ejpmr, 2017,4(09), 135-136

SJIF Impact Factor 4.161

EUROPEAN JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.ejpmr.com

Research Article

ISSN 2394-3211

EJPMR

EFFECTS OF PHENOBARBITAL DOSE ON SERUM LIPID PROFILE IN MALE RATS

Abbas Mohsin Abbas*, Khalid G. Al-Fartosi and Murtada Hafedh Hussein

College of Science, Thi-Qar University, Al-Nasiriya, Iraq.

***Corresponding Author: Abbas Mohsin Abbas**

College of Science, Thi-Qar University, Al-Nasiriya, Iraq.

Article Received on 14/07/2017 **Article Revised on 04/08/2017** **Article Accepted on 24/08/2017**

ABSTRACT

Serum lipid profile changes were investigated depend on dosage amount in 18 healthy male Wistar rats. Serum cholesterol, triglycerides (TGs) and high-density lipoprotein (HDL) levels were measured after a period of treating, low-density lipoprotein (LDL) and very low-density lipoprotein (VLDL) was calculated also. Our data revealed that, the administration of phenobarbital (10 mg\kg) didn't affect serum lipid profile significantly compared to control group in male rats, on the other hand we found that the administration of (20 mg\kg) of phenobarbital caused a significant increase in cholesterol and LDL compare to control group. According to our results we conclude that doubling of the dose cause an increase in cholesterol and LDL and switching from phenobarbital to another drugs or decrease the dosage as possible as could contributes to avoid effects on the lipid metabolism profile of patients with chronic epilepsy.

KEYWORDS: Phenobarbital, Cholesterol, TGs, HDL, LDL, VLDL.

INTRODUCTION

Epilepsy needs long-term and sometimes lifelong treatment. Thus, prolonged antiepileptic use could have some undesirable effects, and several reports have already shown that antiepileptic drugs (AEDs) influence cholesterol and lipoprotein serum levels.[1–5] On the other hand, increased serum concentrations of lipids and lipoproteins are associated with an increased risk of coronary disease.[6] Phenobarbital (PB) is an antiepileptic drug and is the prototype of a large family of lipophilic PB-like compounds that have profound effects in the liver. Its effects on liver physiology are typified by hepatic hypertrophy, hyper proliferation of the smooth endoplasmic reticulum, and induction or repression of numerous genes, especially the genes of cytochrome P450 enzymes.[7–9]

MATERIALS AND METHODS

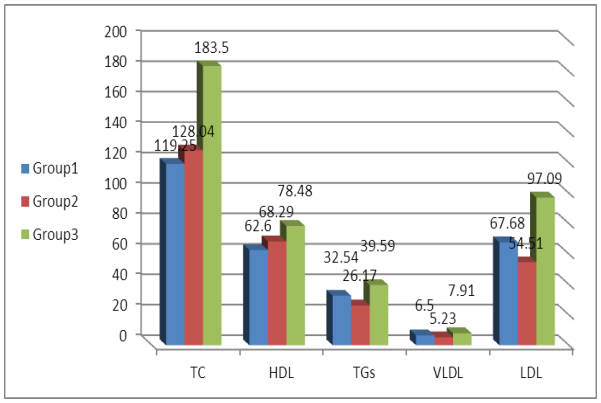
Twelve week old healthy male Wistar rats (150-200 g) were selected for the study. They were housed under controlled conditions of temperature of 23±2ºC and 10-14 h of light and dark cycles respectively. The animals were housed in cages throughout the experiment and had free access to food (animal chow) and water ad libitum, a total of 18 rats were segregated randomly to 3 groups of 6 animals each, control group was administrate orally with 0.2ml of (DMSO) for 20 days the other two groups treated orally with 10mg\kg and 20 mg\kg respectively of Phenobarbital, Body weights were recorded weekly to calculate the dose. The drug was obtained from local pharmacies. The dose and route of administration was based on earlier studies. Powdered form of PB was weighed and dissolved in DMSO (0.2 ml for each animal) and administered orally. Animals were sacrificed week after the last exposure to PB, Fasting samples were taken between 8.00 and 9.00 a.m, serum Cholesterol, HDL and TG levels were determined, LDL and Very low density lipoproteins VLDL was calculated according to the formula of Friedwald et al.[10] In order to detect statistically significant differences between the groups, we used the Student's t-test and One-Way Analysis of Variance (ANOVA). All tests were considered to be significant at a p-value <0.05.

RESULTS

The results of the different variables in the studied groups and controls are shown in the table and the figure below:

Groups	TC Mean ± S.D.	HDL Mean ± S.D.	TGs Mean ± S.D.	VLDL Mean ± S.D.	LDL Mean ± S.D.
Group1	119.25^{b} ±9.03	62.60^{a} ±12.60	32.54^{a} ±7.11	6.5^{a} ±1.42	67.68^{b} ±15.02
Group2	128.04^{b} ±14.87	68.29^{a} ±16.15	26.17^{a} ±4.7	5.23^{a} ±0.94	54.51^{b} ±37.65
Group3	183.50^{a} ±16.91	78.48^{a} ±13.96	39.59^{a} ±9.94	7.91^{a} ±0.81	97.09^{a} ±28.85

Group1: Control, **Group2**: PB (10 mg/kg), **Group3**: PB (20 mg/kg), Different letters refers to a significant difference at p-value <0.05.



The results are given in Table illustrated that: There is no significant changes (p-value <0.05) in serum levels of Cholesterol, TGs, VLDL, LDL and HDL in group that received (10 mg/kg) PB compared with control group. On the other hand the group which received (20 mg/kg) PB showed a significant increase (p-value <0.05) in serum levels of cholesterol and LDL compared with control group.

DISCUSSION

In this study, we have found that administration of (10 mg/kg) phenobarbital medication didn't affects TC, TGs, HDL,VLDL and LDL concentrations compare to control group, while the administration of (20 mg/kg) PB cause a significant increase in the levels of cholesterol and LDL concentrations. Our results are consistent with the findings of some reports and almost similar to those of Eiris *et al.*[11], Verrotti *et al.*[12] Mohamed *et al.*[13] The effects of AEDs on the serum levels of lipids and lipoproteins could be explained on the basis of the different biotransformation pathways of the AEDs, phenobarbital principally metabolized in the hepatic P450 microsomes, this enzyme system also catalyzes the transformation of cholesterol in biliary acids. Thus, PB in chronic treatment might compete with cholesterol in the utilization of those enzymes and this competition could cause a reduction in the transformation of cholesterol in bile acids. Thus, reduced cholesterol biotransformation increases total serum cholesterol levels.[14,15] The increased serum levels of lipids and Lipoproteins are associated with increased risk of coronary heart diseases, high serum cholesterol, LDL and TGs levels are well known risk factors for development of atherosclerosis and coronary heart diseases.[16] Our results suggest a need for careful monitoring of serum cholesterol levels in patients with epilepsy receiving phenobarbital.

REFERENCES

1. Berlit P, Krause K-H, Heuck CC, Schellenberg B. Serum lipids and anticonvulsants. Acta Neurol Scandina, 1982; 66: 328-34
2. Franzoni E, Govoni M, D'Addato S et al: Total cholesterol, high density lipoprotein cholesterol and triglycerides in children recei-ving antiepileptic drugs. Epilepsia, 1992; 33(5): 932-35.
3. Eiris JM, Lojo S, Del Rio MC et al: Effects of long-term treatment with antiepileptic drugs on serum lipid levels in children with epilepsy. Neurology, 1995; 45: 1155-57.
4. Isojarvi JIT, Pakarinen AJ, Myllyla VH: Serum lipid levels during carbamazepine medication. Arch Neurol, 1993; 50: 590-93.
5. Calandre EP, Rodriguez-Lopez MC, Blazquez A, Cano MD: Serum lipids, lipoproteins, and apolipoproteins A and B in epileptic patients treated with valproic acid, carbamazepine or phenobarbi-tal. Acta Neurol Scandina, 1991; 83: 250-53.
6. Castelli WP, Doyle GT, Gordon D et al: HDL cholesterol and other lipids in coronary heart disease: a cooperative lipoprotein pheno-typing study. Circulation, 1977; 55: 767-72.
7. Orrenius S, Ericsson JL, Ernster L. Phenobarbital-induced synthesis of the microsomal drug metabolizing enzyme system and its relationship to the proliferation of endoplasmic membranes. A morphological and biochemical study. J Cell Biol., 1965; 25: 627–639. [PubMed: 4378769]
8. Gonzalez FJ. The molecular biology of cytochrome P450s. Pharmacol Rev., 1988; 40: 243–288. [PubMed: 3072575]
9. Garcia-Allan C, Lord PG, Loughlin JM, Orton TC, Sidaway JE. Identification of phenobarbitone-modulated genes in mouse liver by differential display. J Biochem Mol Toxicol 2000; 14: 65–72. [PubMed: 10630419].
10. Friedwald WT, Levy RI, Frederickson DS: Estimation of the concentration of LDL-c in plasma without use of the preparative ultracentrifuge. Clin Chem., 1972; 18: 499-502.
11. Eirís J, Novo-Rodríguez MI, Del Río M, Meseguer P,Del Río MC, Castro-Gago M: The effects on lipid and apolipoprotein serum levels of long-term carbamazepine, valproic acid and phenobarbital therapy in children with epilepsy. Epilepsy Res., 2000; 41: 1–7.
12. Verrotti A, Domizio S, Angelozzi B, Sabatino G, Morgese G, Chiarelli F: Changes in serum lipids and lipoproteins in epileptic children treated with anticonvulsants. J Paediatr Child Health, 1997; 33: 242–245.
13. Mohamed M. Kantoush, Azza K. El-Shahawy, Samia S. Sokker*, Hanan R. Serag: Effects of Treatment with Antiepileptic Drugs on Serum Lipid Profile in Epileptic Children. Alexandria Journal of Pediatrics, 1998; 12: 1.
14. Luoma PV, Sotaniemi EA, Pelkonen RO et al: Plasma high density lipoprotein cholesterol and hepatic cytochrome P450 concentrations in epileptics undergoing anticonvulsant treatment. Scand J Clin Lab Invest, 1980; 40: 163-67
15. Luoma PV, Sotaniemi EA, Pelkonen RO et al: Serum low density and high density lipoprotein cholesterol and liver size in subjects on drugs inducing microsomal enzymes. Europ J Clin Pharmacol, 1985; 28: 615-18.
16. Heldenberg D, Harel S, Holtzman M, Levtow O, Tamir I. The effect of chronic anticonvulsant therapy on serum lipids and lipoproteins in epileptic children. Neurology, 1983; 33: 510-13.