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Effect of Alpha-Tocopherol on Lipoprotein Profile in Normal and Hyperlipidaemic Rats

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Abstract:*Atherosclerosis is the underlying cause of coronary artery disease, which in turn results from raised oxidized lipoprotein levels. This study was aimed to find out the effect of an anti-oxidant, Alpha-tocopherol, on serum lipoprotein level in rats. Alpha-tocophopherol was administered orally daily in a dose 60mg/kg body weight for 90 days to groups of control and hyperlipidemic rats, and the serum lipoprotein levels (total cholesterol, triglyceride, LDL, HDL, VLDL) were measured on 0, 30, 60 and 90 days of drug administration and compared. The results showed that Alpha-tocopherol in a dose of 6mg/100gm body weight daily orally for 90 days prevented serum lipid parameters to shift in favour of atherosclerosis, both in normal and hyperlipidemic rats.Hence, Alpha-tocopherol has significant hypolipidemic activity in animal model.*

Key words: *dyslipidaemia vitamin E hyperlipidemic diet*

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I. Introduction

Atherosclerotic coronary artery disease (CAD) is the most widely prevalent killer disease all around the globe and its incidence is increasing proportionate to industrialization and modernization. The forerunner of atherosclerosis is hyperlipidaemia, a disorder of lipid metabolism. Clinical and experimental studies reveal that high levels of LDL and TG is closely associated with increased risk of CAD and an inverse relation is found with HDL levels. Effective control of serum lipoprotein levels by drugs can reduce the risk of development of atherosclerotic CAD[1,2.] Hence, drug therapy for hyperlipidaemia is of utmost importance in the treatment of CAD patients.

A crucial step in the pathogenesis of atherosclerosis is oxidative metabolism of low density lipoprotein (LDL), a free-radical driven lipid peroxidation process, where the aldehyde products of lipid hydroperoxide breakdown help to modify the LDL apoprotein[3]. Aldehyde modified apo-B protein has altered receptor affinity, causing it to be scavenged by the macrophages in an uncontrolled manner with the development of 'foam cells' and initiation of the atherosclerotic lesion[4]

Alpha-tocopherol (Vitamin E), a lipid phase antioxidant, might help to prevent oxidation of LDL as well as alter other lipid parameters and prove to be useful in prevention of coronary artery disease[5-6].Anti-oxidants like Vit E consumption have shown to lower risk of coronary disease in men and women, in several studies[7,8].

Hence, this study was undertaken to assess the role of Alpha-tocopherol pre-treatment on serum lipoprotein parameters in normal and hyperlipidaemic rats.

II. Material and Methods

Selection of Animals : Forty adult, male, healthy, Swiss albino rats of either sex, weighing between 150-200gms, were selected randomly from the Central Animal House of Department of Pharmacology, S.C.B. Medical College, Cuttack. They were housed in polypropylene cages and maintained at 23^{o} C in 12: 12 light-dark cycle and given water ad libitum. The Study Protocol was approved by the Institutional Animal Ethics Committee.

Grouping of Animals : Rats were grouped into four groups with ten rats in each group.

a) Control Rats : Group 1 and 2 were supplied with Basal diet (comprising of wheat flour 60%, casein 12%, peanut oil 5%, sucrose 5%, starch 13.8%, mineral mixture 4%, vitamin mixture 0.2%) at 12 noon every day for a period of 3 months. (Group 1 received Normal Saline daily while Group 2 received Alpha-tocopherol daily).

b) HyperlipidemicRats : Rats of groups 3 and 4 were administered with hyperlipidaemic diet (Basal diet + Cholesterol 1 % (in place of starch) for a period of 3 months.(Group 3 received Normal Saline daily while Group 2 received Alpha-tocopherol daily).

Administration of Drugs : Rats of different groups were administered the following drugs daily as given below

Group	Type of Rats	Drug administered	Dose	Route
1	**CONTROL RATS**	Normal Saline	1 ml	Orally daily for 90 days
2	**(On Basal Diet for 90 days)**	Alpha-tocopherol	6mg/100gm bwt	
3	**HYPERLIPIDEMIC RATS**	Normal Saline	1ml	
4	**(High Cholesterol Diet for 90 days)**	Alpha-tocopherol	6mg/100gm bwt	

Collection of Blood Samples : Blood samples were collected from the tail vein of rats using calibrated capillary tubeon days 0, 30, 60 and 90 of drug administration, after overnight fast. Alpha-tocopherol was obtained from E-Merck, Mumbai.

Biochemical Analysis: Estimation of Serum Lipids (Total Cholesterol (TC), Triglycerides (TG), LDL, VLDL and HDL) were done with the help of kits (Pointe Scientific Inc., Michigan, USA) and Spectrophotometer (Systronics UV-Vis Spectrophotometer 118).

Statistical Analysis : Student's Paired t test was used to compare the mean lipoprotein levels at different time intervals within the same group. Unpaired t test was used for comparison between groups.

III. Results

The mean serum lipoprotein concentration (TC, TG, HDL, LDL, VLDL) of rats on basal diet (Control Group) andhyperlipidemicdiet were measured on0, 30, 60 and 90 days of Normal Saline and Alpha-tocopherol treatment, and are depicted below in Table 1.

Table 1. Effect of Alpha-Tocopherol on Serum Lipoprotein Levels in Normal and Hyperlipidemic Rats

LIPID PARAMETERS	RAT GROUP	DRUG TREATMENT	GR NO.	MEAN SERUM LIPOPROTEIN CONC. AT DIFFERENT TIME INTERVALS (in mg/dl ± SEM)		
				Day 30	Day 60	Day 90
TOTAL CHOLESTEROL	Control	N.Saline	1	82.3±0.77	82.3±0.83	82.2±0.87
		Alpha-Tocopherol	2	81.4±0.76	80.9±0.69	79.5±0.7
		P value		> 0.05	>0.05	<0.05*
	Hypolipidemic	N.Saline	3	93.4±0.65	124±0.84	135±0.76
		Alpha-Tocopherol	4	87.3±0.97	99.5±1.19	112.1±1.1
		P value		<0.001*	<0.001*	<0.001*
TRIGLYCERIDE	Control	N.Saline	1	73.3±0.54	73.1±0.53	73.2±0.56
		Alpha-Tocopherol	2	72.6±0.31	71.9±0.34	70.5±0.24
		P value		>0.05	>0.05	<0.001*
	Hypolipidemic	N.Saline	3	96.4±0.76	124±1.05	145±0.78
		Alpha-Tocopherol	4	91.6±0.84	114±1.04	130±1.39
		P value		<0.001*	<0.001*	<0.001*
HDL CHOLESTEROL	Control	N.Saline	1	22.6±0.28	22.4±0.28	22.6±0.31
		Alpha-Tocopherol	2	23.5±0.46	23.2±0.34	24.8±0.29
		P value		>0.05	>0.05	<0.001*
	Hypolipidemic	N.Saline	3	21.5±0.42	20.1±0.48	19.5±0.41
		Alpha-Tocopherol	4	21.9±0.60	21.9±0.51	22.3±0.52
		P value		>0.05	<0.05*	<0.001*
LDL CHOLESTEROL	Control	N.Saline	1	45.0±0.70	45.0±0.72	44.6±0.84
		Alpha-Tocopherol	2	43.8±0.83	42.4±0.74	40.6±0.81
		P value		>0.05	<0.05*	<0.01*
	Hypolipidemic	N.Saline	3	53.0±0.68	78.6±0.70	88.7±0.76
		Alpha-Tocopherol	4	46.3±1.34	55.5±2.21	65.6±0.89
		P value		<0.001*	<0.001*	<0.001*
VLDL CHOLESTEROL	Control	N.Saline	1	14.7±0.11	14.6±0.11	14.6±0.11
		Alpha-Tocopherol	2	14.5±0.06	14.4±0.07	14.1±0.05
		P value		>0.05	>0.05	<0.001*
	Hypolipidemic	N.Saline	3	19.3±0.15	24.8±0.21	28.9±0.16
		Alpha-Tocopherol	4	19.3±0.15	22.7±0.21	26.0±0.28
		P value		>0.05	<0.001*	<0.001*

Unpaired t test - for comparison between Control rats and Hyperlipidemic rats; *p value <0.05 denotes significant difference.

The serum total cholesterol, triglycerides, HDL, LDL and VLDL levels have not changed significantly over 90 days ($p>0.05$) from that of its basal value, in control group of rats treated with N.Saline (Gr-1).

In the rats fed with hyperlipidemic diet and treated with N.Saline (Gr-3), all the lipoprotein parameters increased significantly from 30 days to 90 days of observation ($p<0.001$).

Administration of Alpha-tocopherol to the Control Group of rats (Gr-2) lowered the serum lipoprotein levels significantly on the 90^{th} day of observation ($p<0.05$), compared to the 30^{th} day. But, in the Hyperlipidemic rats, Alpha-tocopheroltreatment (Gr-4) significantly lowered ($p<0.001$) all lipoprotein parameters on 60^{th} day and 90^{th} day, in comparison to the N. Saline treated group (Gr-3).

IV. Discussion

The present study was conducted to investigate the effect of alpha-tocopherolpretreatment on serum lipoprotein profile in normal and hyperlipidemic rats. The serum total cholesterol, triglycerides, HDL, LDL and VLDL levels has not changed significantly ($p>0.05$) from that of its basal value in control group of rats on basal diet over 90 days. This is due to the mineral oil (PUFA) which maintains the lipid profile at constant level. This positively correlates with the findings of Pachori SB et al[9.]

Rats on hyperlipidemic diet showed significant progressive increase all the lipoprotein parameters over the period of 90 days in comparison to basal value ($p<0.001$).

In the Control group of rats, Alpha-tocopherol administration for 90 days was able to significantly lower all the lipoprotein parameters on the 90 day of observation ($p<0.05$), when compared to the N. Saline treated groups. This proves that Alpha-tocopherol can lower the normal lipoprotein parameters in the healthy subjects.

In the Hyperlipidemic groups, Alpha-tocopherol treatment significantly lowered all the lipid values, except HDL which was significantly raised, when compared with the N.Saline treated controls at all the observation days (30, 60 and 90 days) ($p<0.05$), except the HDL and VLDL on 30th day. Thelow range of the latter two lipid parametersin serum,could be reason why there was no early change in their levels.

This study also proves the protective action of Alpha-tocopherolon all lipid parameters. It is known for its anti-oxidant activity, protecting LDL oxidation, and imparting protection against coronary artery disease and acute myocardial infarction in several studies [10-14]. HDL is a major carrier of Alpha-tocopherol and higher levels this vitamin also raises HDL, which can inhibit the binding and initiation of atherosclerosis[15]. Several recommendations are being put forth to include Alpha-tocopherol (Vitamin E) as a drug to prevent development of coronary artery disease [16].

V. Conclusion

Alpha-tocopherol in a dose of 6mg/100gm body weight daily orally for 90 days cansignificantly lower serum lipid parametersand offer significant protection against atherosclerosis, in normal and hyperlipidemic rats.

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