

ORIGINAL RESEARCH PAPER

General Medicine

AN ASSESSMENT OF CALCIUM HOMEOSTASIS ABNORMALITY IN PATIENTS TAKING PROLONGED ANTICONVULSANTS IN TERTIARY CARE

KEY WORDS: Calcium Homeostasis, Anticonvulsants

Dr Hiren Rabadia	M.D.Medicine
Dr. Kolhe Shubham Rajeshwar	First Year Medicine Resident
Dr. Bhadresiya Tarak Yagneshbhai	First Year Medicine Resident
Dr.Gabani Janvi Dilipbhai	First Year Medicine Resident
Dr. Dilipkumar Maghabhai Chaudhary	First Year Medicine Resident
Dr. Amitkumar L. Gamit*	Associate Professor *Corresponding Author

ABSTRACT

This study is to assess calcium homeostasis abnormality in patients taking prolong anticonvulsants admitted in tertiary care hospital.

INTRODUCTION

One of the most well-known disease entities that causes major morbidity is epilepsy. long-term use of anti-epileptic medications that are known to have serious side effects like major changes in bone and mineral metabolism. Hypocalcemia, lower serum 25-(OH) vitamin D concentration, raised serum immunoreactive parathyroid hormone concentration, reduced bone mass, and histologic indications of osteomalacia have been documented in 10-60% of anticonvulsant drug-treated populations. Hypocalcemia, hypocalciuria, decreased 25 hydroxy vitamin D, and high alkaline phosphatase and immunoreactive parathyroid hormone in serum are the most common laboratory findings. Anticonvulsant-induced hypocalcemia can cause seizures in addition to producing bone deformities. Hypocalcemic seizures are a rare and under diagnosed side effect of longterm AED. Hence, evaluation of these anti convulsant induced complications assumes importance in view of their treatable nature, which forms the rationale of my taking up this study

Study Details

A cross sectional study was conducted in patients visiting the Tertiary Care Hospital in South Gujarat in patients who are on AED since one year or more with sample size of 107, All indoor patients above 18 years of age taking antiepileptics for one year or more and willing to give consent were included and Pregnant women, Patients who have taken vitamin D3 and calcium supplements, Patients who have kidney disease and liver disease were not included. A pretested semi structured Performa was used for data collection. All indoor patients of medicine wards who are above 18 years of age, their own informed consent was taken. All patients' medical histories and general physical examination was documented and patients taking antiepileptics since 1 year or more included in study. A blood sample from each patient collected for measuring CBC, S. calcium, S. phosphurus, S. vit D3 level, renal

function test and liver function test. Collected data entered in excel sheet and analysed using EPI info and Open Epi software. Quantitative data was analysed by using measure of central tendency and chi-square applied.

Table 1: Age-group wise distribution of patients (n=107)

Age-group	No of cases (n)	Percent
18-25	38	35.5
26-40	53	49.5
>41	16	15.0

Table 2: Gender wise distribution of patients (n=107)

Gender	No of cases (n)	Percent
Male	54	50.5
Female	53	49.5

Table 3: Distribution of patients according to duration of treatment (n=107)

Duration of treatment	No of cases (n)	Percent	
1 year	68	63.6	
1-2 year	35	32.7	
>2 years	4	3.7	

Table 4: Distribution of patients according to S.calcium level (n=107)

S.Calcium level	No of cases (n)	Percent
Normal	72	67.3
Hypocalcemia	35	32.7
Total	107	100.0

Table 5: Distribution of patients according to S.phosphate level (n=107)

S.phosphate level	No of cases (n)	Percent
Normal	67	62.6
Hypophosphatemia	40	37.4
Total	107	100.0

Table 6: Distribution of patients according to Vit D level (n=107)

Vit D level	No of cases (n)	Percent
Normal	62	57.9
Low	45	42.1
Total	107	100.0

Table 7: Distribution of patients according to number of drugs (n=107)

Number of drugs	No of cases (n)	Percent
1	72	67.3
2	24	22.4
3	8	7.5
>3	3	2.8

Table 10: Association between duration of treatment and S.calcium level

48	20	68	0.55
22	13	35	
2	2	4	1
72	35	107	
	22	22 13 2	22 13 35 2 2 4 72 35 107

Table 11: Association between no. of drugs and S. Calcium level

No of drugs	Normal	Hypocalcemia	Total	P value
1	53	19	72	0.09
2	15	9	24	
3	3	5	8	
>3	1	2	3	
Total	72	35	107	0

Table 12: Association between S.phosphate level and S.calcium level

S.phosphate level	Normal S.Calcium	Hypocalcemia	Total	P value
Normal S. Phosphate	53	19	72	0.04
Hypophosphatemia	19	16	35	
Total	72	35	107	
	Chi-square=3.9	9, df=1		

This table presents significant association between S.phosphate and S.calcium level. (Ch square=3.99, p value=0.04)

Table: 13 Association between Vit D level and S.calcium level

Vit D level	Normal	Hypocalcemia	Total	P value
Normal	59	3	62	0.000
Low	13	32	45	
Total	72	35	107	
	7.4	Chi-square=52.0, df=1	2	

Table 14: Association between seizure control and S.calcium level

Seizure control	Normal	Hypocalcemia	Total	P value
Yes	60	22	82	0.01
No	12	13	25	
Total	72	35	107	

This table found significant association between seizure control and S.calcium level. (Ch square=5.5, p value=0.01) In patients in whom seizure was not controlled, about half of th patients had hypocalcemia.

Table 15: Association between Vit D level and S. Phosphate level

Vit D level	Normal	Hypophosphatemia	Total	P value
Normal	41	21	62	0.37
Low	26	19	45	
Total	67	40	107	
		Chi-square=0.77, df=1		

There was no association found between Vit D level and S.phosphate level. (Chisquare=0.77, p.value=0.37)

Table 16: Association between no. of drugs and S.phosphate level

No of drugs	Normal	Hypophosphatemia	Total	P value
1	55	17	72	0.000
2	10	14	24	
3	2	6	8	
>3	0	3	3	
Total	67	40	107	

This table found significant association between number of anti-convulsant drugs and S.phosphate level. (Chi-square=20.19, p value=<0.001) About three-fourth patients had hypophosphatemia who were taking three anti-convulsant drugs while all the patients had hypophosphatemia who were on more than three anti-convulsant drugs.

Table 17: Association between duration of treatment and S.phosphate level

Duration of treatment	Normal	Hypophosphatemia	Total	P value
1 year	55	13	68	0.000
1-2 year	10	25	35	
>2 years	2	2	4	
Total	67	40	107	

This table presents significant association between duration of treatment and S.phosphate level. (Chi-square=27.29, p value=<0.001)

CASE STUDY DISCUSSION

The aim of the study was to assess the prevalence of hypocalcemia among patients on prolonged anticonvulsant therapy. A cross sectional study was conducted in 107 patients visiting the Tertiary Care Hospital in South Gujarat in patients who are fulfilling the inclusion criteria and on anticonvulsants since I year or more

Associations In Our Study

No significant association found between age-group and S.calcium level.

No significant association was seen between duration of anticonvulsant treatment and S.calcium level.

Significant association was not found between number of anticonvulsant drugs and S.calcium level. Significant association reported between S.phosphate and S.calcium level.

Significant association found between Vit D level and S.calcium level. More than two-third patients found having hypocalcemia who had Vit D deficiency.

Significant association reported between seizure control and S.calcium level. In patients in whom seizure was not controlled, about half of the patients had hypocalcemia No association found between Vit D level and S.phosphate level.

Significant association was seen between number of anticonvulsant drugs and S.phosphate level.

Significant association between duration of treatment and S.phosphate level.

CONCLUSIONS

We conclude that clinical bone disease in adults receiving long-term anticonvulsant therapy is common with evidence of abnormalities in calcium and bone metabolism is quite frequent. Such patients should have serum calcium and phosphorus concentrations should be measured once or twice yearly. If available, measurements of serum Vit D concentration and bone mineral mass are probably the most sensitive methods of detecting and monitoring abnormalities in calcium metabolism. Hence this study concludes that there is significant hypocalcemia and Hypovitaminemia D in patients on prolonged anticonvulsant therapy and serious consideration should be given to long term treatment with vitamin D.

REFERENCES:

- Sridharan R, Murthy BN. Prevalence and pattern of epilepsy in India. Epilepsia [Internet]. 1999 [cited 2021 Nov 20];40(5):631-6. Available from: https://pubmed.ncbi.nlm.nih.gov/10386533/
- Hainn TJ, Halstead LR. Anticonvulsant drug-induced osteomalacia: alterations in mineral metabolism and response to vitamin D3 administration. Calcif Tissue Int [Internet]. 1979 Dec [cited 2021 Nov 20];27(1):13–8. Available from: https://pubmed.ncbi.nlm.nih.gov/223750/
- Kruse K. On the pathogenesis of anticonvulsant-drug-induced alterations of calcium metabolism. Eur J Pediatr [Internet]. 1982 [cited 2021 Nov 20];138(3):202-5. Available from: https://pubmed.ncbi.nlm.nih.gov/ 7117282/
- Holick MF, Maclaughlin JA, Clark MB, Holick SA, Potts JT, Anderson RR, et al. Photosynthesis of previtamin D3 in human skin and the physiologic consequences. Science [Internet]. 1980 [cited 2021 Nov 20]:210(4466):203-5. Available from: https://pubmed.ncbi.nlm.nih.gov/6251551/
- Thomas MK, Demay MB. Vitamin D deficiency and disorders of vitamin D metabolism. Endocrinol Metab Clin North Am [Internet]. 2000 [cited 2021 Nov 20];29(3):611–27. Available from: https://pubmed.ncbi.nlm.nih.gov/ 11033763/
- Bikle DD, Gee E, Halloran B, Kowalski MA, Ryzen E, Haddad JG. Assessment of the free fraction of 25-hydroxyvitamin D in serum and its regulation by albumin and the vitamin D-binding protein. J Clin Endocrinol Metab [Internet]. 1986 [cited 2021 Nov 20];63(4):954-9. Available from: https://pubmed.ncbi.nlm.nih.gov/3745408/
- Bikle DD, Siiteri PK, Ryzen E, Haddad JG, Gee E. Serum protein binding of 1,25- dihydroxyvitamin D: a reevaluation by direct measurement of free metabolite levels. J Clin Endocrinol Metab [Internet]. 1985 [cited 2021 Nov 20];61(5):969-75. Available from: https://pubmed.ncbi.nlm.nih.gov/ 3840175/
- Nykjaer A, Dragun D, Walther D, Vorum H, Jacobsen C, Herz J, et al. An endocytic pathway essential for renal uptake and activation of the steroid 25-(OH) vitamin D3.