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EFFECTS OF ADMINISTRATION OF TWO DIFFERENT DOSES FROM VALPROIC ACID ON LIPID PROFILE IN MALE RATS

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ABSTRACT

Antiepileptic drugs influence, among others, cholesterol and lipoprotein serum level, we designed this study to assume the effects of dose amount on this parameters. In this study Serum cholesterol, HDL, LDL, VLDL and triglycerides (TGs) levels were measured in eighteen healthy male Wistar rats (150-200 g) (subdivide randomly to three groups) after receiving two doses (0.25 mg\kg and 0.5 mg\kg) of Valproic acid (VPA) respectively for twenty day. Compared with controls, rats on (0.25 mg/kg) dose showed nonsignificant reduced TGs, VLDL, Cholesterol and HDL levels, and nonsignificant increase in LDL values, While rats on (0.5 mg/kg) dose showed significant reduced TGs, HDL and VLDL values and nonsignificant reduce in Cholesterol values and non significant increase in LDL values.

KEYWORDS: Cholesterol, Tgs, HDL, LDL, VLDL, Valproic Acid

INTRODUCTION

Epilepsy requires long-term and sometimes lifelong therapy. Thus, prolonged antiepileptic treatment could have some undesirable effects, and several reports have already shown that antiepileptic drugs (AEDs) influence cholesterol and lipoprotein serum levels [1–5].There has been an availability of medications to treat epilepsy for over 100 years. For example, the anticonvulsant property of phenytoin was identified in 1938, and since then, it has become an established antiepileptic drug (AED) therapy, Valproic acid was approved for use in Europe during the 1960s and in the USA in 1978(6). Both drugs are recognized as first-generation AEDs (7).

MATERIALS AND METHODS

Twelve week old healthy male Wistar rats (150-200 g) bred locally in the central animal house in biology department\college of sciences\ Thi-Qar university were selected for the study. They were housed under controlled conditions of temperature of 23±2 ºC 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 0.2 ml of (DMSO) for 20 days the other two groups treated orally with 0.25 mg\kg and 0.5 mg\kg respectively of valproic, Body weights were recorded weekly to calculate the dose. The valproic acid was obtained from local pharmacies. The dose and route of administration was based on earlier studies. Powdered form of valproic acid was weighed in an electronic weighing balance and was dissolved in DMSO (0.2 ml for each animal) and administered orally. Animals were sacrificed week after the last exposure to valproic, 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.*[8]. 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

Mean serum Cholesterol levels were non significantly reduced in the groups receiving (0.25 mg/kg) and (0.5 mg/kg) compare with control. Mean serum TG levels were lower significantly ($p<0.05$) in the groups receiving (0.5 mg/kg) , but not significantly in (0.25 mg/kg) group. Mean serum HDL levels were significantly lower ($p<0.05$) in the group receiving (0.5 mg/kg) , while the reduce was non-significant in the group receiving (0. 25 mg/kg). VLDL levels were significantly lower ($p<0.05$) in the group receiving (0. 5 mg/kg) , but the reduce was not significant in the group receiving (0.25mg/kg). Mean serum LDL levels were non significantly increased in groups receiving (0.25 mg/kg) and (0.5 mg/kg) compare with control (Table 1),(Figure1).

Table 1: Serum values of Cholesterol, TG, HDL, LDL and VLDL (mean, SD, in mg/100 ml)of treated animals and controls.

Groups	Cholesterol Mean ± S.D.	Tgs Mean ± S.D.	Hdl Mean ± S.D.	Vldl Mean ± S.D.	Ldl Mean ± S.D.
0.25 mg\kg	93.29 ±31.12	31.37 ±5.12	52.40 ±5.10	6.27 ±1.02	46.96 ±24.33
0.5 mg\kg	99.93 ±12.35	22.37* ±4.14	39.79* ±10.98	4.47* ±0.82	43.05 ±7.69
Control	103.58 ±37.72	33.89 ±12.71	55.40 ±12.95	6.97 ±2.54	41.40 ±28.8
LSD	42	12.54	8.7	2.47	16.39

* Statistical significance: $p < 0.05$

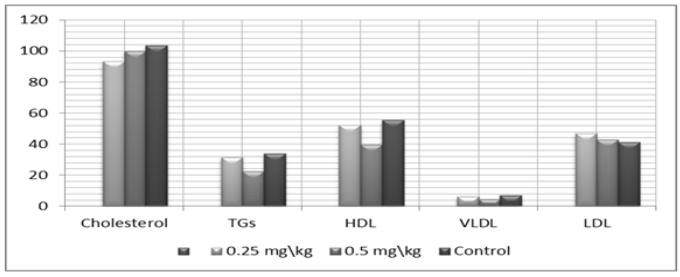

Figure 1: Values of Cholesterol, Tgs, HDL, LDL and VLDL (Mg/100 Ml) Of Treated Groups and Controls.

DISCUSSIONS

The results of profiles assessment showed significant reduction ($p<0.05$) in serum TGs, HDL andVLDL levels in the (0.5 mg/kg) valproic treated male rats in comparison to the control group, This may be explained by the induction of liver enzymes in the antiepileptic fed male rats, a finding similar to other studies in human epileptic patients, (9). In this study the doubled of the valproic dosage effects lipid profile significantly ($p<0.05$) except in cholesterol and LDL levels. Many studies have demonstrated the effects of long-term antiepileptic drugs on the lipid profiles of epileptic patients. There have been reports of lower values of Cholesterol, HDL and LDL or values similar to healthy controls have been found in epileptic patients treated with Valproic [10,11,12,13]. VPA is a well-known enzyme inhibitor, and this may causes the lower values of TGs, HDL and VLDL in this study [14].

CONCLUSIONS

Our findings suggest that the doubled dose were significantly affected TG, HDL and VLDL compare to control group in male rats treated with VPA, indicating a possible toxic effect of this excess in dose amount on lipid metabolism.

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