

DISCORDANT CALCIUM AND PARATHYROID HORMONE WITH PRESUMED EPILEPTIC SEIZURES

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Abstract: *Epileptic seizures are a neurological condition characterized by abnormal electrical activity in the brain, leading to involuntary and unpredictable movements, changes in consciousness, and other symptoms. The study's main objective is to find the discordant calcium and parathyroid hormone with presumed epileptic seizures. This study aims to investigate the association between discordant calcium and parathyroid hormone (PTH) levels and presumed epileptic seizures in a cohort of 200 patients. The study was conducted between June 2022 and December 2022. The study was conducted in collaboration with the neurology department. Patients admitted to the hospital with presumed epileptic seizures were included in the study. This study found that out % of the 200 patients who met the inclusion criteria, 65% had discordant calcium and PTH levels. Among these patients, 80% had low calcium and high PTH levels, while 20% had high calcium and low PTH levels. The logistic regression analysis showed a significant association between discordant calcium and PTH levels and presumed epileptic seizures ($p < 0.05$). In conclusion, the results of this study suggest that abnormalities in calcium and parathyroid hormone (PTH) levels are not a major contributor to the development of epileptic seizures in most patients. While patients with hypocalcemia appeared to have a higher risk of seizures than those with normal calcium levels, most patients with hypocalcemia did not experience seizures.*

Keywords: Discordant Calcium and Parathyroid Hormone, Calcium Levels, Epilepsy, Seizures, Hypocalcemia

Introduction

Epileptic seizures are a neurological condition characterized by abnormal electrical activity in the brain, leading to involuntary and unpredictable movements, changes in consciousness, and other symptoms. While several factors can trigger seizures, such as stress, sleep deprivation, and alcohol consumption, imbalances in calcium and parathyroid hormone levels have been implicated in some cases (Bloem & Stocchi, 2015).

Calcium is essential for many physiological processes, including muscle contraction, nerve function, and bone health. Parathyroid hormone, or PTH, is a hormone produced by the parathyroid glands that regulate calcium levels in the body. When calcium levels are low, PTH is released to stimulate the release of calcium from bones and increase calcium absorption in the gut and kidneys (Camacho et al., 2020). However, when calcium and PTH levels are discordant, meaning that they are not in balance with each other, this can lead to neurological

symptoms, including seizures. The exact mechanisms underlying this association are not yet fully understood, but studies suggest that imbalances in calcium and PTH levels can cause changes in neuronal excitability, leading to abnormal electrical activity in the brain (Heller et al., 1995).

In some cases, calcium and PTH imbalances may result from a primary disorder of the parathyroid glands, such as hyperparathyroidism. This condition is characterized by excessive production of PTH, leading to elevated calcium levels in the blood. Hyperparathyroidism can have various symptoms, including bone pain, kidney stones, and neuropsychiatric disturbances such as depression, anxiety, and cognitive impairment. Additionally, in rare cases, hyperparathyroidism can cause seizures (Zhong, Wang, Wang, You, & Jiang, 2015). On the other hand, hypoparathyroidism, a condition characterized by low PTH levels, can also cause seizures. This condition is usually caused by damage or removal of the parathyroid glands during thyroid or

neck surgery, autoimmune diseases, or genetic disorders. Hypoparathyroidism can lead to low calcium levels, which can cause various neurological symptoms, including seizures, tremors, and muscle cramps (Liang et al., 2019).

It is worth noting that while calcium and PTH imbalances can be associated with seizures, not all patients with these imbalances will experience seizures, and not all patients with seizures will have abnormal calcium and PTH levels. Therefore, calcium and PTH levels should be evaluated as part of the diagnostic workup for patients with suspected seizures, but other causes should also be considered. Discordant calcium and PTH levels can potentially trigger seizures (Moushumi & Rajarshi, 2014). Therefore, it is crucial to investigate and manage any underlying imbalances in these levels in patients with presumed epileptic seizures. Furthermore, identifying and addressing any underlying medical conditions affecting calcium and PTH levels is important for optimal seizure management. It is important to investigate and manage potential calcium and PTH imbalances in patients with presumed epileptic seizures, as correcting these imbalances may help reduce the frequency and severity of seizures. Identifying and addressing any underlying medical conditions affecting calcium and PTH levels, such as kidney disease or vitamin D deficiency, may also be necessary for optimal seizure management (Goswami et al., 2012). The study's main objective is to find the discordant calcium and parathyroid hormone with presumed epileptic seizures.

Methodology

This study aims to investigate the association between discordant calcium and parathyroid hormone (PTH) levels and presumed epileptic seizures in a cohort of 200 patients. The study will be conducted between June 2022 and December 2022. This cross-sectional study was conducted at Avicenna Medical College, Lahore. The study was conducted in collaboration with the neurology department. Patients admitted to the hospital with presumed epileptic seizures were included in the study.

Participants aged 18 years or older who were admitted to the hospital with presumed epileptic seizures and underwent laboratory tests for calcium and PTH levels were included in the study. In contrast, participants who have a history of epilepsy or have been diagnosed with epilepsy, have a history of brain tumor, stroke, or other neurological conditions that can cause seizures, have a history of hyperparathyroidism or hypoparathyroidism, are currently taking medications that can affect calcium or PTH levels or have a history of significant psychiatric or cognitive impairment that may affect

their ability to provide informed consent or participate in the study were excluded from the study.

The neurology department identifies patients who meet the inclusion criteria. After obtaining informed consent, the study team collects demographic and clinical information from the patient's medical and electronic health records. Blood samples were drawn from patients and sent to the hospital's central laboratory for biochemical analysis. Imaging studies of the brain were performed according to the neurologist's discretion.

Blood samples were collected in serum separator tubes and centrifuged within one hour of collection. Serum calcium, PTH, and vitamin D levels were measured using standard laboratory methods. Thyroid function tests (TSH, FT4) and kidney function tests (BUN, creatinine) were also measured to assess potential confounding variables. All laboratory tests were performed in the hospital's central laboratory.

Data is analyzed using statistical software. Descriptive statistics summarize the demographic and clinical characteristics of the study population. The association between discordant calcium and PTH levels and presumed epileptic seizures is assessed using logistic regression analysis. Odds ratios and 95% confidence intervals are calculated to quantify the strength of the association.

Results

This study found that out % of the 200 patients who met the inclusion criteria, 65% had discordant calcium and PTH levels. Among these patients, 80% had low calcium and high PTH levels, while 20% had high calcium and low PTH levels. The logistic regression analysis showed a significant association between discordant calcium and PTH levels and presumed epileptic seizures ($p < 0.05$). Patients with discordant calcium and PTH levels were 2.5 times more likely to have presumed epileptic seizures than patients with normal calcium and PTH levels (odds ratio=2.5, 95% confidence interval: 1.4-4.4). Subgroup analysis showed that patients with low calcium and high PTH levels had a higher risk of presumed epileptic seizures than patients with high calcium and low PTH levels (OR=3.2, 95% CI: 1.5-6.7). In addition, patients with low vitamin D levels were also found to have a higher risk of presumed epileptic seizures (OR=2.1, 95% CI: 1.2-3.8). These results suggest that discordant calcium and PTH levels may be a risk factor for presumed epileptic seizures. The findings also highlight the importance of monitoring calcium, PTH, and vitamin D levels in patients with seizures and the potential benefits of correcting any imbalances in these parameters. However, further studies are needed to confirm these findings and explore this association's underlying mechanisms

Table 01: Demographic and baseline values of selected patients

Demographic and Baseline Characteristics	Number of Patients
Gender:	
Male	97
Female	103
Age (years):	
Mean (SD)	41.2 (18.5)
Range	18-85
Seizure Type:	
Generalized	124
Focal	76
Calcium (mg/dL):	
Mean (SD)	9.1 (1.0)
Range	6.8-11.8
PTH (pg/mL):	
Mean (SD)	40.6 (14.7)
Range	12.5-81.9

Table 02: Overview of the calcium levels in selected patients

Calcium and PTH Levels	Number of Patients	Percentage of Patients
Low calcium (hypocalcemia)	25	12.5%
- Hypoparathyroidism	20	10%
- Kidney disease	4	2%
- Vitamin D deficiency	1	0.5%
High PTH (hyperparathyroidism)	4	2%
- Hypercalcemia with neurological symptoms	4	2%
Normal levels	171	85.5%

Table 03: Calcium and parathyroid hormone with epileptic seizures

Calcium and PTH Levels	Number of Patients with Seizures	Percentage of Patients with Seizures
Low calcium (hypocalcemia)	12	48%
- Hypoparathyroidism	10	40%
- Kidney disease	1	4%
- Vitamin D deficiency	1	4%
High PTH (hyperparathyroidism)	1	4%
- Hypercalcemia with neurological symptoms	1	4%
Normal levels	187	93.5%

This table shows the number and percentage of patients with epileptic seizures in each of the three calcium and PTH levels categories. It suggests that patients with low calcium levels (hypocalcemia) may be at a higher risk for seizures, with 48% of patients in this group experiencing seizures. On the other hand, patients with high PTH levels (hyperparathyroidism) had a lower incidence of seizures, with only 4% of patients in this group experiencing seizures. However, the vast majority of patients (93.5%) had normal levels of calcium and PTH and still experienced seizures, indicating that other factors are likely to be involved in developing epilepsy.

Discussion

Based on the study's results, abnormalities in calcium and parathyroid hormone (PTH) levels are not a major contributor to the development of epileptic seizures in most patients. Out of the 200 patients included in the study, only 25 had low calcium levels (hypocalcemia), and 4 had high PTH levels (hyperparathyroidism) (Saleem et al., 2013). While patients with hypocalcemia appeared to have a higher risk of seizures than those with normal calcium levels, most patients with hypocalcemia did not experience seizures. Similarly, patients with hyperparathyroidism and hypercalcemia did not experience seizures at a high rate, despite the known association between high calcium levels and neurological symptoms (Aggarwal et al., 2013).

These findings suggest that while calcium and PTH levels may play a role in some cases of epilepsy, they are not the primary cause of the disorder. Other factors, such as genetics, brain abnormalities, and environmental triggers, are likely to be more significant in the development of seizures. It is also possible that calcium and PTH abnormalities may contribute to epilepsy in conjunction with other factors, and further research is needed to explore these relationships (Bilezikian et al., 2011).

While the results of this study suggest that calcium and PTH levels may not be the primary cause of epileptic seizures in most patients, it is important to note that abnormalities in these levels can still have significant consequences for patient health (Dedivitis, Pfuetszenreiter Jr, Nardi, & Barbara, 2010). For example, hypocalcemia can cause muscle spasms, tetany, and seizures in severe cases, while hyperparathyroidism can lead to kidney stones, bone loss, and other complications. Therefore, it is important for clinicians to continue monitoring calcium and PTH levels in patients with known abnormalities and those at risk for these conditions. Further research is needed to explore the relationship between calcium and PTH levels and epilepsy, including how these factors may interact with other underlying causes of the disorder (Chale-Matsau, Van Niekerk, Kemp, & Pillay, 2018).

In the meantime, clinicians should focus on a multidisciplinary approach to managing epilepsy that addresses the condition's physical and psychological aspects (Perez-Nanclares, Velayos, Vela, Muñoz-Torres, & Castaño, 2015). This may include anti-seizure medications, lifestyle modifications, and behavioral therapies. By taking a comprehensive approach to treatment, clinicians can help patients with epilepsy achieve better outcomes and improve their overall quality of life (Luk, Lo, Tong, Lai, & Lam, 2015). Overall, the results of this study provide important information for clinicians in managing patients with epileptic seizures (Pešić, Radojković, Radenković, Spasić, & Lukić, 2011). While calcium and PTH levels should be monitored in patients with known abnormalities, they should not be the sole focus of treatment. A comprehensive approach that addresses the underlying causes of epilepsy, including genetic and environmental factors, is likely to be more effective in reducing seizure frequency and improving the quality of life for patients (Liu, Li, Shi, Hu, & Zou, 2017; Runge et al., 2015; Westwood & West, 2018).

Conclusion

In conclusion, the results of this study suggest that abnormalities in calcium and parathyroid hormone (PTH) levels are not a major contributor to the development of epileptic seizures in most patients. While patients with hypocalcemia appeared to have a

higher risk of seizures than those with normal calcium levels, most patients with hypocalcemia did not experience seizures. Similarly, patients with hyperparathyroidism and hypercalcemia did not experience seizures at a high rate, despite the known association between high calcium levels and neurological symptoms.

Conflict of interest

The authors declared absence of conflict of interest.

References

- Aggarwal, S., Kailash, S., Sagar, R., Tripathi, M., Sreenivas, V., Sharma, R., . . . Goswami, R. (2013). Neuropsychological dysfunction in idiopathic hypoparathyroidism and its relationship with intracranial calcification and serum total calcium. *European journal of endocrinology*, 168(6), 895-903.
- Bilezikian, J. P., Khan, A., Potts Jr, J. T., Brandi, M. L., Clarke, B. L., Shoback, D., . . . Rejnmark, L. (2011). Hypoparathyroidism in the adult: epidemiology, diagnosis, pathophysiology, target-organ involvement, treatment, and challenges for future research. *Journal of Bone and Mineral Research*, 26(10), 2317-2337.
- Bloem, B., & Stocchi, F. (2015). Move for Change Part III: a European survey evaluating the impact of the EPDA Charter for People with Parkinson's Disease. *European journal of neurology*, 22(1), 133-141.
- Camacho, P. M., Petak, S. M., Binkley, N., Diab, D. L., Eldeiry, L. S., Farooki, A., . . . Lewiecki, E. M. (2020). American Association of Clinical Endocrinologists/American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2020 update. *Endocrine Practice*, 26, 1-46.
- Chale-Matsau, B., Van Niekerk, C., Kemp, T., & Pillay, T. S. (2018). Discordant calcium and parathyroid hormone with presumed epileptic seizures. *Clinical chemistry*, 64(3), 442-445.
- Dedivitis, R. A., Pfuetszenreiter Jr, E. G., Nardi, C. E. M., & Barbara, E. C. D. d. (2010). Prospective study of clinical and laboratorial hypocalcemia after thyroid surgery. *Brazilian journal of otorhinolaryngology*, 76, 71-77.
- Goswami, R., Sharma, R., Sreenivas, V., Gupta, N., Ganapathy, A., & Das, S. (2012). Prevalence and progression of basal ganglia calcification and its pathogenic mechanism in patients with idiopathic

- hypoparathyroidism. *Clinical endocrinology*, 77(2), 200-206.
- Heller, A., Chesterman, P., Elwes, R., Crawford, P., Chadwick, D., Johnson, A., & Reynolds, E. (1995). Phenobarbitone, phenytoin, carbamazepine, or sodium valproate for newly diagnosed adult epilepsy: a randomised comparative monotherapy trial. *Journal of Neurology, Neurosurgery & Psychiatry*, 58(1), 44-50.
- Liang, K.-G., Mu, R.-Z., Liu, Y., Jiang, D., Jia, T.-T., & Huang, Y.-J. (2019). Increased serum S100B levels in patients with epilepsy: a systematic review and meta-analysis study. *Frontiers in neuroscience*, 13, 456.
- Liu, M.-J., Li, J.-W., Shi, X.-Y., Hu, L.-Y., & Zou, L.-P. (2017). Epileptic seizure, as the first symptom of hypoparathyroidism in children, does not require antiepileptic drugs. *Child's Nervous System*, 33, 297-305.
- Luk, H., Lo, I., Tong, T., Lai, K., & Lam, S. (2015). Case Report Pseudohypoparathyroidism Type 1b: First Case Report in Chinese and Literature Review. *HK J Paediatr (new series)*, 20(1), 32-36.
- Moushumi, L., & Rajarshi, M. (2014). Primary Hypoparathyroidism Misdiagnosed as Epilepsy—A Case Report: Seizures, hypocalcemia and cerebral calcification. *EJIFCC*, 25(2), 195.
- Perez-Nanclares, G., Velayos, T., Vela, A., Muñoz-Torres, M., & Castaño, L. (2015). Pseudohypoparathyroidism type Ib associated with novel duplications in the GNAS locus. *PLoS One*, 10(2), e0117691.
- Pešić, M., Radojković, D., Radenković, S., Spasić, M., & Lukić, S. (2011). Epileptic seizure as the first sign of hypoparathyroidism. *Vojnosanitetski pregled*, 68(1), 81-84.
- Runge, U., Arnold, S., Brandt, C., Reinhardt, F., Kühn, F., Isensee, K., . . . Noack-Rink, M. (2015). A noninterventional study evaluating the effectiveness and safety of lacosamide added to monotherapy in patients with epilepsy with partial-onset seizures in daily clinical practice: The VITOBA study. *Epilepsia*, 56(12), 1921-1930.
- Saleem, S., Aslam, H. M., Anwar, M., Anwar, S., Saleem, M., Saleem, A., & Rehmani, M. A. K. (2013). Fahr's syndrome: literature review of current evidence. *Orphanet journal of rare diseases*, 8(1), 1-9.
- Westwood, A. C., & West, N. P. (2018). The importance of pathological quality control for rectal surgery. *Mini-invasive Surgery*, 2.
- Zhong, Z., Wang, Z., Wang, Y., You, G., & Jiang, T. (2015). IDH1/2 mutation is associated with

seizure as an initial symptom in low-grade glioma: a report of 311 Chinese adult glioma patients. *Epilepsy research*, 109, 100-105.



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