

EFFECT OF ANTI-EPILEPTIC DRUGS ON SERUM LIPIDS IN EPILEPTIC PATIENTS- A CASE-CONTROL STUDY

Ghulam Mujtaba Junejo¹, Naseem Aslam Channa¹, Kamran Khichi¹, Marvi Shaikh^{1,2}, Lubna Noorani³
¹Institute of Biochemistry, University of Sindh, Jamshoro, Pakistan, ²Department of Biochemistry, Indus Medical College, University of Modren Sciences, Tando Muhammad Khan, Sindh, Pakistan, ³Department of Science and Technical Education, Faculty, of Education, Elsa Kazi Campus, Hyderabad, Pakistan

Correspondence:

Prof. Naseem Aslam Channa, Institute of Biochemistry, University of Sindh, Jamshoro, Pakistan

Email: natchanna2000@gmail.com

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ABSTRACT

Epilepsy is a chronic illness, thus antiepileptic drugs are often used extensively. However, this treatment may be linked to metabolic abnormalities in different body systems, including the endocrine system, connective tissues, and liver. Moreover, prolonged use of antiepileptic drugs may lead to adverse effects on serum lipid levels. This study was conducted to explore alterations in serum lipids after the administration of antiepileptic drugs in epileptic patients and compared with healthy volunteers. A total of 200 participants were selected; including 100 epileptic patients and 100 age, gender and locality matched controls having negative personal or family history of epilepsy. All the participants signed written informed consent and were interviewed through a standard questionnaire. Blood samples were collected from all participants, for the analysis of serum lipids. The accurate rapid test used to analyze samples of both groups. Significantly increased concentration of total lipids, total cholesterol, triglyceride and VLDL-C were found in epileptic patients as compared to controls and also in male epileptic patients, whereas, reverse was true for HDL-C. Significant variations were found for total cholesterol, HDL-C, LDL, triglycerides and VLDL-C

in epileptic patients with age group 36 to 46 years, while, the HDL-C was significantly decreased in age group 15 to 35 years. Antiepileptic drugs, especially Episentia alters the serum lipid contents, but the total cholesterol was significantly altered among the users of antiepileptic drugs.

Key Words: antiepileptic drugs, lipid profile, total cholesterol, triglycerides

INTRODUCTION

Epilepsy refers to a disorder of the brain characterized by the periodic and unpredictable occurrence of seizures and the most common neurologic conditions and a significant reason for incapacity and mortality (1, 2). Epilepsy, an illness of the sensory system which can be seen in all age groups. It is reported as the most common non-transmittable disease of the world (3). Epilepsy imposes considerable economic burden on the medical services around the globe. As 70-80% of patients take regular medication after developing epilepsy with the hope to have their seizures controlled with the ideal antiepileptic treatment. Population based investigations suggest the rate of epilepsy in children is around 3.6 to 4.2 per 1000 for children in developing countries and the rate is roughly double in non-industrial countries (4). Antiepileptic drugs are utilized for counteraction of the recurrence of seizures. Most commonly used drugs for epilepsy include carbamazepine (CBZ), phenytoin (DPH), phenobarbitone (PB), sodium valproate, lamotrigine (LTG), Topiramate (TPM), clobazam (CLB), oxcarbazepine (OXC) and levetericitam (LEV) (5). Prolonged use of antiepileptic treatment could have some unwanted effects on the lipid profile of the patients (6). Increase serum concentrations of lipids are related to an increased risk of cardiovascular diseases, may result in ischemic heart disease and stroke (7). The number of patients taking epileptic drugs in Pakistan is also at rise, however there is limited data available to explore pattern of lipid profile in these patients. Thus, this study was designed to investigate the impact of antiepileptic drugs on serum lipid levels.

METHODS

This was a case-control study, carried out at the Institute of Biochemistry, University of Sindh, Jamshoro, Pakistan. The study population was selected from the Dadu district in Sindh. The sample consisted of 50

epileptic patients (cases) and 50 controls who were matched for age, sex, and locality having negative personal or family history of epilepsy. Prior to the commencement of the study, ethical approval was obtained from the Institutional Ethical Committee, and informed written consent was obtained from all participants in their native language.

A standard questionnaire was designed for this study, which included questions about the participants' socio-demographic characteristics, lifestyle, diet, the impact of the sun exposure on them, and the use of anti-epileptic drugs and its duration. Fasting blood samples were collected from all participants for the analysis of lipid profile parameters such as Total Lipids (TL), Total Cholesterol (TC), High Density Lipoprotein Cholesterol (HDL-C), Low Density Lipoprotein Cholesterol (LDL-C), Triglycerides (TG), and very Low-Density Lipoprotein Cholesterol (VLDL-C). Approximately 3ml of blood was drawn from each participants and collected in sterilized sample vials with a screw cap. The serum was separated and stored at -20°C for further analysis. The patient and control samples were analyzed using an accurate and rapid test at the Diagnostic and Research laboratory, Liaquat University of Medical and Health Sciences, Dadu Branch, using same standard protocol.

Statistical analysis

The data collected was entered into Microsoft Office Excel 2010 and Statistical Package for Social Sciences (SPSS version 21.0) for analysis. Descriptive statistics was used to summarize the data, with the mean and standard deviation (\pm SD). In addition, exploratory data analysis was conducted using median, percentage and ratios. The results were further evaluated using logistic regression, with odds ratios and 95% confidence intervals (CI) being calculated using the Stat Chart plus 5.1 software. A p-value <0.05 was considered significant.

RESULTS

In our study, we included a total of 100 participants, consisting of 50 epileptic patients and 50 controls. Among the participants, 84.0% were males and 16.0% were females. The mean age of male subjects was 24.6 years, and the mean age of female subjects was 23.1 years. The educational status of epileptic patients was matriculation, and they had a positive family history of neurological abnormalities and diabetes, as shown in Table 1.

The epileptic patients had significantly elevated levels of serum TL, TC, TG, and VLDL-C as compared to controls. Additionally, HDL-C was significantly decreased in epileptic patients as compared to controls. Among the epileptic patients, male patients had significantly higher levels of TL, TC, TG, and VLDL-C as compared to their female counterparts. There was a significant rise in serum LDL-C, TG, and VLDL-C in the 36-45 age group as compared to the other age groups, as shown in Table 2. Those patients who were taking Episenta (a combination of sodium and valproic acid) showed significantly higher TC. Whereas, non-significantly higher levels of serum TL, TG, LDL-C, and VLDL-C, while their HDL-C levels were lower in Epival drug users. There was a significant difference in the concentrations of total cholesterol among patients who were taking the Epival (Figure 1).

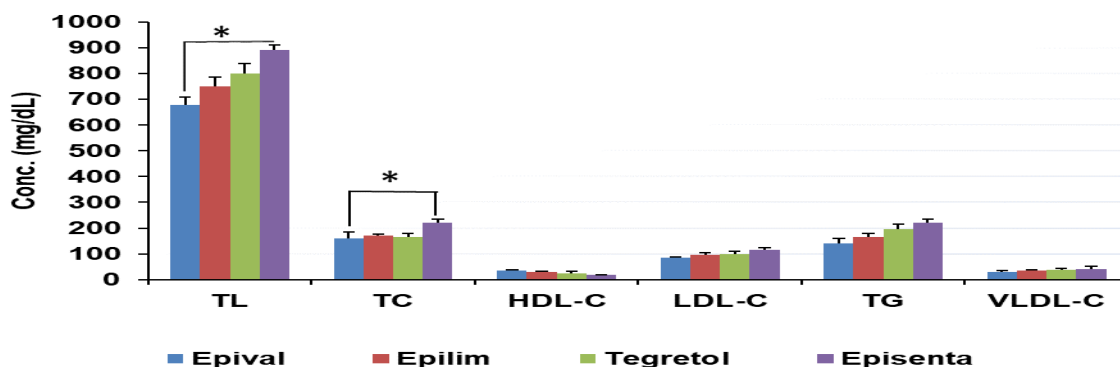


Figure: 1 Antiepileptic drug effects on lipid profile in epileptic patients

Table: Socio-

Characteristics	Epileptic Patients N=50 (%)	Controls N=50 (50)
Gender		
Male	84.0	84.0
Female	16.0	16.0
Age groups(Year)		
15-25	64.0	64.0
26-35	22.0	22.0
36-45	10.0	10
>46	4.0	4.0
Marital Status		
Married	38.0	32.0
Unmarried	62.0	68.0
Occupation		
Government Job	8.0	20.0
Private Job	22.0	23.0
Businessmen	25.0	32.0
Jobless	45.0	25.0
Education		
Primary	15.0	15.0
Matriculation	40.0	30.0
Intermediate	18.0	20.0
Graduation	17.0	30.0
Diploma	10.0	5.0
Comorbidities		
Hypertension	20.0	15.0
Diabetes	15.0	35.0
Hepatitis	25.0	30.0
Heart Disease	10.0	15.0
Neurological disorder	30.0	5.0
Addiction		
Smoking	60.0	50.0
Naswar	10.0	10.0
Paan	30.0	40.0

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demographic characteristic of epileptic patients and controls.

Table: 2 Gender and gender wise comparison of lipid profile in epileptic patients and controls.

	TL	TC	HDL-C	LDL-C	TG	VLDL-C
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Parameters	Range (450- 850)mg/dL Mean ± SD	Range (<200) mg/dL Mean ± SD	Range (45-55) mg/dL Mean ± SD	Range (<130) mg/dL Mean ± SD	Range (<200) mg/dL Mean ± SD	Range (15-25) mg/dL Mean ± SD
Epileptic Patients (n=50)	742.84 ± 30.8	165 ± 16.18	30.95 ± 10.96	91.92 ± 15.92	166.04 ± 16.04	32.94 ± 12.86
Controls (n=50)	623 ± 25.86	140.44 ± 20.45	36.98 ± 5.7	84.9 ± 7.48	129.38 ± 15.6	25.86 ± 6.7
P-value (<0.05)	0.003	0.008	0.0003	0.06	0.0028	0.004
Male Epileptic patients (n=42)	768.64 ± 40.7	171.07 ± 30.66	30.35 ± 7.35	94.47 ± 17.73	172.52 ± 25.6	34.21 ± 16.53
Female Epileptic pa- tients (n=08)	607.37±30.42	134.25±18.5 4	34.12±6.35	78.5±14.6	132±17.66	26.25±3.38
P-value (<0.05)	0.002	0.0025	0.21	0.028	0.007	0.008
15-25 years(n=33)	662.51 ± 98.5	134.25 ± 18.54	33.66 ± 8.47	83.39 ± 15.82	137.42 ± 33.44	27.12 ± 7.01
26-35 years(n=10)	742.84 ± 85.5	145.75 ± 30.96	30.96 ± 9.92	91.92 ± 20.72	166.04 ± 76.57	32.94 ± 15.48
36-45 years(n=05)	1049.8 ± 99.53	165.18 ± 54.16	19.6 ± 10.48	118.2 ± 25.65	285.2 ± 95.64	57.19 ± 141.58
≥46 years (n=02)	1040.34±249. 3	232.73 ± 96.48	25.10 ± 10.18	107.5 ± 22.5	107.5 ± 22.5	52.17 ± 30.52
P-value (<0.05)	0.61	0.002	0.003	0.005	0.001	0.006
(P-value <0.05), TL=Total Lipid, TC= Total Cholesterol, HDL-C= High Density Lipoprotein, LDL-C Low Density Lipoprotein, TG= Triglycerides, VLDL-C Very low density lipoprotein.						

DISCUSSION

A total of 50 epileptic patients and 50 controls participated in this study. There was male predominance of male epileptic patients than female epileptic patients. This finding was consistent with previously reported studies, where A. Gholami *et al.* (2016) and Bano *et al.* (2015), showed more males than females suffering from epilepsy (8, 9). We divided participants into age groups and found that the majority of epileptic patients were 15-25 years age, as reported earlier by Svalheim *et al.*, (2017) that the majority of patients with epilepsy were in the age group 18-35 years with an average age of 31.5 years (10). These findings suggest that epilepsy, as well as gender and age, may influence the lipid profile of patients, and highlights the need for appropriate management of the cardiovascular health of patients with epilepsy.

Antiepileptic medication therapy duration and lipid profile were found to be significantly correlated. Zenteno *et al.* (2007) conducted a study on comorbidities in epileptic patients and found that the majority of patients had neurological disorders, which is consistent with the results of current

study. Mintzer et al. (2016) reported that epileptic patients who were taking antiepileptic drugs had higher levels of TL, TG, and VLDL-C as compared to controls. Similarly, several other studies have also reported elevated levels of TC, TG, HDL-C, and LDL-C, which are comparable with current findings. These studies provide further evidence of the impact of epilepsy and its treatment on serum lipid levels in patients, and highlight the importance of monitoring and managing the cardiovascular health of patients with epilepsy (11, 12). Another study conducted by Mintzer et al. (2018) reported that epilepsy patients had higher serum lipid levels compared to controls, and HDL-C levels were significantly lower in epilepsy patients (13, 14,15).

Mugloo et al. (2017) reported an increase in TL, TC, TG, and LDL-C levels in epileptic patients who were using antiepileptic drugs. They also found that the concentration of VLDL-C was not significantly high in antiepileptic drug users. However, other investigators have reported a negative association between the use of antiepileptic drugs and serum lipid profile (16, 17). These findings further emphasize the impact of specific epilepsy medications on the serum lipid profile of patients and the importance of monitoring their cardiovascular health regularly.

Shah et al. (2016) conducted a study on the lipid profile of patients with epilepsy and found that gender played a significant role in determining the lipid profile. Their findings indicated that male patients with epilepsy had significantly higher levels of serum TL, TC, TG, and VLDL-C when compared to female patients with epilepsy. On the other hand, the levels of HDL-C were found to be higher in female patients with epilepsy than in male patients. These results suggest that gender differences may influence the lipid profile of patients with epilepsy and should be taken into consideration when assessing and managing the cardiovascular health of patients with epilepsy (11).

According to the findings of present study, which is aligned with the research conducted by Irem Fatima et al. in 2009, who reported that male patients with epilepsy have been shown to exhibit higher levels of TC and LDL-C when compared to female patients with epilepsy. This suggests that male patients with epilepsy may be at a higher risk of developing cardiovascular diseases than their female counterparts. However, the same study also revealed that male epileptic patients had higher levels of HDL-C than female epileptic patients, indicating a potential protective effect of HDL-C against the development of cardiovascular disease in male patients with epilepsy (18, 19).

Patients who use Episenta showed significantly higher levels of TC, TL, LDL-C, TG, and VLDL-C when compared to those who were not using Episenta. Conversely, the levels of HDL-C were found to be lower in Episenta users than non-users. The results of our study partially agree with the findings of a previous study conducted by Mintzer et al. (2013), which demonstrates that carbamazepine can significantly reduce serum total cholesterol. While our findings align with Mintzer's results in terms of the reduction in HDL-C levels, they differ in terms of TC and LDL-C levels, which were found to be higher in our study among patients who use Episenta (20). This was a prospective study from patients taking antiepileptic drugs, thus it is the strength of the study, however a small sample size and the 1:1 ratio of cases and controls is taken as a limitation of the study.

CONCLUSION

Antiepileptic drugs significantly alter the serum lipid levels in patients with epilepsy. It is worth noting that the normal ranges for serum cholesterol and its fractions are wide and may vary depending on factors such as gender and age. Specifically, male epileptic patients have higher lipid profiles as compared to female epileptic patients. Regular monitoring of serum lipid levels appears

to be essential for patients undergoing such therapy and proper diet management may reduce the risk of associated clinical manifestations.

Conflict of interest:

Authors declare no conflict of interest

Funding source:

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Ethical Approval:

The study was ethically approved Institutional Ethical Committee, Institute of the Biochemistry University of Sindh, Jamshoro.

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