

LONGTERM EFFECT OF PHENYTOIN ON LIPID PROFILE PARAMETERS IN EPILEPTIC PATIENTS

M.Beg*, S. Afzaal**, A. Kamal***, A. Amir****

ABSTRACT:

Research Problem: What are the factors responsible for decreased incidence of coronary artery disease in epileptics?

Objectives: To evaluate the effect of phenytoin on lipid profile parameters in epileptics and to discuss its implications.

Study Design: Prospective study.

Setting: Neurology clinic of Medicine Department of a teaching hospital.

Participants: Randomly selected epileptic patient attending neurology clinic and admitted to inpatient department of J. N. Medical College Hospital.

Sample Size: 56 epileptic patients.

Study Variables: Phenytoin therapy, lipid profile parameters.

Statistical Analysis: By test of significance.

Result: No significant change in serum levels of total cholesterol, LDL - C, VLDL - C, triglycerides and phospholipids was observed with phenytoin therapy during study. However, serum HDL - C showed a significant increase, both at 12 weeks and 24 weeks ($P < 0.001$) of therapy.

Conclusion: Phenytoin, a commonly used anticonvulsive drug, increases serum HDL - C level significantly, while there is no significant change in other parameters of lipid profile. This rise in HDL - C may provide protection to epileptic patients against atherogenic vascular diseases including coronary artery disease.

Key Words: Serum lipid, Phenytoin, HDL - C, Epilepsy

INTRODUCTION:

Epilepsy forms one of the major public health problems in our country and is the largest group

requiring long-term anticonvulsive therapy. Though these patients come out of agony, they are predisposed to various untowards effects¹ including abnormalities in serum lipid and lipoproteins with possible implication of atherogenic vascular diseases like coronary artery disease^{2,3}, ischaemic cerebrovascular diseases^{4,5} and peripheral vascular diseases⁶. However, the clinicians working on epilepsy have reported decreased incidence of coronary artery disease in epileptics on long-term anticonvulsive therapy but with conflicting results. The present study was, therefore, undertaken to evaluate the effect of phenytoin on various parameters of lipid profile and to discuss its implications.

MATERIAL AND METHODS:

The study comprised of 56 newly diagnosed epileptic patients attending Neurology Clinic or admitted in inpatient department of Medicine who were randomly selected for the study. They were placed on phenytoin 200 - 300 mg. / day orally and 5 ml venous blood was collected after overnight fasting for estimation of various parameters of lipid profile at basal level, 12 weeks and 24 weeks of therapy. 25 comparable subjects served as control.

OBSERVATIONS:

Out of 56 cases, 75% were males and 25% were females. The maximum number of cases were in 11-20 years age group with mean age of 24.22 years (Table - I). Majority of the patients (59%) presented within one year of attack (Table- II) and had primary generalised seizures.

No significant change in levels of various parameters of lipid profile was observed in study group before starting the therapy as compared to the control group, thus, showing that epilepsy per se does not produce any dyslipidemia.

With phenytoin therapy, no significant change was observed in levels of total serum cholesterol, LDL - C, VLDL - C, triglyceride and phospholipids. Serum

* Lecturer, ** Professor and Chairman, *** Resident, Dept. of Medicine, J.N. Medical College, A.M.U., Aligarh

**** Lecturer - cum - Epidemiologist, Dept. of Community Medicine, J.N. Medical College, A.M.U., Aligarh

HDL - C level, however, showed a significant increase both at 12 weeks and 24 weeks of therapy. The rise in level of HDL - C was 14.5%, (males - 16.22% and females - 9.59%) at 12 weeks and 18.63% (males - 19.27%, females - 16.76%) at 24 weeks of therapy as compared to the basal level. Six of our patients failed to show any change in parameters of lipid profile.

DISCUSSION:

Epilepsy is a major public health problem requiring long-term therapy, resulting in large number of untoward effects¹. Various studies have been carried out to study untoward effects in epileptics on long-term anticonvulsive therapy^{2,3,4,5,6}. However, clinicians working on epilepsy have shown a decreased incidence of coronary artery disease in patient of epilepsy receiving long-term anticonvulsive therapy^{7,8,9} but with conflicting results¹⁰.

The present observations of significant increase in HDL - C with insignificant changes in other

parameters of lipid profile in epileptic patients on long-term phenytoin therapy is consistent with studies of other authors.^{11,12,13,14}

Exact mechanism by which phenytoin increases HDL - C is poorly understood but induction of microsomal enzyme system in liver may be an important factor in determining the plasma lipid concentration.¹⁵

CONCLUSION:

The following conclusions can be drawn from the present study:

1. Phenytoin increases significantly serum HDL - C level while there is no significant change in other lipid parameters.
2. The rise in HDL - C may be genetically determined.
3. Rise in HDL - C may provide protection to epileptic patients against atherogenic vascular diseases, including coronary artery disease.

TABLE - I

AGE AND SEX DISTRIBUTION OF CASES AND CONTROL

Age group (years)	Study group				Control group			
	Male	Female	Total	%	Male	Female	Total	%
11-20	20	4	24	42.86	9	3	12	48.0
21-30	14	6	20	35.71	4	3	7	28.0
31-40	8	2	10	17.86	3	2	5	20.0
41-50	0	2	2	3.57	1	0	1	4.0
TOTAL	42	14	56	100	17	8	25	100

TABLE - II

DISTRIBUTION OF CASES ACCORDING TO DURATION OF ILLNESS

Duration (in years)	No. of patients	%
0 - 1	33	59.1
1 - 2	15	26.8
2 - 3	8	14.2
TOTAL	56	100

TABLE-III

LIPID PROFILE IN CONTROL AND STUDY GROUPS BEFORE STARTING PHENYTOIN TREATMENT

Group	Total serum cholesterol	HDL - C	LDL - C	VLDL - C	Triglyceride	Phospholipid
I Control group (n=25)	186±23.25	50.04±43.61	114.8±21.13	21.52±1.53	107.76±7.42	200±33.17
A. Male (n=17)	189.65±26.83	49.41±3.67	118±24.51	22±1.8	110±8.77	199.17±30.92
B. Female (n=8)	178.25±22.47	51.37±3.14	108±12.57	20.5±0.71	103±3.54	201.75±39.76
II Study group (n=56)	192.46±31.23	53.28±6.98	118.82±24.38	20.5±6.38	102.61±31.61	193.21±25.92
A. Male (n=42)	192.95±30.89	53.14±6.89	119.48±24.5	20.43±6.87	101.95±34.07	193.95±22.12
B. Female (n=14)	191±34.75	53.71±7.82	116.86±25.99	20.71±5.06	104.57±25.03	191±37.32

P value

I - II	NS	NS	NS	NS	NS	NS
I _A - II _A	NS	NS	NS	NS	NS	NS
I _B - II _B	NS	NS	NS	NS	NS	NS

Values in mg/dl (mean • SD) (NS: Not significant)

TABLE-IV

LIPID PROFILE IN STUDY GROUP AFTER 12 WEEKS OF PHENYTOIN TREATMENT

Study group	Total serum cholesterol	HDL - C	LDL - C	VLDL - C	Triglyceride	Phospholipid
I Zero week (n=56)	192.46±31.23	53.28±6.98	118.82±24.38	20.50±6.38	102.61±31.61	193.21±25.92
A. Male (n=42)	192.95±30.89	53.14±6.89	119.48±24.5	20.43±6.87	101.95±34.07	193.95±22.12
B. Male (n=14)	191±34.75	53.71±7.82	116.86±25.99	20.71±5.06	104.57±25.03	191±37.32
II 12 weeks (n=42)	201.43±31.46	61.03±11.27	120.18±24.97	21.11±4.16	104.64±20.71	195.32±33.4
A. Male (n=42)	202.05±31.54	61.76±12.54	120.52±24.19	21.05±4.35	103.76±21.73	195.09±35.16
B. Female (n=14)	199.5±33.72	58.86±6.89	119.14±29.25	21.28±3.81	107.28±18.84	196±30

P value

I - II	NS	P<0.001	NS	NS	NS	NS
I _A - II _A	NS	P<0.01	NS	NS	NS	NS
I _B - II _B	NS	P<0.001	NS	NS	NS	NS

Values in mg / dl (Mean • SD) (NS : Not significant)

TABLE - V

LIPID PROFILE IN STUDY GROUP AFTER 24 WEEKS OF PHENYTOIN TREATMENT

Study group	Total serum cholesterol	HDL - C	LDL - C	VLDL - C	Triglyceride	Phospholipid
I Zero week (n=56)	192.46±31.23	53.28±6.98	118.82±24.38	20.50±6.38	102.61±31.61	193.21±25.92
A. Male (n=42)	192.95±30.89	53.14±6.89	119.48±24.5	20.43±6.87	101.95±34.07	193.55±22.12
B. Male (n=14)	191±34.75	53.71±7.82	116.86±25.99	20.71±5.06	104.57±25.03	191±37.32
II 24 weeks (n=56)	202.68±28.96	63.21±9.89	118.36±23.97	21.32±4.14	106.53±19.29	203.25±24.61
A. Male (n=42)	202.19±30.21	63.38±11.04	118.14±24.88	21.09±4.53	105.14±22.28	205.2±25.94
B. Female (n=14)	204.14±27.06	62.71±5.79	119±22.86	22±2.94	110.71±14.6	198±21.98

P value

I - II	NS	P<0.001	NS	NS	NS	NS
I_A - II_A	NS	P<0.001	NS	NS	NS	NS
I_B - II_B	NS	P<0.001	NS	NS	NS	NS

Values in mg / dl (Mean • SD) (NS = Not significant)

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