ORIGINAL ARTCLE

Risk Reduction of Myocardial Infarction by Reducing Cholesterol, Body Weight and Blood Pressure

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ABSTRACT

Sedentary life style, blood pressure, old age, alcohol intake, tobacco smoking, abnormal body mass index and dyslipidemia are major risk factors for atherogenesis leading to morbidity and mortality due to myocardial infarction. The research study was planned to observe effects of Nicotinic acid (niacin) on blood pressure, body weight, bad cholesterol; i.e. LDL-cholesterol and good cholesterol; i.e. HDL-cholesterol. It was single blind placebo-controlled research study, which was conducted at Jinnah Hospital, Karachi, from April 2010 to December 2010. Fifty male and female hyperlipidemic patients were included in the research study, among which 25 patients were on placebo as control group, and 25 were on tablet Niacin, 2.25 grams 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. Body weight and blood pressure of patients were recorded at fortnightly visit. LDL-Cholesterol was calculated by Friedwald formula (LDL= TC- (TG/5 + HDL-C). Serum HDL-cholesterol was determined by direct method. Serum cholesterol and triglycerides were estimated by the enzymatic calorimetric method. Data regarding results were expressed as the mean ± SD and "t" test was applied to determine statistical significance of results. A probability value of <0.05 was the limit of significance. Three patients were dropped from the study due to side effects of Niacin. In three months of treatment with 2.25 grams of niacin HDL-cholesterol increased from 36.41±1.96 to 43.70±1.81 mg/dl, which was highly significant change when analyzed statistically. Niacin has decreased LDL-Cholesterol from 182.58±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. Triglycerides reduced from 169.64±7.60 to 137.35±6.31 mg/dl, which was highly significant (P value <0.001) reduction in three months. Niacin has also reduced Blood Pressure. Difference between mean values of systolic and diastolic blood pressure at day-0 and day-90 were found highly significant (P<0.001). Body weight was reduced from 66.29±194 kg to 64.79±1.82 kg in three months. This change was significant (P<0.01). We concluded from the research study that niacin decreases blood pressure, body weight and LDL-Cholesterol and increases HDL-cholesterol in primary hyperlipidemic patients.

Key words: Blood lipids. Niacin. Systolic BP. Diastolic BP. Cholesterol. Body weight.

INTRODUCTION

Arteriosclerosis is a general term describing any hardening and thus loss of elasticity of medium or large arteries. There are two types of plaque formations stable and unstable. Stenosis (occlusion) over 75% accounts for about 14% of mycondria infractions, while those under 50% occlusions account for more likely it is to be stable.[1-3] Atherosclerosis develops from low-density lipoprotein cholesterol (LDL), colloquially called "bad cholesterol". Most researchers believe that, when this lipoprotein gets through the wall of an artery, oxygen free radicals react with it to form oxidized –LDL. The body's immune system responds by sending specialized white blood cells (marcophages and T-lymphocytes) to absorb the oxidized-LDL. These white blood cells are not able to process the oxidized-LDL, and ultimately grow, then rupture and in so doing deposit the oxidized LDL within the artery wall. This trigtgers more white blood cells thereby continuing the cycle. Eventually the artery become inflamed[4-6].The cholesterol plaque causes the muscle cells in the artery wall to enlarge and form a hard cover over the affected area. This hard cover is what causes a narrowing of the artery, which results in a reduced blood flow and increased blood pressure[7] There are three problems from plaque formation: enlargement, restriction of blood flow, and rupture with clogging. The atheromatous plaques, though

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long compensated for by artery enlargement, will eventually lead to plaque ruptures and stenosis (narrowing) of the artery, and therefore, an insufficient blood supply to the organ it feeds. If the compensating artery enlargement process is excessive, then an aneurysm results. These complications are chronic, slowly progressing and cumulative. The third problem comes from the sudden ruptures, which cause the formation of thrombus that will rapidly slow or stop blood flow. This leads to death of the tissues fed by the artery in approximately 5 minutes. This catastrophic event is called an infraction. When it occurs in a coronary artery is causes a myocardial infraction (MI, a heart attack).[8-10] Nicotinic acid (niacin) has an effect on blood vessels, allowing them to relax, thus allowing better blood flow to all regions of the body, including hands and feet.[11] As compared to its recommended daily allowance (RDA), much high doses of Nicotinic acid (niacin) are used to prevent development of atherosclerosis and to reduce recurrent complications like heart attack, myocardial infarction and peripheral vascular disease.[7-9] The combination of niacin and a cholesterol-lowering drug called simvastatin do dramatically slow the progression of heart disease, reducing risk of heart attack leading to death. Niacin is commonly used to lower elevated LDL-cholesterol and triglyceride levels in the serum and is more effective in increasing HDL-cholesterol levels. A high level of LDL in the blood may mean that cell membranes in the liver have reduced the number of LDL receptors due to increased amounts of cholesterol inside the cell. After a cell has used the cholesterol for its chemical needs and doesn't need any more, it reduces its number of LDL receptors. This enables LDL levels to accumulate in the blood. When this happens, the LDLs begin to deposit cholesterol on artery walls, forming thick plaques. In contrast, the HDLs--the "good" guys--act to remove this excess cholesterol and transport it to the liver for disposal. High doses of Nicotinic acid (niacin) have been shown to raise HDL-cholesterol, and lower LDL-cholesterol and triglycerides. Nicotinic acid is currently used as one of the first-line treatment of hyperlipidemia either alone or in combination with HMG-CoA reductase inhibitors.[6,8,10-12]

MATERIAL & METHODS

Fifty patients of primary hyperlipidemia were enrolled for the research, selected from ward and OPD of Jinnah Hospital, Karachi. Male and female primary hyperlipidemic patients of 17 to 70 years age were selected. Patients with alcohol addiction, hypothyroidism, peptic ulcer, diabetes mellitus, renal disease, hepatic disease, were excluded from the study. Written consent was obtained from all participants. Research study was started after approval by Research Ethics Committee , Jinnah Hospital, Karachi, Pakistan. The study period consisted of 90 days with fortnightly follow up visits. The required information like 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 2.25gm) 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, thrice daily, till end of the study period, i.e. up to day-90. This regimen of dose of drug was applied due to avoidance of it's adverse effects produced by starting with higher doses of the Niacin.22 Patients of drug-2 group were provided placebo capsules, i.e. three capsules, 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 (LDL-Cholesterol = Total Cholesterol-(Triglycerides/5 +HDL-Cholesterol). Data were expressed as the mean ± SD and "t" test was applied to determine statistical significance as the difference. For non significant results P-value >0.05 was used and for significant to highly significant results P-value <0.01 and <0.001 was used, respectively in the research.

RESULTS

Three patients discontinued to take drug in group-1 (Niacin group) due to side effects of the drug like flushing, sensation of heat, and headache. So, out of fifty, 47 patients completed the study period that was three months. Table showing base line and post treatment values is self explanatory. When results were summed up and test parameters were compared, it was seen that, after three months of treatment with niacin, LDL-cholesterol decreased from 182.58±8.74 mg/dl to 119.29±4.08 mg/dl, which

is highly significant (P<0.001). The overall percentage change from day-0 to day-90 was -34.66. 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 3. Niacin has increased HDL-cholesterol from 36.41±1.96 to 43.70±1.81 mg/dl, which is highly significant change (P-value <0.001). In percentage it is 20.02% increase. Triglycerides reduced from 169.64±7.60 to 137.35±6.31 mg/dl, which was highly significant (P value <0.001) reduction in three months. Systolic blood pressure reduced from 125.88±3.48 mm of Hg to 119.70±3.13 mm of Hg in three months. Diastolic blood pressure reduced from 89.11±1.92 to 84.70±1.74 mm of Hg in this duration of treatment with 2.25 grams of Niacin. These changes in both, systolic and diastolic blood pressure are highly significant (P<0.001). Body weight reduced from 66.29±1.94 kg to 64.79±1.82 kg, which is also highly significant (P<0.001) when compared with placebo group.

Table 1: Difference of effects of drug on body weight, systolic, diastolic blood pressure, LDL and HDL-Cholesterol between placebo and niacin group of patients in 3 months of treatment.

Placebo Group (25 patients)				Drug Group (22 patients)			
Parameter	**Pre-treatment**	**Post-treatment**	**P Value**	**Pre-treatment**	**Post-treatment**	**P Value**	**Difference in groups**
HDL-C (mg/dl	69.35±1.76	69.17±1.68	>0.05	66.29±1.94	64.79±1.82	<0.001	2.01%
Systolic BP	84.25±1.99	120.75±2.18	<0.01	125.88±3.48	119.70±3.13	<0.001	3.28%
Diastolic BP	150.75±2.67	82.00±1.82	<0.01	89.11±1.92	84.70±1.74	<0.001	2.27%
LDL-C(mg/dl)	122.75±219	148.80±2.28	>0.05	182.58±8.74	150.41±6.94	<0.001	33.4%
TG	48.45±4.80	146.20±4.20	>0.05	169.64±7.60	137.35±6.31	<0.001	17.52%
HDL-C(mg/dl)	35.50±1.13	35.75±1.07	>0.05	36.41±1.96	43.70±1.81	<0.001	19.32%

Key:(Drug Group is on niacin 2.25 gm, ± indicates standard error of mean, BP stands for blood pressure, Body weight is measured in kilograms, blood pressure is measured in mm of Hg, P Value >0.05 indicates non significant, P Value <0.01 indicates significant, P Value <0.001 indicates highly significant, Figures in parentheses indicate number of patients)

DISCUSSION

There are various drug groups which are used as hypolipidemic agent and among all lipid lowering drugs, niacin appears to be the best HDL upraising and LDL lowering agent. In our research, HDL-cholesterol increased from 36.41±1.96 to 43.70±1.81 mg/dl and LDL-Cholesterol levels decreased by 34.66% in men and women with high LDL-C levels treated with 2.25 grams of Niacin. Reduction in body weight was 2.26%. Systolic blood pressure decreased 4.90% and diastolic blood pressure reduced 4.94% in three months of treatment with same dose of niacin as used in LDL lowering and HDL upraising dose. Triglycerides reduced from 169.64±7.60 to 137.35±6.31 mg/dl, which was highly significant (P value <0.001) reduction in three months. These results match with the results of study conducted by S. Lamon-Fava et al[13] who observed almost same changes in LDL-Cholesterol, body weight and blood pressure. HDL-cholesterol is not increased as much as in our research study. Their research proved only 11.09% increase in HDL cholesterol. In their study LDL-C reduced 29.75%, systolic BP 2.89%, diastolic BP 3.98% and body weight 2.94%, in 90 days of treatment with three grams of niacin in 47 primary hyperlipidemic patients. Results of study conducted by P. Tuohimaaa and M. Jarvilehtob[14] also match with our study results. In their results LDL cholesterol reduced 31.98%, systolic blood pressure 3.87%, diastolic blood pressure 3.87% and body weight 2.91%. They observed remarkable increase in HDL cholesterol in 15 female hyperlipidemic patients when two grams of niacin was used for 4 months. David H. Blankenhorn et al[15] observed that niacin is very effective among all lipid lowering drugs, that can reduced LDL cholesterol and increase HDL cholesterol remarkably. They proved 30.12% reduction in low density lipoprotein cholesterol, 17% decrease in triglycerides and 20.56% increase in high density lipoprotein cholesterol when 3 grams of niacin was used in 20 hyperlipidemic patients for three months. These results also coincide with our results regarding LDL and HDL cholesterol. Results of research study conducted by Y. Koh et al[16] are in contrast with our results who observed only 12.99% decrease in LDL-Cholesterol by using three grams of niacin in 13 hyperlipidemic patients for the period of three months. In their observation systolic and diastolic blood pressure was reduced 0.19 and 2.51%

respectively. Body weight was reduced 2.90%. These findings do not match with our results, except body weight. The reason for difference may be due to small sample size and environmental factors. Their patients strictly followed step-I diet, along with taking drug. M. C. Cheung et al[17] proved 24.03% reduction in concentration of LDL cholesterol, 10.32% reduction in serum triglycerides and 11.87% increase in HDL cholesterol. Their observation is in contrast with our observation, probably due to small sample size and low dose of the drug in our study. They used 4.4 grams of niacin in 87 hyperlipidemic patients for the period of 8 months. M. B. Elam et al[18] used 2.5 grams of niacin in 30 hyperlipidemic patients for four months and observed 20% increase in HDL cholesterol and only 13% decrease in LDL cholesterol. Result of one of the parameter that is HDL cholesterol matches with our result but in another parameter that is LDL cholesterol results of his study and our research results are in contrast. The reason of this contrast may be the cases of secondary hyperlipidemia, they included in their study. We excluded secondary hyperlipidemic patients in our research work. In his study 10 patients discontinued to take part in research as agreed initially. The reason for this remarkable dropout was urticaria, warmth feeling and redness on dependant parts of the body by taking niacin.

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