

ORIGINAL ARTICLE**Chronic intake of Valproic acid Decreases total Cholesterol Level in adult population**

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ABSTRACT

Background: Valproic acid (VA) serve as the antimigraine, anti-mental disturbances agent and antiepileptic medicine. After using VA, metabolic rearrangements seen in patients that include alteration in lipoproteins levels; however, this topic is still under discussion and disputable.

Aim: To discuss the effects of VA after using for long duration on total levels of cholesterol in adult.

Methods: About Eighty candidates participated and they were divided into two groups namely, case group (40 candidates) and control groups(40 candidates). All the candidates were asked for collection of venous blood sample in order to determine total cholesterol serum level among them via aid of enzymatic cholesterol oxidase phenol 4-aminoantipyrine peroxidase. By the aid of the logistic regression analysis, the relationship of the long-term VA treatment and the level of total cholesterol was obtained. With respect to our analysis, there is a co relation between total levels of cholesterol and long term usage of VA ($P=0.003$).

Results: There were no noteworthy link for age, sex, body BMI, height medication usage, smoking, diabetes mellitus and VA dosage , except combination of anti-epileptic drugs

Conclusion: In a net shell, by using VA for long duration, the total level of cholesterol in adults reduces.

Keywords: Lipid profile, side effects, total cholesterol, valproic acid

INTRODUCTION

Valproic acid (VA) is short chained, branched fatty acid that is mostly indicated in case of migraine, mental disturbances and epilepsy⁴. After using VA for longer duration, there is increase in levels of leptin and insulin and subsequently increase in risk factor for hypercholesterolemia⁶.

For atherosclerosis, hypercholesterolemia serves as a major risk factor⁸. By increasing the level of cholesterol in individuals, the risk for coronary health diseases in productive ages multiplies by 3.78–4.32⁴. Many case researches proved that there is an increase in rate of deaths in patients of atherosclerosis with epilepsy⁸. The final impact of VA on total levels of cholesterol is still disputable. Some case researches depicted that there are noteworthy changes in total cholesterol levels while some case studies demonstrates no impact of VA on total levels of cholesterol². Due to these disputes, we documented the relationship between use of VA for longer duration and its effect on total serum cholesterol levels among adult.

MATERIALS AND METHODS

After approval from Ethical Committee this case research was conducted by using VA among candidates for duration of 6 month 2020 with respect to inclusion criteria

candidate age should be 20 years or above where as exclusion criteria included if candidate was taking carbamazepine, phenytoin, gemfibrozil and statins and previously having back ground of dyslipidemia before VA usage. These all criteria were analyzed during interview of candidates and then final conformation was made by checking medical records of each candidate.

Total candidates participated were Eighty. From 80, 40 candidates were categorized into case group in which candidates had cholesterol levels greater than 200mg/dL and whereas 40 candidates were placed in control group, in which total cholesterol level of candidate was equal or less than dL .Sampling method was utilized for selection of candidates. All the candidates were made to fast about 8 hours at least for testing cholesterol levels intravenously.

The total level of cholesterol was tested by aid of Cholesterol kit and preparation of sampling was done with respect to manufacturer insert kit and performed using parameters such as, body mass index (BMI), sex, smoking history, usage of other medications, anti epileptic drugs and diabetes mellitus were by aid of Chi-square test, whereas data such as weight, age, BMI, height of body and daily VA dosage were accessed by aid of two-independent sample T-test because of the normal distribution of data. By the aid of Chi-square test, the relation between VA treatment usage (long term) and cholesterol levels of candidates were accessed then with logistic regression continued.

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RESULTS

Results depicted that there were no noteworthy link for age, sex, body BMI, height medication usage, smoking , diabetes mellitus and VA dosage, except combination of anti-epileptic drugs [Table 1].

Table 1: Demographic characteristics of the participants (*n*=80)

Variable	Increase cholesterol%	Normal cholesterol%	p
Male	55	45	0.002
Female	43	57	
Medication	23	6	0.003
Diabetics	7	3	0.003
Antiepileptic drug	17	19	0.002

Recently, there is no case research depicted a cutoff point of time-associated to the linkage of the time of treatment of VA and total cholesterol levels, herewith we utilize cutoff points 12 months duration, got via Receiver Operating Characteristic (ROC) curve.

The total effects of treatment of VA for longer duration on levels of total cholesterol is depicted in Table 2. This depicted that long term usage VA for more than 12 months of duration has been linked with decline in total serum levels of cholesterol (*p*= 0.003).

Table 2: link between valproic acid treatment duration and total serum levels of cholesterol

Valproic acid treatment duration	High cholesterol %	Normal cholesterol	p
>12	42	58	0.003
<12	57	43	0.003

Analysis of data was then made by aid of logistic regression for the variable timet via VA treatment, combination of anti-epileptic drug and total serum the level of cholesterol. An association was found via result that suggested that there was a link between VA treatment time and total serum cholesterol levels (*p*=0.003 for the long term use of VA), so this suggested that usage of VA for more than duration of 12 months has been associated with risk of 3.53 times lesser as compared to usage of VA for less than duration of 12 months.

DISCUSSION

The levels of cholesterol relation with VA treatment (long term) was depicted at the cut-off point of duration of 12 months. Use of VA after 12 months depicts a noteworthy link between duration of treatment via VA and cholesterol level. Candidates who utilized VA more than duration of 12 months were at risk of 3.52 times smaller in cholesterol levels as compared to candidates who had VA administration for 12 months or less than that.

Our case results are same as the results of case research via Nisha *et al.*, 2018 who did comparison of cholesterol level in epilepsy patients who were diagnosed recently and compared results with level of cholesterol in patients who were under treatment of VA for greater than 12 months for epilepsy. The case research suggested that cholesterol level in candidates treated with already VA was less as compared to candidates who were recently

diagnosed with epilepsy⁴. Moreover, the result of our case reach was same to reach study of Kantouch *et al.*, which depicted that total cholesterol level was lower in children who had epilepsy and given treatment with VA as compared to the control group¹⁰. In addition, Abidemi *et al.*, did experiment on alloxan-induced Wistar rats that depicted via using VA there was reduction in triglyceride, LDL and total cholesterol⁹.

The conclusion of our case reach also got similarity with case reach of Kantouch *et al.*, which depicted that total cholesterol level and triglycerides, in kids who were treated with VA for epilepsy was lower as compared to control group⁷. In addition, Abidemi *et al* by aid of alloxan-induced Wistar rats depicted that reduction significantly in total cholesterol levels, LDL levels and triglycerides after administration of VA⁸.

The conclusion of this case research proved that candidates who were administered VA for greater than 12 months of duration were less likely to develop (3.53 times less) high levels of cholesterol as compared to candidates who were administered VA for less than 12 months of duration. This depicts that after using VA for more than 12 months, there is decline in total serum cholesterol levels. It can also be said that long duration usage of VA is linked with improvement in lipid profile of patients (especially total cholesterol). Decline in total serum cholesterol levels can be associated with VA usage for long duration due to the fact that it causes betterment in organs which are linked with metabolism of cholesterol. With respect to case research by Huang *et al.*, 2017, VA has impact on oxidative stress specially in the endoplasmic reticulum by the aid of glycogen synthase kinase 3β which is associated with metabolism of cholesterol and pathologies related to atherosclerosis¹⁰.

Moreover, it is also hypothesized that usage of VA contributes to the differentiation, proliferation and improving functional ability of beta cells of pancreas so therefore, overall improving secretion of insulin via beta inhibitory mechanism in histone deacetylase (HDAC)⁸. A protein known as HDAC is involved in process of recovery of beta cell damage in pancreas so overall aid in making insulin secretion better¹¹.

CONCLUSION

The use of VA for more than 12 months decreases the level of total cholesterol.

Conflict of interest: Nil

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