

EFFECTS OF VITAMIN B-3 ON SELECTED CORONARY HEART DISEASE RISK FACTORS; A PLACEBO CONTROLLED EXPERIMENTAL STUDY

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ABSTRACT

Background: Well recognized and explained risks factors for development of atherosclerosis include hypertension, old age, sedentary life style, smoking and high serum lipid levels. **Objective:** To determine the effects of niacin on blood pressure, body weight, low density lipoprotein (LDL) and high density lipoprotein (HDL). **Patients and Methods:** This single blind placebo controlled experimental study was conducted at Jinnah Hospital, Karachi, from June 2009 to December 2009. Forty hyperlipidemic patients of both sexes were included in the research study, among which 20 patients were on placebo as control group, and 20 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 was calculated by Friedwald formula ($LDL = TC - (TG/5 + HDL-C)$). Serum HDL was determined by direct method. Serum cholesterol and triglycerides were estimated by the enzymatic calorimetric method. Data regarding results were expressed as the mean \pm SD and "t" test was applied to determine statistical significance of results. A probability value of <0.05 was taken as significant. Three patients were dropped from the study due to side effects of niacin. **Results:** In three months of treatment with 2.25 grams of niacin, HDL increased from 36.41 ± 1.96 to 43.70 ± 1.81 mg/dl, which was highly significant change when analyzed statistically. Niacin decreased LDL from 182.58 ± 8.74 mg/dl to 119.29 ± 4.08 mg/dl, which was highly significant ($p < 0.00$) statistically. Overall, percentage change from day-0 to day-90 was 34.66. Triglycerides reduced from 169.64 ± 7.60 to 137.35 ± 6.31 mg/dl, which was highly significant ($p < 0.001$) reduction in three months. Niacin has also reduced blood pressure, the 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 ± 1.94 kg to 64.79 ± 1.82 kg in three months. This change was significant ($p < 0.01$). **Conclusion:** 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: Vitamin B3, low density lipoprotein, high density lipoprotein, triglycerides, body weight, blood pressure.

INTRODUCTION

There are basically two forms of vitamin B3, niacin (or nicotinic acid) and niacinamide (or nicotinamide). Niacin is the only form of vitamin B3 that has been shown to reduce low density lipoprotein (LDL) and triglycerides and increase high density lipoprotein (HDL). Hence, niacin can help reduce the risk of heart disease. Niacin also provides benefits for energy production and metabolism and may be useful in the management of depression and anxiety.¹ Niacin relaxes the blood vessels, thus allowing better flow to all regions of the body, including hands and feet. Inositol hexaniacinate is one form of niacin that can have this kind of effect on the circulatory

system. High doses of niacin are used to prevent development of atherosclerosis and to reduce recurrent complications such like heart attack and peripheral vascular disease.² Circulation disorders are painful and often debilitating problems. Intermittent claudication is a circulation disorder characterized by painful cramping in the calf region, brought on by walking. Another aggravating disease caused by poor circulation is Raynaud's disease, causing pain and numbness in the extremities when exposed to cold.³ The combination of niacin and a cholesterol-lowering drug called simvastatin, may dramatically slow the progression of heart disease, reducing the risk of heart attack, and even death.⁴ Niacin is commonly used to lower elevated LDL and triglyceride levels in the blood and is more effective in increasing HDL levels than other cholesterol-lowering medications. High doses of niacin have been shown to raise HDL and lower LDL and triglycerides.⁵ Niacin is currently used as one of the first-line treatments of high cholesterol either alone or in combination with other cholesterol-lowering drugs. Niacinamide, which is also present in vitamin B-3, does not have the same effects as niacin on cholesterol levels.⁶ Overall, the use of niacin to treat or prevent high levels of blood cholesterol and triglycerides and reduce the risk of cardiovascular

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disease is well substantiated.⁷ This single blind, placebo controlled experimental study was planned to observe effects of niacin on blood pressure, body weight, low density lipoprotein (LDL), triglycerides and high density lipoprotein (HDL) in our population.

PATIENTS AND METHODS

The single blind placebo controlled experimental study, was conducted at Jinnah Hospital, Karachi and duration of study was 6 months, starting from June 2009 to December 2009.

40 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 and 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 of each patient was recorded on a proforma, specially 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 tablets, containing equal amounts of partly grinded wheat & similar in appearance to drug I) groups. Patients of drug-1 group were advised to take tab niacin (250 mg), half tablet thrice daily, after meal for 2 days, then one tablet, TID after meal for 2 days, 2 tablets thrice daily after meal for 2 days, and finally the maintenance dose of 3 tablets, thrice daily, till the end of the study period, i.e. up to day-90. This regimen of drug dosage (called "titration of niacin") was applied to avoid adverse effects produced by starting with higher doses of niacin. Patients of drug-II group were provided placebo tablets, i.e. three tablets, 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. Data was expressed as the mean \pm SD and t-test was applied to determine statistical significance. 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 in this study. Serum LDL was calculated by Friedwald formula (LDL-Cholesterol=Total Cholesterol-(Triglycerides/5+HDL-Cholesterol).⁸

RESULTS

Three patients withdrew from group-1 (niacin group) due to side effects of the drug like flushing, sensation of heat and headache. Table I is showing base line and post treatment values. When results were analysed and test of significance was applied, it was seen that, after three months of treatment with niacin, LDL 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 level decreased from 150.75 ± 29.67 mg/dl 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 ($p < 0.001$), as shown in the Table. I. Niacin increased HDL from 36.41 ± 1.96 to 43.70 ± 1.81 mg/dl, which is highly significant change statistically. ($p < 0.001$). 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 ($p < 0.001$) 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.

DISCUSSION

Various drug groups are used as hypolipidemic agent and among all lipid lowering drugs, niacin appears to be a good HDL raising and LDL lowering agent. In

Table: I

Effects of drug (Niacin) on body weight, systolic, diastolic blood pressure, triglyceride (TG), low density lipoprotein (LDL) and high density lipoprotein (HDL) compared with placebo in 3 months of treatment.

Placebo Group (20 patients)				Drug Group (17 patients)			
Parameter	Pre-treatment	Post-treatment	P value	Pre-treatment	Post-treatment	P value	Difference in groups
Body weight(Kg)	69.35±1.76	69.17±1.68	>0.05	66.29±1.94	64.79±1.82	<0.001	2.01%
Systolic BP (mm of Hg)	122.72± 219	120.75±2.18	<0.01	125.88±3.48	119.70±3.13	<0.001	3.28%
Diastolic BP (mm of Hg)	84.25± 219	82.00±1.82	<0.01	89.11±1.92	84.70±1.74	<0.001	2.27%
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%
TG	148.45±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±.13	35.75±1.07	>0.05	36.41±1.96	43.70±1.81	<0.001	19.32%

our research, HDL increased from 36.41±1.96 to 43.70±1.81 mg/dl and LDL 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 by 4.90% and diastolic blood pressure reduced by 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 J. M. S. Lee et al, who observed almost same changes in LDL-Cholesterol, body weight and blood pressure.⁹ HDL-cholesterol is not increased as much as in our research study. Their research showed only 11.09% increase in HDL cholesterol. In their study, LDL-C reduced by 29.75%, systolic BP by 2.89%, diastolic BP by 3.98% and body weight by 2.94% in 90 days of treatment with three grams of niacin in 47 primary hyperlipidemic patients. Results of the study conducted by Allen J. Taylor et al, also coincide with our study results.¹⁰ In their study, LDL cholesterol reduced by 31.98%, systolic blood pressure by 3.87%, diastolic blood pressure by 3.87% and body weight by 2.91%. They observed remarkable increase in HDL cholesterol in 15 female hyperlipidemic patients when two grams of niacin was used for 4 months. Guyton JR, observed that niacin is very effective among all

lipid lowering drugs, that can reduce LDL cholesterol and increase HDL cholesterol remarkably.¹¹ They showed 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 Bays H E and McGovern ME 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.¹² In their observation systolic and diastolic blood pressure was reduced by 0.19 and 2.51%, respectively. Body weight was reduced by 2.90%. These findings do not favour our results, except in 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 the drug. Taylor AJ et al also showed a 24.03% reduction in concentration of LDL cholesterol, 10.32% reduction in serum triglycerides and 11.87% increase in HDL cholesterol.¹³ 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. F. A. Jaffer 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.¹⁴ Result of one of

the parameter, that is HDL cholesterol, matches with our result but in another parameter, 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. Our study hence supports the previously shown/proven facts that niacin has a markedly beneficial impact on the cholesterol and triglyceride levels of primary hyperlipidemics. In his study, 10 patients discontinued to take part in research as agreed initially. The reason for this remarkable drop out was urticaria, warmth feeling and redness on dependant parts of the body by taking niacin. Mechanism by which aspirin blocks niacin-induced flushing is explained by A. Muller et al, as cyclo-oxygenase pathway is responsible for production of prostaglandin D2, which causes vasodilatation and feeling of warmth, when a person uses niacin.¹⁵

CONCLUSION

We concluded from this study that Vitamin B3, when used in high doses, can decrease LDL and increase HDL, which is beneficial for human body especially for human heart.

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