hip fracture probability and the variation of bone mineral density in total femur (Spearman’s coefficient 0.248, p=0.04). There was no correlation between FRAX-based major fracture probability and the variation of bone mineral density in the spine or femur. When we separately analyze the relationship between the variation in total hip BMD and the FRAX-based fracture risk, depending on whether it is a secondary or primary OP, we find that the correlation is stronger and only remains in secondary OP (Spearman’s coefficient 0.348, p=0.03).

Conclusion: Our data suggest that teriparatide could be an important weapon in the treatment of secondary cause OP, particularly cortisone, and in patients at high fracture risk, although further larger studies are needed to confirm these findings.

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THE EFFICACY, SAFETY AND OUTCOME AFTER 5-8 YEARS OF PARENTERAL ANTI-OSTEOPOROTIC THERAPY EVALUATED AT A DISTRICT GENERAL HOSPITAL IN THE UK

Z. Alkutobi, D. Laila, T. Jones, A. Nandagudi, Basildon and Thurrock University Hospitals NHS Foundation Trust, Rheumatology, Basildon, United Kingdom; Basildon and Thurrock University Hospitals NHS Foundation Trust, Rheumatology, Basildon, United Kingdom; Basildon and Thurrock University Hospitals NHS Foundation Trust, Internal Medicine, Basildon, United Kingdom

Background: Parenteral anti-osteoporotic medications are frequently recommended for the management of primary and secondary osteoporosis by NICE (1) and EULAR (2) guidelines.

Objectives: This audit aimed at evaluating the efficacy, adherence and safety profile of denosumab (D), zoledronate (Z) and teriparatide (T).

Methods: The data of patients initiating D, Z and T from 2012-2021 were retrospectively reviewed using electronic medical records at Basildon hospital.

Results: We enrolled 146 patients diagnosed with low bone density and following treatment (3-6 years D (n: 50), 4-5 years Z (n: 50) and 2 years T (n: 46). More than 92% were Caucasian females; 41.7% were above 80 years. T group had more pronounced reduction in bone mineral density (BMD) with a mean T-score (spine:-3.9, hip:-2.6, neck of femur:-2.7); followed by Z group (spine:-2.6, hip:-2, neck of femur:-2.5) and D group (spine:-2.3, hip:-2.2, neck of femur:-2.3). Primary prevention was in 26% and secondary prevention in 73.9%; with the commonest fractures at the vertebrae at 40%.

Conclusion: D, Z and T were well tolerated and could effectively either maintain or improve the BMD at both spinal and hip sites and prevent fragility fractures and T was associated with the most pronounced soar in BMD. There were few cases of deterioration mainly at the hip area with all groups.

The course of T was stopped earlier in 28.2% of the cases due to the difficulty in taking injections or side effects including nausea, gastric upset, myalgia, insomnium, poor renal function, raised PTH, ALP and calcium. Dental issues (not osteonecrosis) were the reason to stop Z and D in 2% of each group and 8% choose to discontinue D after developing other non-related comorbidities. There were no fragility fractures during the treatment courses.

The outcome after reviewing 91.3% of those who completed or stopped the T course shows 39% commenced on D whereas 35.7% and 19% on Z and alendronate respectively leaving 7.1% on drug holiday. After completion of the 10th D, 78.5% of the reviewed patients were continued on further D injections whereas 3.5% were switched to T and 17.8% given drug holiday. For those who were reviewed after the 5th Z, 94% were switched to D and 5.8% given drug holiday.

EFM: 4.4% 6%

Primary bisphosphonate therapy did not show significant influence on the later effects of D, Z or T on BMD. After completion of the treatment for the 3 groups, only 30.87 % of the reviewed cases were advised for drug holiday and majority were switched to D as Z and T is limited to 5 and 2 years course respectively. Heterogeneity in decision making exists due to variability in recommending these medications, patient preference and mode of administration. To optimize the adherence and effects of anti-osteoporotic medications, stratified guidelines is required for the long term use of these medications and discontinuation of D.

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THE ACCURACY OF OSTEOPOROTIC FRACTURE RISK PREDICTION IN PATIENTS WITH RHEUMATOID ARTHRITIS USING THE PREDICTIVE MODEL DEVELOPED AT V.A. NASONOVA RESEARCH INSTITUTE OF RHEUMATOLOGY (RUSSIA) AND FRACTURE RISK ASSESSMENT TOOL (FRAX)

P. Kozhevnikova, P. Kovalenko, S. Glukhova, I. Dzydykina, A. Lila; V.A. Nasonova Research Institute of Rheumatology, Laboratory for the Study of Comorbid Infections and Safety Control of Drug Therapy, Moscow, Russian Federation

Background: FRAX is a computer-based algorithm that calculates the 10-year probability of a major osteoporotic fracture and the 10-year probability of hip fracture. However, FRAX has several limitations in assessing the risk of fracture in patients with rheumatoid arthritis (RA).

In 2013V.A. Nasonova Research Institute of Rheumatology (Russia) developed a predictive mathematical model for assessing the risk of osteoporotic fractures in RA, which includes 2 main risk factors: cumulative glucocorticoid dose (GC), decrease in BMD in the femoral neck to osteoporosis, and 2 additional factors: for patients under 65 years of age - the presence of ischemic heart disease, and for people over 65 - a history of gastric ulcer or duodenal ulcer.

Objectives: To compare accuracy of osteoporotic fracture risk prediction in patients with RA using the predictive model developed at V.A. Nasonova Research Institute of Rheumatology (IR) and FRAX.

Methods: This monocentric (single-center) prospective study included 70 patients with RA, aged 40 to 80 years. The follow-up period - 8.0 ± 1.2 years; mean age at the baseline was 55.4 ± 7.8 years old; the mean disease duration at...