ORIGINAL ARTICLE

Good and Bad Cholesterol; New and Novel Considerations on Vitamins

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ABSTRACT

Risks of development of atherosclerosis include already having family history of the disease, old age, male gender, sedentary life style, chronic continuous smoking and/or intake of alcohol, blood lipid levels, body weight and blood pressure. So the research study was planned to examine the effects of 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 June 2009 to December 2009. Forty male and female hyperlipidemic patients 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-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. Interest also attaches to our findings that 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: Vitamins.Body Weight.HDL-Cholesterol.LDL-Cholesterol.Blood Pressure.

INTRODUCTION

"Good" and "Bad" cholesterol refer to the type of carrier molecule that transports the cholesterol in human body. These carrier molecules are made of protein and are called apoproteins. They are necessary because cholesterol and other fats (lipids) can't dissolve in water, which also means they can't dissolve in blood. When these apoproteins are joined with cholesterol, they form a compound called lipoproteins. The density of these lipoproteins is determined by the amount of protein in the molecule "Bad" cholesterol is the low-density lipoprotein (LDL) , the major cholesterol carrier in the blood. High levels of these LDLs are associated with atherosclerosis. "Good" cholesterol is the high-density lipoprotein (HDL); a greater level of HDL--think of this as drain cleaner you pour in the sink--is thought to provide some protection against artery blockage.[1] The levels of HDL, LDL and total cholesterol are all indicators for atherosclerosis and heart attack risk. People who have a cholesterol level of 275 or greater (200 or less is desirable) are at significant risk for a heart attack, despite a favorable HDL level. In addition, people who have normal cholesterol levels but low HDL levels are also at increased risk for a heart attack.[2] Heart attack and Myocardial Infarction due to atherosclerosis are leading cause of morbidity and mortality through out the world. Moderately high levels of serum triglycerides with low levels of blood HDL-cholesterol

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is scientifically well proved risk for developing atherosclerosis. It is well explained that atherosclerosis, if not stopped at earlier steps may lead to development of myocardial infarction or heart attack.[3,4] Despite substantial medical progress in the past three decades, coronary heart diseases remain the major health problem in most of the industrialized countries. The disease remains a common cause of morbidity and mortality throughout the world. Each 1% increase in the serum cholesterol concentration results in 2-3% increase in CHD risk. The levels below 200 mg/dl are classified as desirable blood cholesterol, those 200 to 239 mg/dl as borderline high blood cholesterol and those 240 mg/dl and above as high blood cholesterol. The cut point that defines high blood cholesterol (240 mg/dl) is a value above which risk of CHD rises steeply. The cut points recommended are uniform for adult men and women of all ages.[1-3,5-7] There are various drugs which decrease total cholesterol, triglycerides, LDL-Cholesterol and increase HDL-Cholesterol in primary hyperlipidemic patients, but nicotinic acid is the best LDL-Cholesterol lowering agent among the lipid lowering drugs. Nicotinic acid has another beneficial effect that it reduces body weight and blood pressure. Niacin increases HDL-Cholesterol 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 coronary heart disease.[8] Niacin inhibits the activity of lipoprotein lipase causing decrease in lipolysis and so decreased VLDL secretion from hepatocytes. 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.[6,9-10]

MATERIAL & METHOD

Research study was conducted at Jinnah Hospital Karachi, Pakistan, from June 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 20 to 70 years age were 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 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 (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. 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 in the research.

RESULTS

Hypolipidemic dose of vitamin B-3 is 100 times greater than its RDA. So it was observed in the study that three patients withdrew from group-1 (Niacin group) due to side effects of the drug like flushing, sensation of heat, and headache. So, out of forty, 37 patients completed the study period, that was three months. 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 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, as shown in table no: 1. 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, as shown in table no 2. 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. 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: Effects of drug on body weight, systolic, diastolic blood pressure, LDL and HDL-Cholesterol in drug group of patients (n=17)

Parameter	Pre-treatment	Post-treatment	Change in %	
Body weight	66.29±1.94	64.79±1.82	2.26%	P<0.001
Systolic BP	125.88±3.48	119.70±3.13	4.90%	P<0.001
Diastolic BP	89.11±1.92	84.70±1.74	4.94%	P<0.001
LDL-C(mg/dl)	182.58±8.74	119.29±4.08	34.66%	P<0.001
HDL-C (mg/dl)	36.41±1.96	43.70±1.81	20.02%	P<0.001

Key: (Drug group is on niacin 2.25 grams, ± indicates standard error of mean, BP stands for blood pressure, body weight is measured in kilograms, blood pressure is measured in mm of Hg, figures in parentheses indicate number of patients, P value <0.001 is regarded as significant)

Table 2: Effects of placebo on body weight, systolic, diastolic blood pressure, LDL and HDL-Cholesterol, in placebo group of patients (n=20)

Parameter	Pre-treatment	Post-treatment	Change
Body weight	69.35±1.76	69.17±1.68	0.25%(P>0.05)
Systolic BP	122.75±2.19	120.75±2.18	1.62%(P<0.05)
Diastolic BP	84.25±1.99	82.00±1.82	2.67%(P<0.05)
LDL-C(mg/dl)	150.75±2.67	148.80±2.28	1.29%(P>0.05)
HDL-C (mg/dl)	35.50±1.13	35.75±1.07	0.70%(P>0.05)

Key: (± indicates standard error of mean, BP stands for blood pressure, body weight is measured in kilograms, blood pressure is measured in mm of Hg, figures in parentheses indicate number of patients, P value <0.05 is regarded as significant and P value >0.05 stands for non significant)

Table 3: 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 (n=20)				Drugs Group (n=17)			
Parameter	**Pre-treatment**	**Post-treatment**	**P Value**	**Pre-treatment**	**Post-treatment**	**P Value**	**Difference in groups**
Body weight	69.35±1.76	69.17±1.68	>0.05	66.29±1.94	64.79±1.82	<0.001	2.01%
Systolic BP	122.75±219	120.75±2.18	<0.01	125.88±3.48	119.70±3.13	<0.001	3.28%
Diastolic BP	84.25±1.99	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%
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

Flushing, urticaria and sensation of heat in the body are main side effects and reason for low compliance of the drug Niacin. In our study three patients discontinued to take niacin due to these effects. Other patients were convinced for continuing therapy, by taking aspirin 250 mg, before taking 1st dose of niacin at morning, every day. 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. These results match with the results of study conducted by Izzat NN et al[11] 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 Hiatt J G et al[12] 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. Hunninghake DB[13] observed that niacin is very effective among all lipid lowering drugs, that can reduced LDL cholesterol and increase HDL cholesterol remarkably. He proved 30.12% reduction in low density lipoprotein cholesterol 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 Schetman G and Hiatt J[14] 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 1.19 and 1.78% 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. Patients in their study strictly followed step-I diet, along with taking drug. Rader DJ[15] proved 27.03% reduction in concentration of LDL cholesterol and 10.71% increase in HDL cholesterol. This observation is in contrast with our observation, probably due to small sample size and low dose of the drug in our study. He used 4.4 grams of niacin in 87 hyperlipidemic patients for the period of 8 months. Pearson TA et al[16] used 2 grams of niacin in 20 hyperlipidemic patients for 3 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 their 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. Various pathological conditions do mask primary hyperlipidemia, like diabetes mellitus, primary hypertension, hypothyroidism, alcohol intake, liver disease, etc.

CONCLUSION

We concluded from the research study that Vitamin B-3 is effective hypolipidemic drug, when used in specific doses, even better monotherapy for primary hyperlipidemia as compared to other expensive hypolipidemic agents.

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