ORIGINAL ARTICLE

Niacin is Major Drug for Lowering LDL - Cholesterol

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ABSTRACT

Objective: Study was planned to examine the effects of Niacin (Vitamin B-3) on serum LDL-Cholesterol levels

Design: Single blind placebo controlled study.

Place and duration of study: Study was conducted at department of Pharmacology, Basic Medical Sciences Institute (BMSI), Jinnah Postgraduate Medical Centre (JPMC), Karachi, from January 2002 to July 2002

Patient and methods: Forty hyperlipidemic patients were included, among which 20 patients were on placebo as control group, and 20 were on tablet Niacin, 2 gram daily, in divided doses for the period of three months. Patients with diabetes mellitus, peptic ulcer, renal disease, hepatic disease, hypothyroidism and alcoholism were excluded from the study. Serum LDL-cholesterol was calculated by Friedwald formula(LDL-Cholesterol = Total Cholesterol-(Triglycerides/5 +HDL-Cholesterol) described by Delong et al (1986) and Beamount et al (1970).Data were expressed as the mean ± SD and "t" test was applied to determine statistical significance as the difference. A probability value of <0.05 was the limit of significance.

Results: Three patients were dropped from the study due to side effects of Niacin. Niacin has decreased the levels of LDL-Cholesterol from182.58±8.74 mg/dl to 119.29±4.08 mg/dl, which was highly significant (P<0.001), when compared statistically by paired "t" test. Overall percentage (%) changes from day-0 to day-90 were -34.66

Conclusion: Finally we concluded from this study that Niacin decreases the risk of CHD by decreasing LDL-Cholesterol

Key words: Niacin.LDL-Cholesterol. Atherosclerosis. Primary hyperlipidemia

INTRODUCTION

Hypertension and coronary heart disease (CHD) are of great importance. CHD is the cause of death in 30% of males and 22% of females in England and Wales[1].

In Pakistan 46% cardiac deaths are due to myocardial infarction and 23% are due to other subsets of ischemic heart disease.70% of these patients die even before any medical help is made available to them. Major risk factors associated with the development of CHD include gender, age, cigarette smoking, diabetes mellitus, hypertension and hyperlipidemia[2]. LD-L is major risk factor for the development of atherosclerosis and then to CHD[3].

Certain plasma lipoproteins are linked to accelerated atherogenesis. The lipoproteins that contain apoprotein (apo) B-100 have been identified as the vehicles in which cholesterol is transported into the artery wall. These atherogenic lipoproteins are the LDL, IDL, VLDL and LP (a) lipoproteins. Oxidations of lipoproteins lead to their uptake by receptors on these cells, forming foam cells in which cholesteryl esters accumulate[4].

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Atherosclerotic disease of both coronary and peripheral arteries appears to be a dynamic process. Evidence from studies both in animals and in humans indicate that progression can be slowed if elevated serum concentrations of the atherogenic lipoproteins can be reduced. Reversal of atheromas has been demonstrated in animals and, more recently, in humans following drug treatment of hyperlipidemia[5].

There are various drugs which decrease total cholesterol, triglycerides, LDL-C and increase HDL-C in primary hyperlipidemic patients, but Niacin is the best LDL-C decreasing agent among the lipid lowering drugs.6 Niacin inhibits the activity of hormone sensitivity lipase causing decrease in lipolysis and so decreased VLDL secretion from hepatocytes.7 Factors responsible for decreased production of VLDL include inhibition of lipolysis with a decrease in free fatty acids in plasma, decreased hepatic esterification of triglycerides, and a possible direct effect on the hepatic production of apolipoprotein-B. Niacin also increases HDL-C by reducing its catabolism. It also decreases plasma fibrinogen levels and increase tissue plasminogen activator. All of these factors influence the process of atherogenesis and CHD[3].

PATIENTS AND METHODS

This study was conducted at department of Pharmacology and therapeutics, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, from January to July 2002. Forty patients of primary hyperlipidemia were initially enrolled in this study, selected from ward and OPD of National Institute of Cardiovascular Diseases, Karachi. Newly diagnosed and untreated primary hyperlipidemic patients of either sex, age range from 17 to 70 years were randomly selected. Patients with diabetes mellitus, peptic ulcer, renal disease, hepatic disease, hypothyroidism and alcoholism were excluded from the study by available laboratory investigation, history and clinical examination. After explaining the limitations, written consent was obtained from all participants. The study period consisted of 90 days with fortnightly follow up visits. The required information such as name, age, sex, occupation, address, previous medication, date of follow up visit and laboratory investigations, etc of each patient was recorded on a proforma, especially designed for this study. Initially a detailed medical history and physical examination of all patients were carried out. All the base line assessments were taken on the day of inclusion (Day-0) in the study and a similar assessment was taken on Day-90 of research design. After fulfilling the inclusion criteria patients were randomly divided into two groups, i.e. Drug-1(tab: Niacin 2gm) and Drug-2(placebo capsules, containing equal amounts of partly grinded wheat) groups. Patients of drug-1 group were advised to take Tab: Niacin (250 mg), half tablet thrice daily, after meal for 2 days, then by increasing the dose one tablet, TID, after meal for 2 days, then 2 tablets, thrice daily after meal for 2 days, then the maintenance dose of 3 tablets per day after meal, thrice daily, till end of the study period, i.e. up to day-90. This regimen of dose of drug (called titration of Niacin) was applied due to avoidance of it's adverse effects produced by starting with higher doses of the Niacin.17 Patients of drug-2 group were provided placebo capsules, i.e. one capsule, TID, after meal for 90 days. Patients were called every 2 weeks for follow up to check blood pressure, weight, pulse rate and general appearance of the individual. Drug compliance to the regimen was monitored by interview and counseling at each clinical visits. Serum LDL-cholesterol was calculated by Friedwald formula[9] (LDL-Cholesterol=Total Cholesterol-(Triglycerides/5 +HDL-Cholesterol) described by Delong et al (1986)[10] and Beamount et al (1970)[11]. Data were expressed as the mean ±SD and "t" test was applied to determine statistical significance as the difference. A probability value of <0.05 was the limit of significance.

RESULTS

Out of 40 patients, 37 completed the over all study period. Three patients withdrew from one group (Niacin group) due to side effects of the drug like flushing, sensation of heat, urinary and headache. Tables showing base line and post treatment values are self explainatory. When results were summed up and test parameters were compared, it was seen that, after 90 days of treatment with Niacin, LDL-Cholesterol decreased from 182.58±8.74 mg/dl to 119.29±4.08mg/dl, which is highly significant (P<0.001). The overall percentage change from day-0 to day-90 was -34.66, as shown in table. In placebo group at day-0, LDL-Cholesterol level was 150.75±2.67 mg/dl, which decreased to 148.80±2.28 mg/dl, which is non-significant (P>0.05).The overall percentage decrease in the parameter was -1.29.The difference between mean values among placebo group and Niacin group is 33.4, which is highly significant (<0.001) as shown in the table:

Table 1: Changes in LDL-Cholesterol in Niacin group of patients (n=17)

Parameter	At day-0	At day-90	% Change
LDL-C (mg/dl)	182.58 ±8.74	119.29 ±4.08	-34.66

Key: ± indicates standard error of mean
Figures in parentheses indicate number of patients

Table 2: Changes in LDL-Cholesterol, in placebo group of patients (n=20)

Parameter	At day-0	At day-90	% Change
LDL-C (mg/dl)	150.75 ±2.67	148.80 ±2.28	-1.29

Key: ± indicates standard error of mean
Figures in parentheses indicate number of patients

Table 3: Difference of changes in LDL-Cholesterol between placebo and Niacin group of patients in 90 days of treatment.

PLACEBO GROUP (n=20), NIACIN GROUP (n=17)
Parameters: LEL-C (mg/dl)

Baseline	Post Treatment	P Value	% Difference in groups
150.75 ±2.67	148.80 ±2.28	>0.05	33.4
182.58 ±8.74	150.41 ±6.94	<0.001	

Key: ± indicates standard error of mean
P Value >0.05 indicates non significant
P Value <0.001 indicates highly significant
Figures in parentheses indicate number of patients

DISCUSSION

Among the lipid lowering drugs, Niacin appears to be the best LDL decreasing agent. In our study, LDL-Cholesterol levels decreased by 34.66% in men and women with high LDL-C levels treated with a medium dose of Niacin (2 gm/day).The drug has another advantage of being inexpensive. Levels of LDL-C go maintained throughout 3 months of study period with the therapy. This finding coincides with the study of Martin-jadraque et al[12]. Treatment with placebo capsules for 90 days, LDL-Cholesterol was decreased 1.29% as compared to 3.7% decrease in a study by lipid Research Clinics.13 7% increase in HDL-Cholesterol has also been quoted in another study by Rivellese et al[14]. It was demonstrated by Miller et al[15] that long distance runners have much less LDL-Cholesterol concentration than do more sedentary subjects. The decrease in LDL-C concentration by physical training may be a consequence of enhanced catabolism of triglycerides rich lipoproteins (VLDL). It was observed by McKinney et al[l6], that high dose of crystalline Niacin decreased 39% in concentration of LDL-C. This observation is in contrast with our observation, probably due to small sample size and low dose of the drug. They used 6gm of Niacin in 80 patients for the period of four months.

Drop out rate in our study was 9% and most of the patients discontinued treatment due to development of side effects like flushing, urticaria and sensation of heat in the body. Other patients were convinced for continuing therapy, by dose concentration regimen (titration) of Niacin or taking aspirin 250mg OD, before taking 1st dose of drug at morning. Wilkin et al, have described the mechanism by which aspirin blocks Niacin induced flushing[17]. Stern et al[13] has mentioned that tolerance is developed for flushing, urticaria and hotness in body, by dose titration of Niacin.

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