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Study of lipid profile and liver function in children on anticonvulsant drugs

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Abstract

Several studies have reported that commonly used antiepileptic drugs like phenytoin, and carbamazepine increase serum High Density Lipoproteins Cholesterol (HDL-C) levels, while some others documented no such effect. Further, some researchers also observed that valproic acid and other newer antiepileptic drugs like lamotrigine and levetiracetam has no influence on serum lipid profile. The present study was planned to assess and compare serum lipid profile and liver function in children on commonly used antiepileptic drugs like carbamazepine and valproic acid attending Neurology OPD of a tertiary care hospital in Pune, India compared to normal subjects.

Keywords: lipid profile, liver function, drugs

Introduction

Epilepsy refers to a disorder of brain characterised by the periodic and unpredictable occurrence of seizure. The term 'Seizure' refers to a transient alteration of behaviour due to the disordered, synchronous, and rhythmic firing of populations of brain neuron ^[1]. The episodes of seizures are unpredictable and their frequency is highly variable. As per WHO, epilepsy is one of the most common serious brain disorder that affects not only the individual, but also disturbs the family and the society in general. WHO estimates that 8 per 1000 population worldwide have epilepsy, with higher prevalence in developing countries as compared to developed countries. Further, there are approximately 10 million people estimated to be with epilepsy in India accounting for 1/5th of the global burden ^[2]. Epilepsy occurs in men and women and can begin at any age, but is most frequently diagnosed in early life or in old age. Up to 5% of the world's population may have a single seizure at some time in their lives, but a diagnosis of epilepsy is reserved for those who have recurring seizures, i.e. at least two unprovoked seizures. The anticonvulsants also commonly known as antiepileptic drugs are a diverse group of pharmaceuticals used in the treatment of epileptic seizures. The goal of an anticonvulsant is to suppress the rapid and excessive firing of neurons that start a seizure. Treatment of epilepsy is often a lifelong affair. Several studies have reported that commonly used antiepileptic drugs like phenytoin, phenobarbital and carbamazepine, increase serum HDL-C levels, while some others documented no such effect. Further, some researchers also observed that valproic acid and other newer antiepileptic drugs like lamotrigine and levetiracetam has no influence on serum lipid profile ^[3]. Serum concentration of certain lipids and lipoproteins in children are important risk factors for the development of coronary heart disease in later life. Considerable data has suggested that besides total cholesterol (TC), elevated triglyceride (TG) concentrations, increased LDL-C and decreased HDL-C contribute to cardiovascular diseases. Thus, assessing changes in serum lipid levels following antiepileptic drugs may be useful to choose the safest drug and prevention of cardiovascular complications in later life ^[4]. The effect of antiepileptic drugs on serum lipid levels had already been documented in western literature. However, information in this regard is scarce from India. So, the present study was planned to find and compare the effect of conventional and newer antiepileptic drugs on lipid profile of epileptic patients.

Materials and Methodology

This is an analytical cross sectional case control study done at tertiary hospital of Pimpri, India. The study was carried out over the period of two years. assuming the mean LDL of 77.86 in Valproic acid group with standard deviation of 7.4 and mean LDL 117.93 in carbamazepine group with standard deviation of 15.78 at significance level of 5 % and power of 80%, sample size works out to be 68 in each group. Total 204 children were included in this study (68 in Valproate group, 68 in carbamazepine group, 68 in control group) All seizure disorder patients were treated for atleast 6 months. Children between 2-15 years were included in this study. Children who received monotherapy with Carbamazepine and Valproic acid for atleast 6 months were our cases. Age and sex matched healthy controls were enrolled from OPD

Statistical analysis

Descriptive statistics explained using mean ± SD. Inferential statistics was used depending on the nature of variables. We used one-way-ANOVA and followed by independent test for comparison with control group and statistically significant was considered at p-value <0.05

Observation and Result

Table 1: Comparison of age in group A, group B and group C

Group	n	Age (Yrs)		F Value	P Value
		Mean	SD		
Group A	68	6.68	2.334	0.89	0.41
Group B	68	6.54	1.958		
Group C	68	6.22	1.819		

Group A Vs Group B: P>0.05 Group A Vs Group C: P>0.05 Group B Vs Group C: P>0.05

It was observed that the mean age of patients in group A was 6.68±2.334 yrs, while of Group B and group C was 6.54±1.958 and 6.22±1.819 respectively. And the difference observed in the three group was not significant.

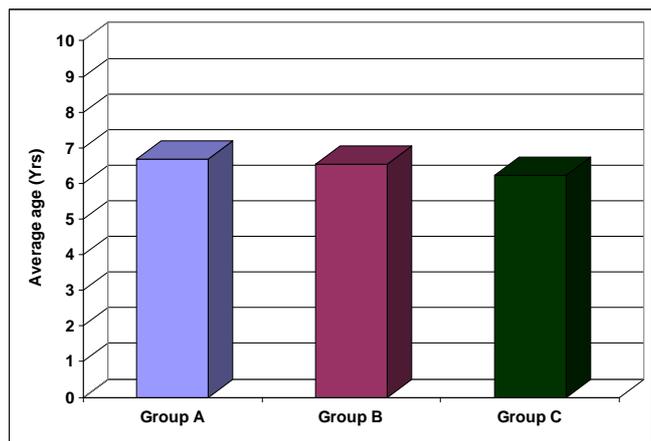


Fig 1: Bar diagram showing comparison of age in group A, group B and group C

Table 2: Sex wise distribution of cases in group A, group B and group C

Sex	Group A	Group B	Group C	Total
Male	37	37	37	111
Female	31	31	31	93
Total	68	68	68	204

Chi-square = 0, P = 1

The sex distribution among all the three study groups was equal with 37 male and 31 female children each.

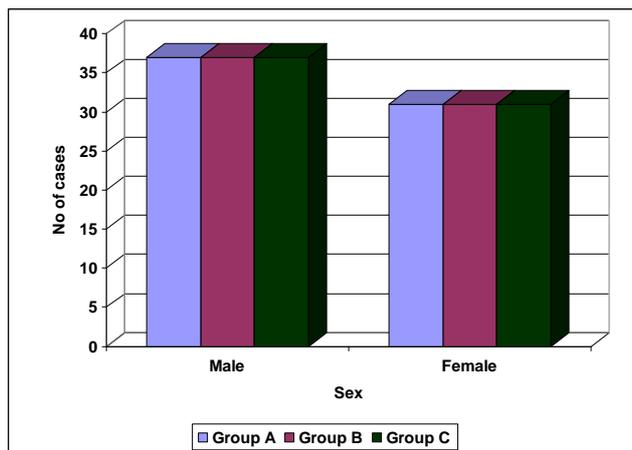


Fig 2: Bar diagram showing sex wise distribution of cases in group A, group B and group C

Table 4: Comparison of BMI in group A, group B and group C

Group	n	BMI		F Value	P Value
		Mean	SD		
Group A	68	14.96	0.71	2.78	0.064
Group B	68	14.69	0.71		
Group C	68	14.81	0.61		

Group A Vs Group B: P>0.05 Group A Vs Group C: P>0.05 Group B Vs Group C: P>0.05

The mean BMI of group A was 14.96±0.71 while of group B and group C was 14.69±0.71 and 14.81±0.61 respectively and difference were not statistically significant.

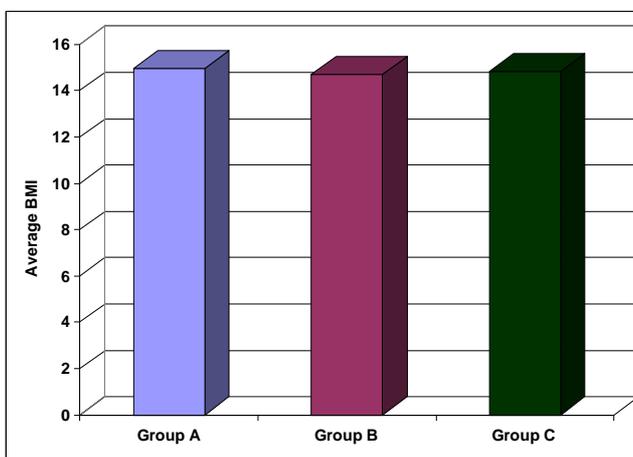


Fig 3: Bar diagram showing comparison of BMI in group A, group B and group C

Table 5: Comparison of serum Cholesterol in group A, group B and group C

Group	n	Sr. Cholesterol (mg/dl)		F Value	P Value
		Mean	SD		
Group A	68	191.22	19.068	9.63	<0.0001
Group B	68	181.38	17.200		
Group C	68	179.57	13.148		

Group A Vs Group B: P<0.002 Group A Vs Group C: P<0.0001 Group B Vs Group C: P>0.05

The mean serum cholesterol level of group A Children was $191.22 \pm 19.068 \text{mg/dl}$ while that of group B and group C was $181.38 \pm 17.200 \text{mg/dl}$ and $179.57 \pm 13.148 \text{mg/dl}$ respectively but difference were statistically significant. The difference observed in serum cholesterol level in group A Vs group B and group A Vs group C was statistically significant. But the difference observed in group B Vs group C was not significant.

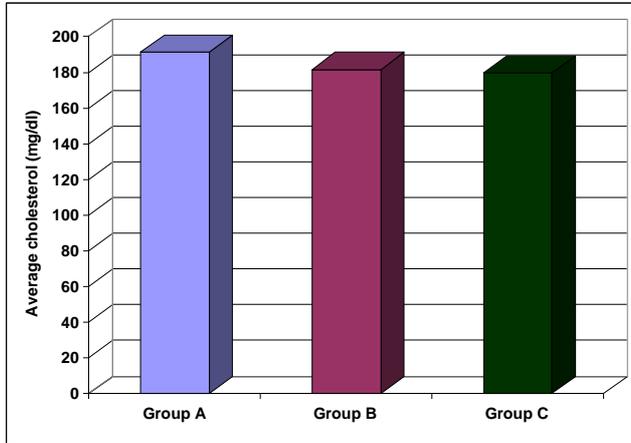


Fig 4: Bar diagram showing comparison of serum Cholesterol in group A, group B and group C

Table 6: Comparison of LDL cholesterol in group A, group B and group C

Group	LDL cholesterol (mg/dl)			F Value	P Value
	n	Mean	SD		
Group A	68	93.96	11.156	22.56	<0.0001
Group B	68	83.88	10.778		
Group C	68	84.46	6.989		

Group A Vs Group B: $P < 0.0001$ Group A Vs Group C: $P < 0.0001$ Group B Vs Group C: $P > 0.05$

The mean LDL levels were raised in group A children ($93.96 \pm 11.156 \text{mg/dl}$) as compared to group B ($83.88 \pm 10.778 \text{mg/dl}$) and group C ($84.46 \pm 6.989 \text{mg/dl}$) and the difference was also statistically significant. The difference observed in LDL in group A Vs group B and Group A Vs group C was statistically significant. But the difference observed in group B Vs group C was not significant.

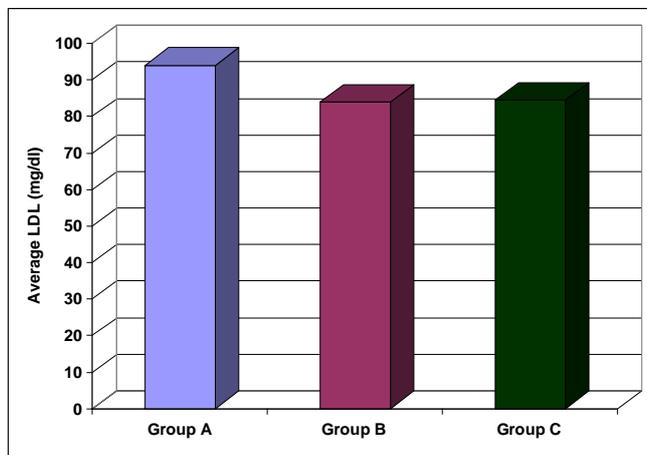


Fig 5: Bar diagram showing comparison of LDL cholesterol in group A, group B and group C

Table 7: Comparison of HDL cholesterol in group A, group B and group C

Group	HDL cholesterol (mg/dl)			F Value	P Value
	n	Mean	SD		
Group A	68	67.43	6.537	45.29	<0.0001
Group B	68	59.57	5.765		
Group C	68	58.50	5.570		

Group A Vs Group B: $P < 0.0001$ Group A Vs Group C: $P < 0.0001$ Group B Vs Group C: $P > 0.05$

The rise in mean serum cholesterol in group A ($67.43 \pm 6.537 \text{mg/dl}$) was statistically significant as compared to group B ($59.57 \pm 5.765 \text{mg/dl}$) and group C ($58.50 \pm 5.570 \text{mg/dl}$) but difference were statistically significant. The difference observed in HDL in group A Vs group B and group A Vs group C was statistically significant. But the difference observed in group B Vs group C was not significant.

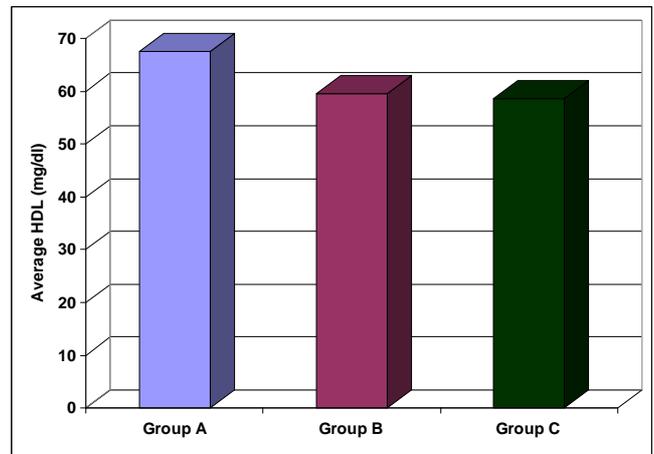


Fig 6: Bar diagram showing comparison of HDL cholesterol in group A, group B and group C

Table 8: Comparison of Triglyceride in group A, group B and group C

Group	Triglyceride (mg/dl)			F Value	P Value
	n	Mean	SD		
Group A	68	141.62	13.567	18.46	<0.0001
Group B	68	131.43	12.372		
Group C	68	129.93	10.490		

Group A Vs Group B: $P < 0.0001$ Group A Vs Group C: $P < 0.0001$ Group B Vs Group C: $P > 0.05$

While comparing the mean serum triglyceride it was seen that in group A the serum triglyceride level was $141.62 \pm 13.567 \text{mg/dl}$, while in group B and group C was $131.43 \pm 12.372 \text{mg/dl}$ and $129.93 \pm 10.490 \text{mg/dl}$ but difference were statistically significant. The difference observed in Triglyceride in group A Vs group B and group A Vs group C was statistically significant. But the difference observed in group B Vs group C was not significant.

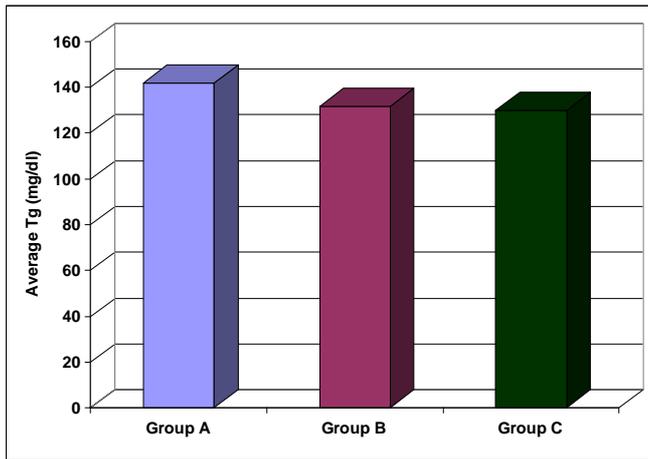


Fig 7: Bar diagram showing comparison of Triglyceride in group A, group B and group C

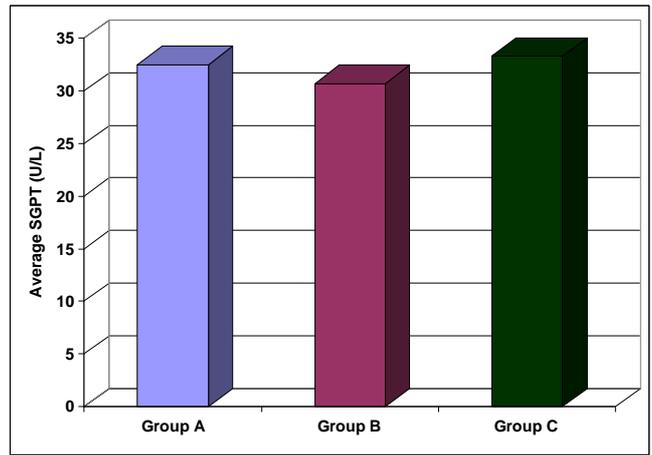


Fig 9: Bar diagram showing comparison of SGPT in group A, group B and group C

Table 9: Comparison of SGOT in group A, group B and group C

Group	n	SGOT (U/L)		F Value	P Value
		Mean	SD		
Group A	68	32.44	17.230	0.40	0.67
Group B	68	33.75	13.775		
Group C	68	34.94	17.686		

Group A Vs Group B: $P > 0.05$ Group A Vs Group C: $P > 0.05$
Group B Vs Group C: $P > 0.05$

The mean SGOT among group A, group B and group C was 32.44 ± 17.230 U/L, 33.75 ± 13.775 U/L and 34.94 ± 17.686 U/L. the difference observed in the SGOT level in all the three groups was not significant.

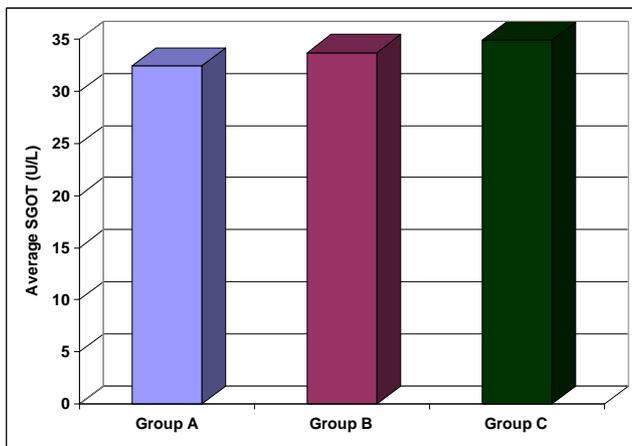


Fig 8: Bar diagram showing comparison of SGOT in group A, group B and group C

Table 10: Comparison of SGPT in group A, group B and group C

Group	n	SGPT (U/L)		F Value	P Value
		Mean	SD		
Group A	68	32.49	15.075	0.52	0.60
Group B	68	30.69	15.259		
Group C	68	33.26	15.086		

Group A Vs Group B: $P > 0.05$ Group A Vs Group C: $P > 0.05$
Group B Vs Group C: $P > 0.05$

The mean SGPT level was 32.49 ± 15.075 U/L in group A while that was 30.69 ± 15.259 U/L and 33.26 ± 15.086 U/L in group B and group C respectively. And the difference observed in these groups was statistically non significant.

Table 11: Comparison of total Bilirubin in group A, group B and group C

Group	n	Total bilirubin (mg/dl)		F Value	P Value
		Mean	SD		
Group A	68	0.356	0.1297	3.37	0.036
Group B	68	0.325	0.1262		
Group C	68	0.300	0.1209		

Group A Vs Group B: $P > 0.05$ Group A Vs Group C: $P < 0.05$
Group B Vs Group C: $P > 0.05$

The total bilirubin in group A, group B and group C was measured to be 0.356 ± 0.1297 mg/dl, 0.325 ± 0.1262 mg/dl and 0.300 ± 0.1209 mg/dl respectively but difference were statistically significant. The difference observed in Total Bilirubin level in group A Vs group C was statistically significant. But the difference observed in group A Vs group B and group B Vs group C was not significant.

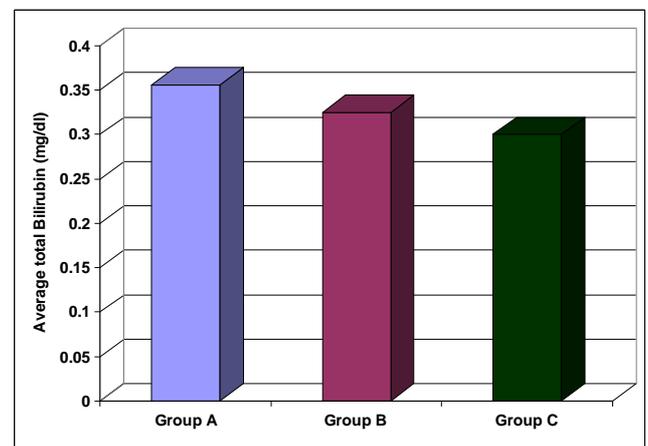


Fig 10: Bar diagram showing comparison of total Bilirubin in group A, group B and group C

Table 12: Comparison of direct Bilirubin in group A, group B and group C

Group	n	Direct bilirubin (mg/dl)		F Value	P Value
		Mean	SD		
Group A	68	0.168	0.0921	0.79	0.46
Group B	68	0.169	0.0935		
Group C	68	0.151	0.0872		

Group A Vs Group B: $P > 0.05$ Group A Vs Group C: $P > 0.05$
Group B Vs Group C: $P > 0.05$

The mean direct bilirubin level in group A was 0.168 ± 0.0921 mg/dl while that in group B and group C was 0.169 ± 0.0935 mg/dl and 0.151 ± 0.0872 mg/dl respectively but difference were not statistically significant.

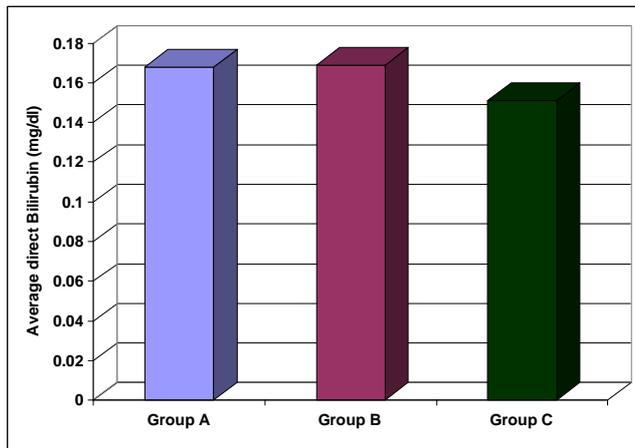


Fig 11: Bar diagram showing comparison of direct Bilirubin in group A, group B and group C

Table 13: Comparison of serum ALP in group A, group B and group C

Group	n	Sr. ALP (IU/L)		F Value	P Value
		Mean	SD		
Group A	68	92.72	37.429	0.79	0.46
Group B	68	99.56	40.240		
Group C	68	99.99	35.795		

Group A Vs Group B: $P > 0.05$ Group A Vs Group C: $P > 0.05$
 Group B Vs Group C: $P > 0.05$

The mean serum ALP in group A, group B and group C was 92.72 ± 37.429 IU/L, 99.56 ± 40.240 IU/L and 99.99 ± 35.795 IU/L respectively. And the difference observed in the three groups was not significant.

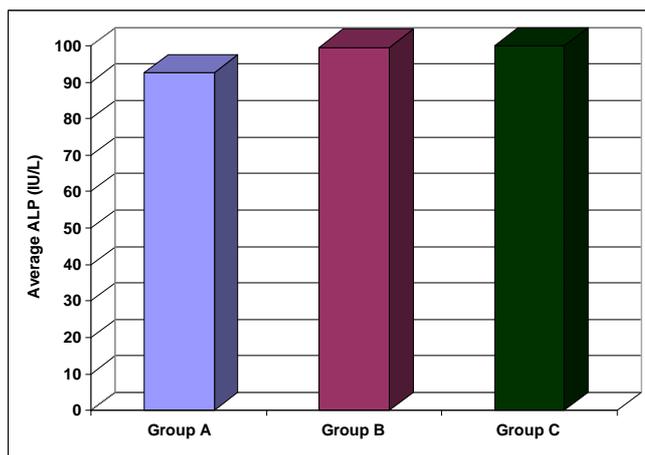


Table 14: Bar diagram showing comparison of serum ALP in group A, group B and group C

Summary

The mean age of patients in group A was 6.68 ± 2.334 yrs, while of Group B and group C was 6.54 ± 1.958 and 6.22 ± 1.819 respectively. The sex distribution among all the three study groups was equal with 37 male and 31 female children each. The mean BMI of group A was 14.96 ± 0.71 while of group B and group C was 14.69 ± 0.71 and 14.81 ± 0.61 respectively. 191.22 ± 19.068 mg/dl was the mean

serum cholesterol level of group A Children while that of group B and group C was 181.38 ± 17.200 mg/dl and 179.57 ± 13.148 mg/dl respectively. The difference observed in serum cholesterol level in group A with group B and group C was statistically significant. But the difference observed in group B with group C was not significant. The mean LDL levels were raised in group A children (93.96 ± 11.156 mg/dl) as compared to group B (83.88 ± 10.778 mg/dl) and group C (84.46 ± 6.989 mg/dl) and the difference was also statistically significant. The difference observed in group B and group C was not statistically significant. The rise in mean serum cholesterol in group A (67.43 ± 6.537 mg/dl) was statistically significant as compared to group B (59.57 ± 5.765 mg/dl) and group C (58.50 ± 5.570 mg/dl). The difference in mean serum HDL in group B and group C was not statistically significant. While comparing the mean serum triglyceride it was seen that in group A the serum triglyceride level was 141.62 ± 13.567 mg/dl, while in group B and group C was 131.43 ± 12.372 mg/dl and 129.93 ± 10.490 mg/dl. The rise in serum triglyceride in group A was statistically significant as compared to group B and Group C. The mean SGOT among group A, group B and group C was 32.44 ± 17.230 U/L, 33.75 ± 13.775 U/L and 34.94 ± 17.686 U/L. the difference observed in the SGOT level in all the three groups was not significant. The mean SGPT level was 32.49 ± 15.075 U/L in group A while that was 30.69 ± 15.259 U/L and 33.26 ± 15.086 U/L in group B and group C respectively. And the difference observed in these groups was statistically non significant. The total bilirubin in group A, group B and group C was measured to be 0.356 ± 0.1297 mg/dl, 0.325 ± 0.1262 mg/dl and 0.300 ± 0.1209 mg/dl respectively. The difference in group A and group C was not statistically significant. The mean direct bilirubin level in group A was 0.168 ± 0.0921 mg/dl while that in group B and group C was 0.169 ± 0.0935 mg/dl and 0.151 ± 0.0872 mg/dl respectively. The mean serum ALP in group A, group B and group C was 92.72 ± 37.429 IU/L, 99.56 ± 40.240 IU/L and 99.99 ± 35.795 IU/L respectively. And the difference observed in the three groups was not significant.

Conclusion

Thus it can be concluded from the results and discussion that the serum lipid profile of children on carbamazepine monotherapy attending paediatric and Neurology OPD was deranged whereas the lipid profile of children on valproic acid monotherapy was slightly raised as compared to control group but it was not statistically significant. Liver function test was not deranged in either of the group. The lipid profile was raised statistically significantly in the children with seizure disorder on carbamazepine monotherapy as compared to valproic acid monotherapy and control group. While lipid profile in valproic acid monotherapy group was also raised as compared to control group but the difference was not statistically significant. The liver function test was not deranged in carbamazepine monotherapy and valproic acid monotherapy group.

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