Longterm antiepileptic treatment and bone turnover

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Introduction

In recent years, there is more and more evidence suggesting that epilepsy and its treatment may have negative effects on bone mineralization and calcium metabolism. While long term use of CYP450 inducing antiepileptic drugs is often associated with bone turnover threw alteration of vitamin D metabolism, mechanism of reduced BMD in long term treatment with antiepileptics non inducing liver enzymes remains unclear. **Objectives:** Therefore, we decided to measure serum levels of 25-OHD, calcium and osteocalcin (OCLN) in epilepsy patients taking lamotrigin (LTG) (n = 50) and caprbamazepine (CBZ) (n=50) in monotherapy for a period of at least twelve months. Also, for each participant, mineral density (BMD) was evaluated by dual-energy X-ray absorptiometry method.

Methodology

A cross-sectional study in patients under treatment with CBZ monotherapy was carried out between the years 2016 to 2017, in Epilepsy Center at Neurology Clinic in Sarajevo. Only patients with CBZ and LTG monotherapy for a period of at least twelve months were entered in this study (n=50). Patients who had any condition known to affect bone metabolism (e.g., renal disease, recent fracture, hyperparathyroidism, Paget disease, osteoporosis) or taking any drug known to cause or treat osteoporosis, were excluded. The results were compared with age-matched healthy controls, with no evidence of metabolic bone disease (n=30).

All participants were asked to complete a questionnaire including medical history, fractures, falls and injuries, and vitamin D or calcium supplements.

Bone mineral density (BMD) was evaluated by dual-energy X-ray absorptiometry method called DXA technology.

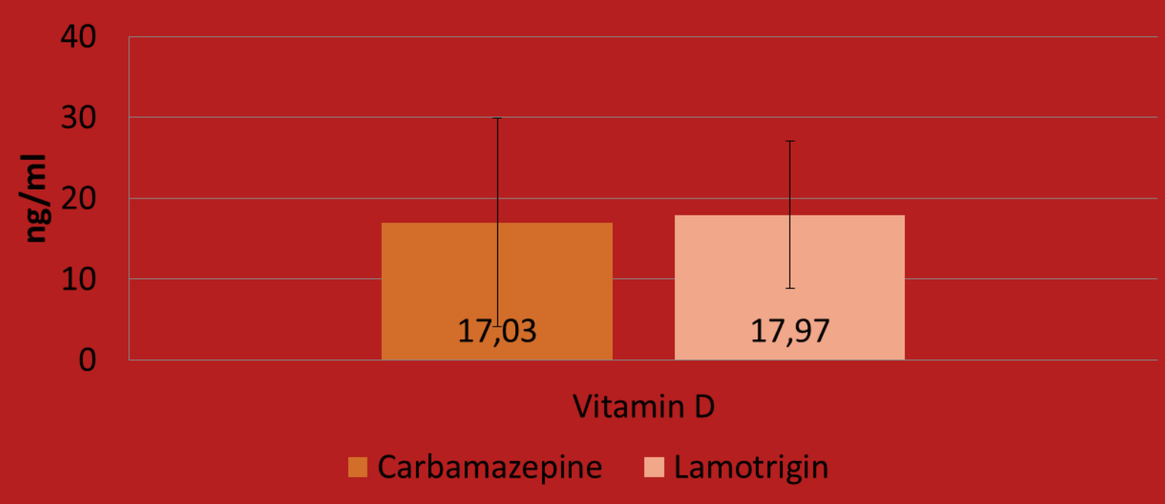
DXA was performed using a Hologic QDR-4000A densitometer (Hologic, Bedford, MA, U.S.A.). DXA measured bone mineral content (BMC in grams) and bone area (BA, in square centimeters), then calculated "area" BMD in g/cm2 by divided BMC by BA. T-score, the value used for diagnosis osteoporosis, is the mean BMD of a young-adult reference population from the patients' BMD divide by the standard deviation (SD) of young-adult population. Z-score, used to compare the patients' BMD to a population of peers, calculates by subtracting the mean BMD of an age, ethnicity and sex-matched reference population from the patients' BMD and divide by the SD of the reference population.

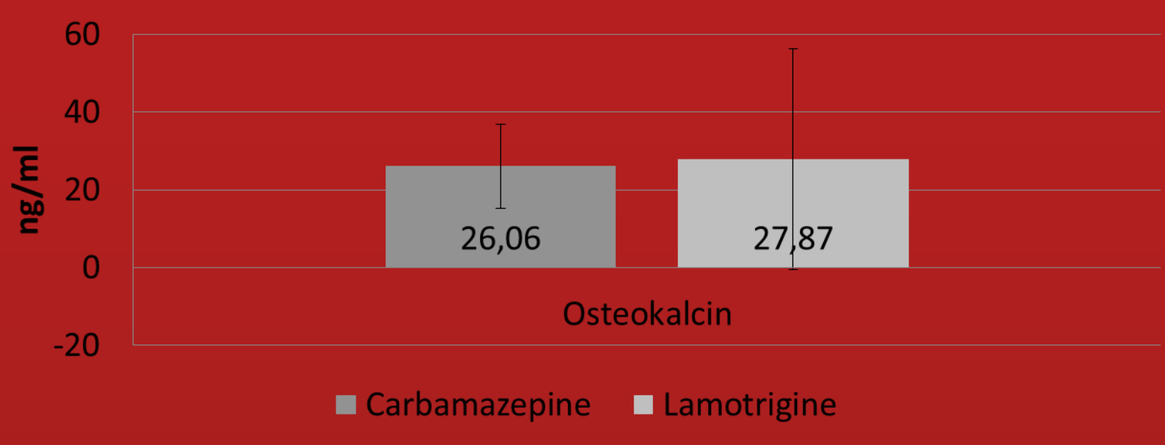
For each subject the level of vitamin D and osteocalcin in serum was determined in laboratory findings.

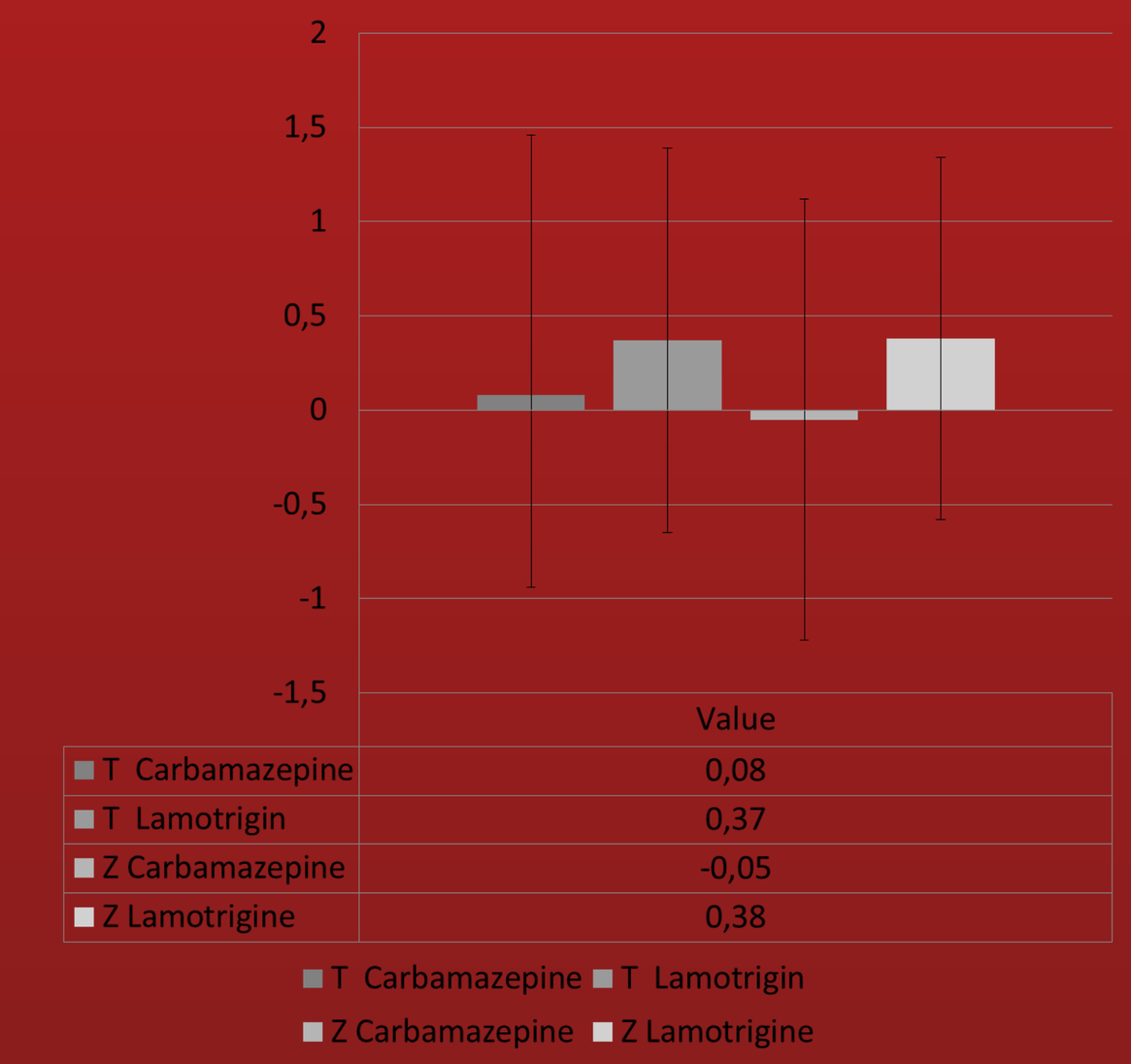
Serum 1, 25-dihydroxyvitamin D (3) (normal range, 20–74 pg/ml) was measured by radioimmunoassay. Serum osteocalcin level was determined by Elisa.

Results

The average value of vitamin D in serum was significantly lower in both groups compared to the normal reference range but there was no statistically significant difference in LTG group compared to CBZ group (Vit D 17.97±9.15 vs. 17.03±12.86 , p=0,680). The average value of osteocalcin in serum was significantly higher in both groups compared to the normal reference range but there was no statistically significant difference in LTG group compared to CBZ group (OCLN 27.87±28.45 vs. 26.06±10.78, p=0,124). The average value of calcium in serum was significantly lower in both groups compared to the normal reference range but there was no statistically significant difference in LTG group compared to CBZ group (Ca 1.01 ±0.06 vs. 1.02±0.12, p=0,435). BMD value in CBZ group was lower than in LTG group (T. score CBZ: 0.08± 1.38 vs. T. score LTG: 0.37± 1.02, p=0,224; Z score CBZ:-0.05±1.17 vs. Z score LTG: 0,38±0,96, p=0,046) but difference was statistically significant only for Z score.







Conclusion

Longterm antiepileptic therapy is associated with bone disease, as evidenced by biochemical abnormalities and decreased BMD.