Effect Of Anticonvulsant Drugs On Lipid Profile In Epileptic Patients

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Citation

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Abstract

One hundred and twenty patients with epilepsy who had been on various anticonvulsant drugs were selected for the study of their lipid profile. We found a significant increase in serum levels of triglyceride, total cholesterol, HDLc and VLDLc in patients receiving combination therapy of either Phenytoin and Phenobarbitone or Phenytoin and Carbamazepine or Phenytoin alone. Patients receiving Carbamazepine alone had significant increase in serum levels of triglyceride and VLDLc but no significant changes in serum levels of total cholesterol & HDLc in this group. A significant correlation between duration of anticonvulsant therapy and lipid profile was established. Our results indicated the long-term use of anticonvulsant therapy significantly raises total cholesterol level and therefore cholesterol should be regularly checked in patients undergoing such treatment.

INTRODUCTION

Epilepsy is one of the most common disorders of the nervous system. Prevalence of epilepsy is estimated at over two million cases in United States ([1,2]) and there are approximately six million people suffering from epilepsy in India alone with the prevalence rate of 9/1000. In most studies, prevalence rates lie between 4 and 10 per 1000 population ([3,4]). Recent advances in the diagnosis of epilepsy include the development of clinical classification of epileptic seizures and the recognition of specific epileptic disorders. Though the incidence of seizures complications have decreased with the use of appropriate anticonvulsant therapy but incidence of various metabolic and endocrinal abnormalities remained same despite of treatment in epileptic patients. Anticonvulsant drugs are used in large quantities during long-term antiepileptic therapy and the treatment may be associated with various metabolic abnormalities in connective tissues, endocrine system and the liver ([5]). Anticonvulsants may alter liver function and increase the activity of hepatic microsomal enzyme system ([5,6]). This enzyme induction phenomenon is associated with an altered metabolism of various substances such as drugs and lipids ([5,6]). This anomaly has focused attention on changes in lipid profile during long-term anticonvulsant therapy especially by alter liver function and increase the activity of the hepatic microsomal enzyme system ([6,7]). The clinical significance of these changes has not yet been clearly established. The present study was undertaken to study the effect of anticonvulsant drugs on serum levels of triglyceride, total cholesterol, HDLc, LDLc and VLDLc.

MATERIALS AND METHODS

PATIENTS AND SPECIMEN COLLECTION

One hundred and twenty cases of epilepsy, which had been on various anticonvulsant drugs for a period varying from 3-15 years, attending epilepsy clinic of Sardar Vallabh Bhai Patel hospital, LLRM medical college, Meerut, UP, were selected for the present study. Patients suffering with diabetes mellitus, nephrotic syndrome, myxoedema and familial hypercholesterolemia, which might affect the blood lipid, were excluded. Sixty healthy individuals preferably relatives of patients were selected to serve as normal control.

After an overnight fast, 5 ml blood samples of patient and control were collected in vacuum tubes and allowed to clot at room temperature for 60-120 minute followed by centrifugation at 3000 g for 10 min. at 40C. Serum was stored at -200C, for estimation of lipid profile.

ESTIMATION OF TRIGLYCERIDE

Estimation of triglyceride was performed by method described by Kaplan 1985 ([8]) by using commercially available kit from Sigma- Aldrich. In Brief, 10 microliter of serum was mixed with 1000 microliter of reaction solution. The absorbance of sample was measured against the reaction solution. The Increase in absorbance, measured at 540 nm, due to the formation the Quinoneimine dye, is directly

proportional to the triglyceride concentration in the sample. The increase in absorbance was directly proportional to the glycerol concentration in the sample. True serum triglycerides were calculated by subtracting the free glycerol concentration in the sample from total triglycerides.

ESTIMATION OF TOTAL CHOLESTEROL

Estimation of Total cholesterol was performed by method of Pelkonen et al. 1975 ([7]) CHOD-PAP method by using commercially available kit from Sigma-Aldrich. In brief, 0.02 ml of serum was mixed with 2 ml of reaction solution (Enzyme solution with colour reagent). The absorbance of samples was measured at 540nm against the reagent blank value.

ESTIMATION OF SERUM HDLC

Estimation of serum HDLc was performed as described by Nikkila et al. 1978 ([9]) CHOD-PAP method by using commercially available kit from Sigma-Aldrich. In brief, 0.2 ml of serum was mixed with 0.5 ml of precipitating reagent solution and centrifuged at 4000 rpm for 10 minute. 0.1 ml of clear supernatant was mixed with 1 ml of reaction solution. The amount of colour produced was directly proportional to the concentration of HDL cholesterol in the sample. The absorbance of samples was measured at 540 nm against the reagent blank value.

ESTIMATION OF SERUM VLDLC

Estimation of VLDLc was calculated by Sattyanaryanan 1999 ([10]). The value of VLDLc was calculated by density gradient centrifugation method based on formula:

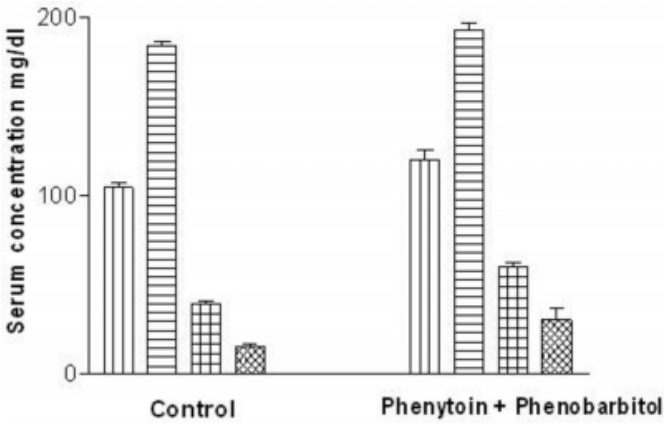
VLDLc = total cholesterol - (HDL + LDL). The estimated values of VLDLc were expressed in mg/dl.

RESULTS

The increased level of serum triglyceride, total cholesterol, HDLc and VLDLc in epileptic patients was observed on combination therapy of Phenytoin and Phenobarbitone was 134.62 ±18.16 mg/dl, 199.48±16.34mg/dl, 71.34±5.84 mg/dl and 26.92 ±3.64 mg/dl respectively as compare to normal control (Fig-1).

Figure 1

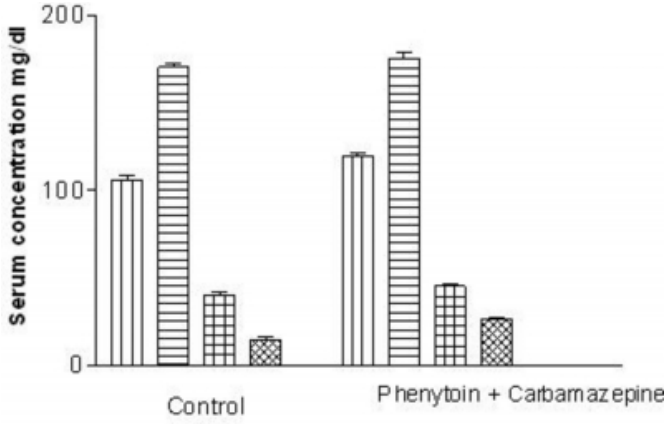
Figure 1



A significant increase in serum triglyceride, total cholesterol, HDLc and VLDLc in epileptic patients was observed on combination therapy of Phenytoin and Carbamazepine was 130.12 ±18.04 mg/dl, 193.14±16.28 mg/dl, 67.56±5.72 mg/dl and 26.02 ±3.58 mg/dl respectively as compare to normal control (Fig-2).

Figure 2

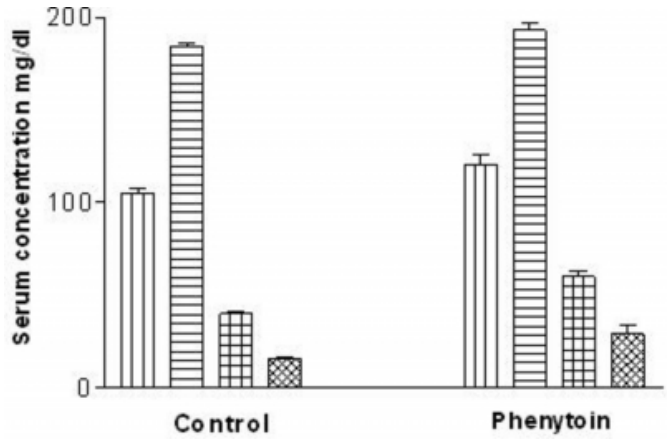
Figure 2



The increased level of serum triglyceride, total cholesterol, HDLc and VLDLc in epileptic patients was observed in Phenytoin alone was 122.18 ±17.06 mg/dl, 183.13±16.13 mg/dl, 63.56±5.59 mg/dl and 24.44 ±3.41 mg/dl respectively as compare to normal control (Fig-3).

Figure 3

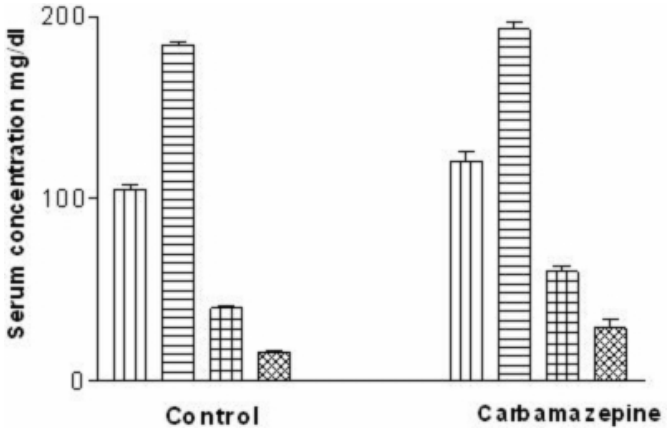
Figure 3



Patients receiving Carbamazepine alone have significant increase in serum levels of triglyceride 121.72 ±17.42 mg/dl and VLDLc 24.34 ±3.43 mg/dl but no significant changes in serum levels of total cholesterol 176.34±15.82 mg/dl & HDLc 53.78±4.76 mg/dl was observed in this group as compare to normal control (Fig-4).

Figure 4

Figure 4



DISCUSSION

The present study was carried out on one hundred and twenty cases of epilepsy patients attending epilepsy clinic of SVBP Hospital, Meerut. The most common seizure type observed was primary generalized tonic -clonic. Significant correlation between duration of anticonvulsant therapy and lipid profile was established. The longer the duration the greater was the increase in serum triglyceride, total cholesterol, HDLc and VLDLc. The increased level of serum triglyceride, total cholesterol, HDLc and VLDLc was observed in epileptic patients on combination therapy of either Phenytoin and Phenobarbitone or Phenytoin and Carbamazepine and monotherapy of Phenytoin alone as compare to normal control.

Patients receiving Carbamazepine alone have significant increase in serum levels of triglyceride and VLDLc but no significant changes in serum levels of total cholesterol & HDLc was observed in this group as compare to normal control.

Several workers reported an increase in tryglycerides in epileptic patients on long-term treatment with phenobarbitone ([11,12,13]). Pelkonen et al. 1975, Nikkila et al. 1978 and Luoma et al. 1979 ([7,9,14]) reported an increase in tryglycerides, cholesterol and HDLc in epileptics on long-term treatment with Phenytoin. Linvingston S 1976 ([15]) reported an increase in tryglycerides in 35 epileptics on long-term treatment with Carbamazepine. An increase in tryglycerides, cholesterol and VLDLc in epileptics on long-term treatment of anticonvulsant drugs was observed by Reynolds et al. 1976 ([16]). Our findings are in concordance with the other studies of correlation between duration of anticonvulsant therapy and lipid profile level ([7,16,17,18,19]). Combination therapy of either Phenytoin and Phenobarbitone or Phenytoin and Carbamazepine stimulates the hepatic synthesis of cholesterase and increase the formation and pool size of bile acids, which in turn raise the level of intestinal absorption of cholesterol by facilitating micelle formation. An increase in serum cholesterol may be regarded as an adverse effect on long-term anticonvulsant treatment as it increases the risk of coronary heart disease. Therefore the serum cholesterol level should be regularly monitored in patients undergoing such therapy.

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