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Original Research Article

A Prospective Study of Lipid Profile Changes In Patients on Anti-Epileptic Drug Therapy

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ABSTRACT

Introduction: Epilepsy is one of the commonest neurological disorders often requiring long term treatment with anti-epileptic drugs (AED's). Many biochemical side-effects occur in patients who take AED's for chronic diseases. Alterations in Serum Lipid Profile due to AED's can have serious implications for the patients in future in the form of an adverse cardiovascular or cerebrovascular event. Increase in Serum cholesterol, especially LDL Cholesterol accelerates atherosclerotic changes in the form of plaque formation in arteries. Since, most epileptic patients are of younger age group, an early and rapid start of atherosclerosis in them will have an adverse cardiovascular impact in later age.
Materials and Methods: A prospective study was done on 30 newly diagnosed epilepsy patients. Blood samples were collected before starting anti-epileptic drugs and repeated after 8 months of drug treatment. Samples were also taken from 20 healthy age and sex matched controls. All samples were analysed for Serum Lipid profile on Beckman-Coulter fully automatic analyser.
Results: Total Cholesterol and LDL cholesterol were significantly higher ($p<0.05$) after 8 months of AED's use. Triglyceride levels though raised, were not statistically significant. ($p>0.05$)
Conclusion: Adverse impact on blood lipids occurs due to long term use of AED's which necessitates corrective action to halt adverse vascular events in future.

Key words: Anti-epileptic drugs (AED's), Epilepsy, lipid profile, LDL, atherosclerosis

INTRODUCTION

Epilepsy is one of the commonest chronic neurological disorders with a high worldwide prevalence. Etiology of Epilepsy is not clearly known. Most of the cases are idiopathic, while genetic, traumatic and pathological changes in nervous system can also result in seizure disorders. There are approximately 10 million people living with epilepsy in India accounting for1/5th of the global burden. [1] It is characterised by recurrent, usually unprovoked, epileptic seizures, as well as by the cognitive, psychological, and social consequences of this condition. [2,3] These seizures are transient signs and/or symptoms of abnormal, excessive or hyper-synchronous neuronal activity in the brain. [4] Anxiety, fear and social stigma often surround the patients suffering from epilepsy. This is very common in developing countries even today and can impact the quality of life of not only the epilepsy patients but also their families.

Treatment of epilepsy is usually by medication and rarely surgical. Anti-epileptic drugs (AEDs) are frequently used for several conditions including, epilepsy, migraine and psychiatric conditions. Most of the times, patients suffering from

epilepsy require long term or lifelong medication with anti-epileptic drugs (AED's). People with epilepsy respond to the treatment with AED's approximately 70% of the times. Epileptic patients are more commonly treated with a single drug based therapy (mono-therapy) as Polytherapy can cause more side-effects in these patients.

Since many of these AED's, especially the more commonly used older AED's like carbamazepine, phenytoin and phenobarbital are enzyme inducers, they have adverse metabolic and biochemical consequences. They are known to adversely affect Lipid profile by increasing serum cholesterol, LDL and triglyceride levels. However, since many studies also report rise in HDL-Cholesterol levels, the net result of AED's on vascular system is controversial. This is because; high HDL levels are cardio protective. Epilepsy patients treated with older enzyme inducing drugs like carbamazepine or phenytoin for long periods have increased levels of cholesterol, LDL and total homocysteine. All these changes may increase the risk of adverse cardiovascular and cerebrovascular events. [5] This is because; high serum lipid levels are known to cause atherosclerotic changes in blood vessels. Since, atherosclerosis starts at an early age in the form of fatty streaks which later form fibrous plaques, high lipid levels in young people will make them more prone to thrombotic cardiovascular events in future. This demands early intervention, more so in Indian population as Indians are more prone to cardiovascular disease (CVD) risk. [6]

MATERIALS AND METHODS

The present study was carried out in the Department of Biochemistry in collaboration with the Department of Neurology and Psychiatry of Sardar Patel Medical College & PBM hospital, Bikaner. The study plan was approved by the Ethics Committee of the Institute. A total number of 50 participants of age between 10-60 years were chosen and they were divided into 2 groups, Group-I: Newly diagnosed epilepsy patients (n=30) and Group-II: Healthy controls (n=20).In this prospective study 30 newly diagnosed patients of epilepsy were enrolled. Cases with pre-existing cardiovascular disease, metabolic syndrome and other co-morbidities were excluded from study group. Fasting blood samples (5 ml) were collected by venepuncture under aseptic conditions from cases before starting of any drugs. For comparison of baseline level in cases, samples were also taken from 20 healthy controls. Most of the cases were prescribed monotherapy with carbamazepine and phenytoin. Repeat collection of blood samples was done after 8 months of anti-epileptic therapy in cases. Consent was taken from all the patients before each sample collection. Haemolysed samples were discarded. Lipid profile (Total. Cholesterol, Triglycerides, LDL, HDL and VLDL) was analysed on Beckman-Coulter fully automatic analyser.

STATISTICAL METHODS

Mean and SD of all the data was recorded in Microsoft Excel. GraphPad software was used to analyse statistical significance of data. Baseline levels of cases before starting AED's was compared with that of healthy control by the unpaired student t-test. Lipid profile after 8 months of anti-epileptic therapy in cases was compared with their baseline levels (before starting AED's) by the paired t-test. P-value of <0.05 was considered statistically significant.

RESULTS

Both cases and age matched controls were compared for baseline level of total cholesterol, LDL, HDL, VLDL and Triglycerides (table1). No significant difference ($p > 0.05$) was found between both groups which means that lipid profile was normal in epilepsy patients before starting AED's.

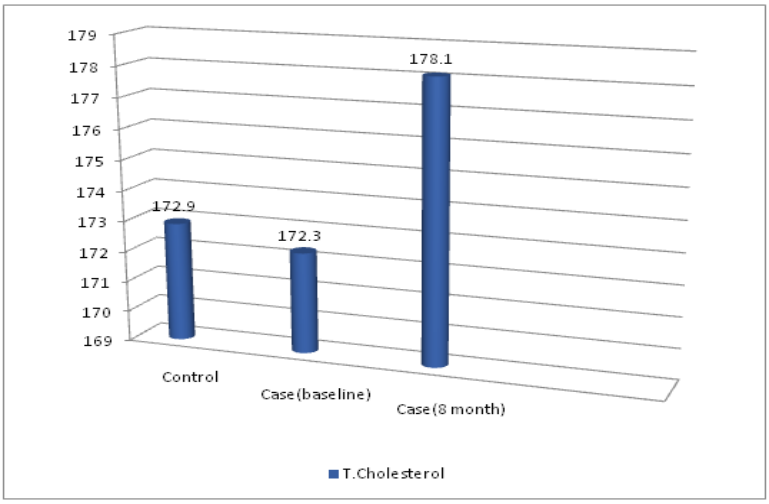
Table1: Baseline characteristics of cases(n=30) and control(n=20) group

Characteristic	Controls (Mean ±SD)	Cases (Mean ±SD)	P-value	Stat.significance
Age (years)	33.70 ±12.23	27.57 ±13.4	0.1074	Non-significant
T.Cholesterol(mg/dl)	172.90±47.88	172.30±24.18	0.9443	Non-significant
Triglycerides(mg/dl)	109.70±30.87	118.30±42.81	0.4388	Non-significant
LDL (mg/dl)	109.60±32.26	107.80±25.94	0.8307	Non-significant
HDL (mg/dl)	41.40±7.037	40.90±8.248	0.8250	Non-significant
VLDL (mg/dl)	21.93±6.175	23.67±8.562	0.4388	Non-significant

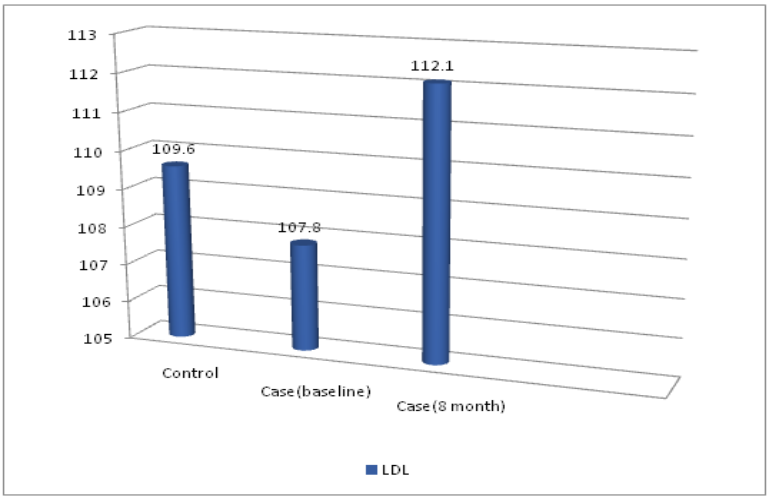
After 8 months of treatment with AED's, a statistically significant increase ($p<0.05$) in Total. Cholesterol and LDL Cholesterol levels was seen in epilepsy patients as compared to their baseline levels before the start of anti-epileptic therapy (table 2). Also, the mean serum level of Triglycerides, VLDL and HDL Cholesterol also increase on treatment with AED's, but, it is not statistically significant.($p>0.05$)

Table 2: Lipid Profile before and after AED's (8 month) in cases (n=30)

Characteristic	Before AED (Mean ±SD)	After AED (Mean ±SD)	P-value	Stat. significance
T. Cholesterol (mg/dl)	172.30±24.18	178.10±30.10	0.0045	Significant
Triglycerides(mg/dl)	118.30±42.81	123.30±46.52	0.0600	Non-significant
LDL(mg/dl)	107.80±25.94	112.10±32.57	0.0419	Significant
HDL(mg/dl)	40.90±8.248	41.37±7.421	0.3100	Non-significant
VLDL(mg/dl)	23.67±8.562	24.67±9.304	0.0600	Non-significant



Table/Figure 3- Total Cholesterol (mg/dl) in control and cases(before and after AED's)



Table/Figure 4-Serum LDL(mg/dl) in control and cases(before and after AED's)

DISCUSSION

Our results show statistically significant increase in serum total cholesterol and LDL Cholesterol on treatment with AED's. The metabolic effects involving lipids in patients treated with the anti-epileptic drugs like phenobarbital, carbamazepine, or phenytoin can be explained by highly elevated levels of plasma 4 beta-hydroxycholesterol in these patients. [7]

The lipid raising effect of AED's may be due to the induction of CYP enzymes. CYP450 enzyme system is involved in the synthesis and metabolism of cholesterol and enzyme inducing drugs also stimulate the endogenous hepatic synthesis of cholesterol. [8]

Previous studies done for similar investigations in patients with epilepsy also showed similar results. Yilmaz.E et al. demonstrated an increase in serum total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglyceride concentrations after 3 months of treatment with carbamazepine. [9] Nikolaos T et al. also found that lipid levels increase on long term treatment with AED's. [10] Lossius M et.al demonstrated that withdrawal of carbamazepine in long term users of the drug results in return of lipid profile to normal levels. [11] However, Manimekalai K et.al observed that no significant difference was observed in mean LDL cholesterol levels in patients on oxcarbazepine when compared to that of control group. [12]

Most of these adverse biochemical changes can be explained by enzyme inducing effect of older AED's which raise not only lipid but also homocysteine levels in blood. As such, AED's drugs which are not enzyme inducers (some newer drugs like levetiracetam) can be a better option for use in patients with high lipid levels.

CONCLUSION

The use of AED's for long term duration alters the Lipid profile in patients. More prospective studies are needed to differentiate the effect of different types of AED's (old and new) on serum Lipid levels. Our results indicate the need for regular monitoring of lipid profile in epileptic patients receiving AED's. Also, adjuvant drug therapy with Lipid lowering agents may be considered in epileptic patients above 50 years of age who show altered lipid levels on treatment with AED's.

REFERENCES

1. Nelson Lorene, Neuroepidemiology- From Principles to Practice, Oxford University Press London,UK, 1st edition, 2003
2. Chang BS, Lowenstein DH. Epilepsy. N Engl J Med 2003;349:1257-66.
3. Fisher RS, van Emde Boas W, Blume W, et al. Epileptic seizures and epilepsy: definitions proposed by the International League Against Epilepsy (ILAE) and the International Bureau for Epilepsy (IBE). Epilepsia. 2005 Apr. 46(4):470
4. Berg A, Berkovic S, Brodie MJ et al. 2010. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005–2009. Epilepsia 51: 676–685.
5. Hamed SA, Hamed EA, Hamdy R, Nabeshima T. Vascular risk factors and oxidative stress as independent predictors of asymptomatic atherosclerosis in adult patients with epilepsy. Epilepsy Res. 2007; 74:183–192
6. Joshi P, Islam S, Pais P et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. JAMA. 2007; 297:286–294. doi: 10.1001/jama.297.3.286.
7. Bodin K, Bretillon L, Aden Y, Bertilsson L, Broomé U, Einarsson C et al. Antiepileptic Drugs Increase Plasma Levels of 4β-Hydroxycholesterolin Humans. Journal of Biological Chemistry.2001;276(42):38685-38689.
8. Gibbons GF. The role of cytochrome P450 in the regulation of cholesterol biosynthesis. Lipids. 2002;37:1163–70.]
9. Yilmaz E, Doşan Y, Gürgöze MK, Güngör S. Serum lipid changes during anticonvulsive treatment serum lipids in epileptic children. Acta Neurol Belg. 2001 Dec;101(4) 217-220. PMID: 11851028.

10. Nikolaos T, Stylianos G, Chryssoula N, et al. The effect of long-term antiepileptic treatment on Serum cholesterol (TC, HDL, LDL) and triglyceride levels in adult epileptic patients on monotherapy. Med Sci Monit 2004; 10: 50-52
11. Lossius M, Nakken K, Mowinckel P, Taubøll E, Gjerstad L. Favorable change of lipid profile after carbamazepine withdrawal. Acta Neurologica Scandinavica. 2015;134(3):219-223.
12. Manimekalai K, Visakan B, Salwe KJ, et al. Evaluation of Effect of Antiepileptic Drugs on Serum Lipid Profile among Young Adults with Epilepsy in a Tertiary Care Hospital in Pondicherry. J Clin Diagn Res 2014; 8: 5-9

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