Effect of antiseizure medications on calcium profile, thyroid profile and bone mineral density in children- A case control study

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INTRODUCTION

- Patients with epilepsy require long-term therapy with antiseizure medications (ASMs).
- ASMs are known to be associated with decreased bone mineral density (BMD), altered bone turnover, and increased risk of fracture.[1]
- A number of biochemical abnormalities like hypocalcaemia, hypophosphatemia, low biologically active vitamin D levels, and increase in parathormone (PTH) level have been reported in patients on ASMs.[2]

OBJECTIVES

- To compare mean levels of Serum Calcium, Phosphorus, Alkaline phosphatase, T4 and TSH between cases and controls.
- To estimate proportion of children with low bone mineral density (BMD) amongst cases and controls (defined as those with Z scores below -2).
- To estimate correlation of BMD, calcium and Thyroid profile with number, duration and type of ASM (inducers vs non inducers)
- To estimate correlation of BMD with factors like duration of sunlight exposure and physical activity .

61.58% of cases and 4.6% controls had received Vit-D supplementation prior to enrolment in the study (in last 1 year).

MATERIAL & METHODS

This is a prospective case-control study conducted from April 2018 to December 2021. Cases were recruited from the epilepsy unit-

Inclusion criteria:

Children aged 5-18 years, on ASM for 1 or more years.

Exclusion criteria:

Children with intellectual disability, un co-operative patients who are unable to lie down during DEXA scan, with cerebral palsy, on prolonged steroids.

Controls were siblings of these cases.

Both the groups were studied for Serum calcium, phosphorus, alkaline phosphatase, T_3, T_4 and TSH and Dual-energy X-ray absorptiometry (DEXA). DEXA-Z score were calculated for AP spine and dual femur. Different factors affecting the BMD like duration of therapy, type of drug (enzyme inducer vs non inducers) were analysed.

All Statistical Analysis was done by using SPSS software with version 25.0. Mann-Whitney U test was used to test the significant median difference between groups for continues variable who follows non-normal distribution. Z-test for difference between two proportion was used to test significant difference between two proportions.

Through out results 5% level of significance was used, all results was shown by 95% of confidence. P-value less than 0.05 considered as significant.

RESULTS

Total enrolled
Cases -78
Controls - 48

No significant difference noted between Physical /other Parameters in cases vs controls

There was no difference between median Calcium, Thyroid Levels or Z scores. Children on ASM for more than 3 y had significantly lower BMD. No Effect of type or Number of ASM, or Vitamin D Supplementation. (30% vs 33%)

Table-1

		Mean	p-value
Age(yr.)	Cases	11.26 ±3.66	0.76
	Control	11.46 ±3.47	
Weight in kg	Cases	35.47 ±17.30	0.79
	Control	36.32 ±16.98	
Height in Meters	Cases	1.41 ±0.20	0.73
	Control	1.42 ±0.19	
BMI	Cases	16.87 ±4.62	0.85
	Control	17.03 ±4.54	

Parameter	Cases N = 78	Controls N = 48	P value
Sunlight exposure > 60 mins	47	34	0.551
Physical activity > 60 mins	38	27	0.328

Table-2

Parameter	Cases (n = 78)	Control (n = 48)	P- value
Sr Calcium (mg/dL)	9.76	9.71	0.55
Sr Po4 (mg/dL)	4.89	4.96	0.67
Alk PO_4 (U/L)	552.50	488.50	0.29
Free T_4 (ug/dl)	0.99	1.06	0.09
TSH (ulU/ml)	1.95	1.94	0.56
A-P Spine (Z score)	-1.1	-0.9	0.436
Dual Femur (Z score)	-1.0	-1.0	0.391
Low BMD	24 (30.76%)	10 (20.83%)	0.22

Table-3

Parameter	Category	Total no. N=78	Low BMD N = 24	P value
Duration of therapy	<= 2 years	27	6	0.0006
	> 2 years	51	18	
No. of ASM	Single	44	14	0.253
	Poly	34	10	
Type of ASM	Inducers	33	10	0.253
	Non-inducers	45	14	

Table-4

Parameter	Category	Total no.	High SAP levels N = 53	P value
Duration of therapy	<=2 years	27	20	0.01
	>2 years	51	33	
Number of ASMs	Single	44	26	0.847
	Poly	34	27	
Type of ASM-	Inducers	33	27	0.847
	Non-inducers	45	26	

Serin et al[3] and a metanalysis by Zhang et al.[4] showed no difference in biochemical (Serum Calcium and Sr Phosphorus) and BMD Z scores. However, Coppola et al[5] and Hasaneen et al[6] showed more severe effects on biochemical profile and Z scores on ≥2 years of ASMs.

LIMITATIONS

Low sample size; We did not have age and sex matched analysis due to fewer numbers, as parents of all siblings did not consent for the study. The study was halted for 2 years during the covid pandemic. Vit D levels were not measured.

CONCLUSION

 # Prevalence of low BMD was 30% amongst cases and 20% amongst controls.

 # Duration of ASM longer than 3 years had significant effect on bone health.

Recommendations and areas of future research

The study should be done in larger number of patients with age and sex matched controls, with longer follow up, Vit D levels should be added.

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