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Derangement of lipid profile in antiepileptic drugs treated patients in local population

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Abstract: Epilepsy is the third most common neurological disorder. It is not a single entity. The abnormal electrical activity may result in a variety of events, including loss of consciousness, abnormal movements, a typical or odd behavior or distorted perceptions falls seizers. Epilepsy is a chronic disorder and often requiring years of treatment. A large number of drugs are used for the treatment of epilepsy. The choice among the antiepileptic drugs depends on its effectiveness and side effects. Our retrospective study investigated the effect of antiepileptic drugs on lipid profile. Serum lipid profile was measured in 160 patients in which 40 patients were not started any antiepileptic drug .The remaining 120 patients were receiving antiepileptic drugs (AEDs). 40 control subjects were taken from general population for comparison. The height, weight and body mass index (BMI) and lipid profile of antiepileptic drugs treated patients were compared with control and untreated group. The weight and body mass index of antiepileptic drugs treated group was significantly increased when compared to the control group. Total Cholesterol (TC), Triglyceride (TG), High density lipoprotein (HDL-C), low density lipoprotein (LDL-C), ratio TC/HDL-C and ratio LDL-C/HDL-C were investigated for each group of drugs and controls. TC, TG, LDL-C, ratio TC/HDL-C and ratio LDL-C/HDL-C were significantly increased in patients who were on AEDs when compared with control but HDL-C of all drug treated groups showed significantly decreased when compared with control group. There was significant change in lipid profile was seen in AEDs treated group when compared with control group. Ratio TC/HDL-C and ratio LDL/HDL-C alteration showed the risk of atherosclerosis and cardiovascular diseases. Anti-epileptic drugs also alter the BMI and so it could potentially facilitate the development of diabetes mellitus. Our results additionally suggest that there is a need for careful monitoring of lipid profile in adult epileptic patients. Anti-epileptic drugs alter the BMI and so it could potentially facilitate the development of diabetes mellitus. Long term prospective studies are required to evaluate the risk of atherosclerosis caused by alteration in serum lipid levels which may lead to the cardiovascular disease.

Key words: Epilepsy, antiepileptic drugs, BMI, lipid profile.
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INTRODUCTION

Epilepsy is the third most common neurological disorder. It is not a single entity. The abnormal electrical activity may result in a variety of events, including loss of consciousness, abnormal movements, a typical or odd behavior or distorted perceptions1. About 50 million people worldwide have epilepsy and 90% of these being in developing countries[2]. Highest seen in people younger than 30 years of age. It is a common medical problem in Pakistan. Based on the available data that 1.38 million people are suffering from epilepsy in Pakistan[3].

Epilepsy is usually controlled but cannot be cured with medication although surgery may be considered in difficult cases. It is a chronic disorder and often requiring years of treatment. The choice among the antiepileptic drugs depends on its effectiveness and side effects. The first anticonvulsant was bromide suggested in 1857 by Charles Locock. Adverse effects of epilepsy and its treatment can impact general health for many decades. Antiepileptic drugs are well known to alter weight causing either wait gain or loss. These drugs also affect on the metabolism of lipid and glucose[4]. Epidemiological, clinical and experimental investigations have shown that alteration in serum lipids predisposes to atherosclerosis and Cardiovascular diseases CVD[5,6].The patients undergoing long-term treatment with valproic acid (VPA) are prone to develop different features of the metabolic syndrome (MS) like insulin resistance (IR) and proatherogenic lipid profile. Patients showed high BMI on VPA mono therapy [7]. The present study investigated serum lipid status of adult epileptic patients who had been receiving different antiepileptic drugs and newly diagnosed epileptic patients who had not been started any AEDs in our population.

MATERIALS AND METHODS

This retrospective study was conducted in the Department of Biochemistry, University of Karachi with the collaboration of Neurology Department of a tertiary care hospital, Karachi. We studied 160 patients with Epilepsy aged between 14 to 53 years of both sex. 40 of them had not received any antiepileptic drug. Those who were on regular medication other than AEDs, alcoholism and pregnant/ lactation females were excluded. Written consent was taken from the patients and control subjects who fulfilled the criteria. Weight and height were recorded as per standard techniques and body mass index (BMI) was also calculated. The control

group consisted of 40 healthy age and sex-matched individuals from general population.

Venous blood sample (5 ml) was drawn from anticubital vein and serum was separated. Sample was collected in the morning after an over night fast for both patients and controls. Serum was analyzed for lipid profile on the same day. Estimation of total cholesterol was performed by CHOD – PAP method by using commercially available kit.(Randox Laboratries LTD) and Serum HDL-C was estimated by CHOD – PAP method by using commercially available HDL – cholesterol precipitating reagent Randox. Triglyceride was also estimated by GPO – PAP method by using commercially available kit of Randox. Very low density lipoproteins (VLDL) and LDL - C were calculated using Friedewald formula i.e LDL Cholesterol = Total Cholesterol - (HDL Cholesterol + TG/5) Or LDL cholesterol = Total Cholesterol – (HDL cholesterol + 0.2 Triglyceride) and VLDL-C = TG/5, LDL-C = TC – HDL-C – VLDL-C.

Statistical analysis

Statistical analysis was performed by using by using SPSS version 11. Statistical comparison between the groups were performed by using Analysis of variance (ANOVA) . In all statistical analysis only p value < 0.05 will be considered significant.

RESULTS

A total of 200 subjects (age 14-53 years) irrespective of sex were included in this study which were divided into three groups.

Group A: consist of 40 health subjects age, sex matched control.

Group B: consist of 40 patients which were newly diagnosed and were not taking any antiepileptic drugs.

Group C: consist of 120 patients which were on different AEDs.

Table 1 showed Comparison between age, weight, height and BMI of group A ,B and C. There was no significant difference in age and height in group A, B and C but a significant increase in weight and BMI was shown in group C. Weight of group C was significantly increased when compared with group B ($p<0.01$) and BMI was also significantly increased when compared with group A and B. ($p<0.01$)

Table 2 Showed a significant difference in Lipid Profile of three groups. There was a significant increased in Total Cholesterol (TC), Triglyceride (TG)) , Ratio TC/HDL-c and Ratio LDL-c /HDL- c in group C when compared with group A and B ($p<0.001$). HDL-C is significantly decreased in group C when compared with group A and B but HDL-c was also significantly decreased in group B when compared with group A ($p<0.001$) .LDL-c of group C was significantly increased when compared with group A ($p<0.001$). VLDL of group C was significantly increased when compared to group B ($p<0.001$). Ratio TC/HDL-c and Ratio LDL-c/ HDL-c of group B was also significantly increased when compared to group A ($p<0.001$). TC, TG, LDL-c, Ratio TC/HDL-c and Ratio LDL-c / HDL-c were significantly increased in those patients who were on antiepileptic drugs when compared with control ($p<0.001$) but HDL-c of AEDs treated group was significantly decreased when compared with control ($p<0.001$).

Table 1: Comparison of biophysical parameters in Groups A, B, and C.

	Controls Group A (n=40)	Patients without AEP drugs Group B (n=40)	Patients with AEP drugs Group C (n=120)	P-value
Age (years)	27.5±9.73	28.1±12.55	31.7±12.31	0.083
Height (inches)	64.7±3.76	64.0±4.93	63.4±4.76	0.262
Weight (Kg)	60.2±8.65	55.0±11.01	64.7±14.07 ◊	0.001
BMI	21.7±2.63	20.9±3.18	25.1±5.30 *	0.001

Values are mean±SD,*Significant as compared to group A and B ($p<0.01$),◊ Significant as compared to group B ($p<0.01$).

Table 2: Comparison of lipid profile in groups A, B, and C.

Biochemical parameters	Controls Group A (n=40)	Patients without AEP drugs Group B (n=40)	Patients with AEP drugs Group C (n=120)	P-value
Total cholesterol (mg/dl)	141.5 ±13.31	150.9 ±33.29	168.9 ±48.81 *	0.001
Triglyceride (mg/dl)	140.5 ±8.38	131.6 ±28.16	158.8 ±52.99 *	0.001
HDL-c (mg/dl)	41.6 ±3.24	37.4 ±5.76 ↑	34.9 ±4.04 *	0.001
LDL-c (mg/dl)	71.61 ±2.78	87.2 ±24.31	100.5 ±40.56 ↑	0.001
VLDL	28.1 ±3.52	26.3 ±5.66	31.8 ±10.61 ◊	0.001
Ratio Total Cholesterol/ HDL-c	3.4 ±0.32	4.1 ±1.07 ↑	4.8 ±1.38 *	0.001
Ratio LDL-c/HDL-c	1.7 ±0.29	2.3 ±0.84 ↑	2.8 ±1.87 *	0.001

Values are mean±SD, *Significant as compared to groups A and B ($p<0.01$), ↑ Significant as compared to Group A ($p<0.01$), ◊Significant as compared to Group B ($p<0.01$)

DISCUSSION

Epilepsy is a chronic disorder and often requiring years of treatment and different antiepileptic drugs are used to control the seizures. Anti-epileptic medications often results in weight gain[9] and these results are matched with our study. In our study the BMI of group C was significantly increased when compared with group A and B ($p<0.001$). The adverse effects of individual AEDs on weight and serum lipid profile was also reported [4] .The patients who were on Valporic acid (VPA) monotherapy showed high BMI when compared with control [7]. These results matched with our results and showed that BMI of patients who were on AED drugs was significantly increased as compared to the group A and B.

There are contradictory reports on the relationship of AEDs with serum lipid profile[10] .The results of this study matched with the results of our study where we have found significantly increased levels of TC, TG and LDL-C. Present study showed the increased TC/HDL-C ratio and LDL-C / HDL-C ratio indicating a high risk of atherosclerosis . It had also suggested that increased in ratio following Carbamazepine therapy might increase the risk of atherosclerosis[5.] . Alteration in serum lipid profile falling long term antiepileptic treatment has been reported [11.] There results showed TC and ratio TC / HDL-C was significantly increased where as HDL-C was decreased and these results are consistent with the present findings where TC, TG, LDL-c levels were significantly increased and HDL-c was significantly decreased. Ratio TC/HDL-C and Ratio LDL-C / HDL-C was significantly increased which is a good predictor of atherosclerosis.

It is reported that children treated with CBZ had high levels of TC, TG, LDL-C & HDL-C [12].In present study it is observed that AEDS increased TC, TG, LDL-C but HDL-C decreased significantly. Adult epileptic patients had less exercise and are physically less active as compared to the children. It may be a cause of decreased HDL-C levels in adult epileptic patients. Previously it is reported that patients with epilepsy doing less exercise and had sedentary life style had decreased HDL-C levels and increased risk of acute myocardial infarction (AMI)[6] .

Some authors reported that there was no significant change in lipid profile when treated with Valproic acid [5,13] . However patients on Valproic acid had significantly lower TC, LDL-C, TC/HDL-C ratio and LDL-C/ HDL-C ratio when compared with the control group [14]. The patients who were on Sodium Valporic acid showed high BMI when compared with Lamotrigine treated patients[7] .It is observed in present study that BMI of AEDs treated patients was significantly increased as compared to without AEDs patients and control group . In present study BMI was significantly increased in epileptic patients following the treatment of antiepileptic drugs. Increased BMI, less exercise, sedentary life style and on treatment of different antiepileptic drugs may cause increased risk of atherosclerosis and acute myocardial infarction in epileptic patients.

CONCLUSION

The present study showed significant derangement of lipid profile and BMI in antiepileptic treated patients. The use of antiepileptic drugs could potentially facilitate the development of diabetes mellitus, atherosclerosis and cardiovascular diseases in later stage of life. The present findings suggest that there is a need of careful monitoring of lipid profile, weight and BMI. It should be regularly checked in patients undergoing such treatments. Long term prospective studies are required to evaluate the risk of atherosclerosis caused by alteration in serum lipid levels which may lead to cardiovascular diseases.

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