ORIGINAL ARTICLE

Niacin Decreases the Risk of Coronary Heart Disease

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ABSTRACT

Objective: Study was planned to examine the effects of Niacin on serum Total cholesterol and LDL-Cholesterol

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 2006 to July 2006.

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 total cholesterol was calculated by enzymatic caloricmeter method. 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 serum total cholesterol from 253.00±7.73 to 189.94±3.85 (mg/dl), which was highly significant statistically. Percentage change was -24.92. The drug 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 in this parameter.

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

Key words: Niacin. LDL-Cholesterol. Serum total cholesterol. Atherosclerosis. Primary hyperlipidemia

INTRODUCTION

Coronary Heart Disease (CHD) is caused by narrowing of the coronary arteries that feed the heart. Like any muscle, the heart needs a constant supply of oxygen and nutrients, which are carried to it by the blood in the coronary arteries[1]. When the coronary arteries become narrowed or clogged by cholesterol and fat deposits--a process called atherosclerosis--and cannot supply enough blood to the heart, the result is coronary heart disease[2]. If not enough oxygen-carrying blood reaches the heart, you may experience chest pain called angina[3]. If the blood supply to a portion of the heart is completely cut off by total blockage of a coronary artery, the result is a heart attack. This is usually due to a sudden closure from a blood clot forming on top of a previous narrowing[4].

Cholesterol is a waxy, fat-like substance that occurs naturally in all parts of the body and that your body needs to function normally. It is present in cell walls or membranes everywhere in the body, including the brain, nerves, muscle, skin, liver, intestines, and heart.5 Human body uses cholesterol to produce many hormones, vitamin D, and the bile acids that help to digest fat. It takes only a small amount of cholesterol in the blood to meet these needs[6]. If human body have too much cholesterol in bloodstream, the excess is deposited in arteries, including the coronary arteries, where it contributes to the narrowing and blockages that cause the signs and symptoms of heart disease[7].

Niacin is a natural substance. In fact, it's vitamin B3. Like other vitamins, it keeps the body's metabolism working properly. The Recommended Daily Allowance (RDA) for vitamin B3 is only 18 mg a day. That's far less than the amount needed to improve cholesterol level in the body[8].

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In the doses needed to improve cholesterol, niacin is a drug, and a potent one. On average, it can lower LDL ("bad") cholesterol by 10% to 25%. Statins and other lipid-lowing drugs do even better, but niacin outshines them all for lowering triglyceride levels (down 20% to50%) and raising HDL ("good") cholesterol levels (up 15% to35%)[9].

PATIENTS AND METHOD

Study was conducted in the department of Pharmacology, Basic Medical Sciences Institute, Jinnah Postgraduate Medical Centre, Karachi, from January to July 2006.Forty patients of primary hyperlipidemia were enrolled in the study, selected from ward and OPD of NICVD, Karachi. Previously diagnosed and untreated primary hyperlipidemic patients of either sex, age range from 21 to 60 years were randomly selected. Patients with peptic ulcer, hepatic disease, alcoholism, hypothyroidism, diabetes mellitus, and renal disease were excluded from the study as these pathological conditions can mask hyperlipidemic abnormality of the patient.10 After explaining the limitations, written consent was obtained from all participants. The study period consisted of 90 days with fortnightly follow up visits. Name, age, sex, occupation, address, previous medication, date of follow up visit and laboratory investigations, etc of each patient was recorded on a Performa, especially designed for the study. 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 divided in 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 Vitamin B-3.[11] 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 total cholesterol was estimated by the enzymatic calorimetric method (Rivelles et al 1994) using kit cat. # 303113050 by Eli Tech Diagnostic, France.12 Triglycerides were also estimated by enzymatic calorimetric method, using kit Cat. # 304710050 by Eli Tech Diagnostic. France. HDL- C was determined by using kit Cat. # 303210040 by Eli Tech Diagnostic, France. Serum LDL-cholesterol was calculated by Friedwald formula[13]@ (LDL-Cholesterol = Total Cholesterol-(Triglycerides/5 +HDL-Cholesterol) described by Delong et al (1986)[14] and Beamount et al (1970)[15]. 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, urticaria and headache. Tables showing base line and post treatment values are self explanatory. When results were summed up and test parameters were compared, it was seen that, after 90 days of treatment with Niacin, serum total cholesterol decreased from 253.00±7.73 mg/dl to 189.94±3.85 mg/dl, which is highly significant statistically (P<0.001). The overall percentage change from day-0 to day-90 was -24.92, as shown in table no 1. LDL-Cholesterol in these patients at day-0 was 182.58±8.74 mg/dl, which reduced by 90 days of treatment to 119.29±4.08 mg/dl, which is highly significant statistically (P<0.001) as shown in table 1. The overall percentage change from day-0 to day-90 was -34.66, as shown in table no 1. In placebo group at day-0, serum total cholesterol level was 215.95±2.47 mg/dl, which decreased to 208.70±5.38 mg/dl, which is significant statistically (P>0.05).The overall percentage decrease in the parameter was -3.35 as shown in table no 2. LDL-Cholesterol in placebo group at day-o was 150.75±2.67 mg/dl which reduced to 148.80±2.28 mg/dl, which is non significant statistically (P>0.05) (Table 3).

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

Parameter	At day-0	At day-90	% Change
Total cholesterol (mg/dl)	253.00±7.73	189.94±3.85	-24.92
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 Total cholesterol and LDL-Cholesterol, in placebo group of patients (n=20)

Parameter	At day-0	At day-90	% Change
Total cholesterol (mg/dl)	215.95±2.47	208.70±5.38	-3.35
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 Total cholesterol and LDL-Cholesterol between placebo and Niacin group of patients in 90 days of treatment.

PLACEBO GROUP (n=20)				NIACIN GROUP (n=17)			
Parameter	Baseline	Post Treatment	P Value	Baseline	Post Treatment	P Value	% Difference in groups
Total cholesterol (mg/dl)	215.95±2.7	208.70±5.38	<0.05	253.00±7.73	189.94±3.85	<0.001	21.57
LDL-C (Mg/dl)	150.75±2.67	148.80±2.28	>0.05	182.58±8.74	150.41±6.94	<0.001	33.4

P Value >0.05 indicates non significant P Value <0.05 indicates 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 drug for decreasing total cholesterol and LDL-Cholesterol. In our study, total cholesterol decreased 24.92% in 90 days of treatment with Niacin in primary hyperlipidemic patients. Our results matches with the study of Henken et al[16] who saw same changes in 98 primary hyperlipidemic patients when treated with 3 gram Nicotinic acid for the period of 3 months. In their results total cholesterol was decreased 23.81%. Another study by Crouse JR[17] also accords with our study, who observed 22.22% decrease in serum total cholesterol in 20 hyperlipidemic patients by giving 2 gram Nicotinic acid for the period of four months. Our results regarding decrease in serum total cholesterol level contrasts with the results of research study conducted by Garg and Grundy[18] when they used 2 gram Niacin in 13 male diabetic patients for the period of eight weeks. 15% decrease level in serum total cholesterol was observed by them. This contrast in results may be due to gender, sample size and secondary hyperlipidemia. Diabetes mellitus usually deteriorates when Niacin is given to treat dyslipidemia of diabetic patients. Exact mechanism of this phenomenon is not clear. Garg and Grundy stated that by interfering with triglycerides synthesis in liver, Niacin may enhance utilization of fatty acids at the expense of glucose; if so, this could lead to enhanced hepatic glucose output, potential cause of hyperglycemia. 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-Idraque et al[19]. 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[20]. Change in placebo group results may be due to their compact, comprehensive study and large sample size. 7% increase in HDL-Cholesterol has also been quoted in another study by Rivellese et al.[21]It was demonstrated by Miller et al[22] 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). Our study also matches with the study taken at Lipid Research Centre, Montreal by Tato et al[23]. Their study was double blind placebo controlled. They observed same changes in LDL-Cholesterol;ie 34.21% decreased LDL-C by Niacin in 45 primary hyperlipidemic male and female patients. It was observed by McKinney et al[24], that high dose of crystalline Niacin decreased 49% in concentration of LDL-C. This observation is in contrast with our observation, probably due to our small sample size and low dose of the drug. They used 6gm (Slow-Release preparation) of Niacin in 180 patients for the period of seven months. Remarkable change in our and their results may be due to immediate release preparation of the Niacin, we used in our study. Our results do not match with the results of research study by Kane et al[25], who observed much less decreased LDL-Cholesterol levels (19%) in eleven hyperlipidemic patients, when treated by Niacin for the period of two months. This difference in results of two research studies may be due to very small sample size and lesser duration of drug exposure, used in their research study. Three patients discontinued taking Niacin 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 250 mg OD, before taking 1st dose of drug at morning. Wilkin et al, have described the mechanism by which aspirin blocks Niacin induced flushing.[26] Stern et al[27] has mentioned that tolerance is developed for flushing, urticaria and hotness in body, by dose titration of Niacin.

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