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Short communication

Correlation of Vitamin D and Zinc concentration with therapy outcome in epilepsy patients from Republic of North Macedonia

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Introduction

Epilepsy is one of the most common neurological diseases; more precisely it is the second most common neurological disease in the world. This disease affects the neurological system and has an immense impact on other human systems. It is widely known that epileptic patients taking anticonvulsants have decreased vitamin D levels (Holló et al., 2014) and zinc (Ma et al., 2015), contributing to various other comorbidities.

Vitamin D plays a crucial role in the metabolic pathway of calcium absorption, which closely relates to bone formation and density. It has been shown that epilepsy patients who suffer from vitamin D insufficiency are prone to bone damage and are more often exposed to fractures (Holló et al., 2014). Additionally, vitamin D receptors and the 1-alpha–hydroxylase enzyme, which is responsible for the formation of the active form of vitamin D, have been found to be present in all brain tissues, thus increasing its recognition as an important neuronal modulator (Elmazny et al., 2020).

Zinc plays a vital role as a neuromodulator in the pathophysiology of epileptic and seizure occurrences. Studies have shown that epileptic patients on anticonvulsant therapy have decreased zinc levels in their plasma and serum (Doboszewska et al., 2019).

Antiepileptic therapy and different medications for the treatment of epilepsy contribute to lower vitamin D and zinc levels in epileptic patients. Evidence shows that many epileptic medications are usually CYP-450 inducers, thus converting vitamin D into inactive metabolites (Holló et al., 2014). Each antiepileptic drug or antiepileptic therapy has its own impact on vitamin D metabolism and zinc levels.

Considering the before-mentioned correlations, this deficiency of vitamin D and zinc may be significantly higher in drug-resistant patients exposed to more than one antiepileptic drug. In this study, we aim to understand the difference in vitamin D and zinc plasma levels between drug-resistant and non-drug-resistant adult epileptic patients.

Materials and methods

Study design

The samples were collected between June and August 2022. Sixty-three epileptic patients on anticonvulsant therapy were included, of which 23 were drug-resistant cases, and the other 40 were non-drug-resistant patients. The patients included in this study varied from 16 to 70 years old. Patients taking vitamin D and other mineral supplements were excluded from this study.

We collected basic patient information regarding this study's needs through a questionnaire distributed to the University Clinic for Neurology. The questionnaire consisted of questions about basic information for the patient, age, what medications they are using, type of

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epilepsy, intensity and frequency of the seizures, days of sunlight exposure, duration of seizures, and BMI.

Plasma vitamin D levels were measured by collecting 3 ml of venous blood. The samples were centrifuged at 1374 g, and the plasma was immediately separated into 1.5 mL tubes and stored at -80 ℃ until the analysis time.

Plasma levels of 25-OH vitamin D were measured using a commercially available enzyme immunoassay competition method with a final fluorescent detection (VIDAS® 25 OH Vitamin D Total) kit by bioMerieux, France. According to the supplier's reference range for vitamin D, a concentration of less than 20 ng/mL25 OH vitamin D in plasma is defined as deficient, 20-29 ng/mL is defined as insufficient, and 30-100 ng/mL as sufficient.

Plasma levels of zinc were measured using a commercially available colorimetric test kit by Gesan, Italy. According to several studies, concentration lower than 60 μg/dL was defined as insufficient, and the reference range was 60-120 μg/dL.

We used the Statistical Package for Social Sciences (SPSS 20.0; IBM, USA) for data analysis.

Results and discussion

The goodness of fit of the obtained data was tested using the Kolmogorov-Smirnov & Shapiro-Wilk test. The obtained results indicate a normal distribution of our data with $p > 0.05$.

The statistical association of the sample data regarding vitamin D and zinc concentration in drug-resistant patients and patients on mono or polytherapy was evaluated using the Pearson coefficient for point-biserial correlation.

The acquired results indicate a moderate positive correlation between the vitamin D concentration and the therapy outcome (Pearson coefficient = 0.462 and $p < 0.05$). It was determined that there is no statistically significant correlation between the Zn concentration and the therapy outcome (Pearson coefficient = 0.176 and $p > 0.05$). The statistical analysis of the results regarding the influence of the type of therapy (mono or polytherapy) on the vitamin D and Zn concentrations indicates that there isn't a statistically significant correlation.

Conclusion

The obtained results in this study, carried out for the first time on a patient population in North Macedonia, are in accordance with other published studies in this area of interest. Vitamin D concentration could influence the outcome of antiepileptic therapy in patients with the diagnosed epileptic syndrome.

Eighty-one percent of the examined patients had a lower vitamin D concentration than the reference value. This is particularly significant considering that the study was conducted from April to July when there is a high exposure to sunlight. This points to the need for additional vitamin D therapy in patients receiving antiepileptic treatment.

A more significant number of patients is needed in further studies for more accurate statistical confirmation of the obtained results.

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