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Research Article

STUDY TO DETERMINE THE EFFECTS OF HYPOLIPIDEMIA ON NICOTINIC ACID (A SINGLE BLIND PLACEBO CONTROLLED RANDOMIZED TRIAL)

Dr Syed Jahanzaib Naqvi¹, Dr Hafza Azam², Dr M Hasham Arshad¹

¹ University College of Medicine and Dentistry, University of Lahore

² Ameer-ud-Din Medical College, Lahore

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Abstract:

Objective: The study was planned to determine the nicotinic effects on body weight, blood pressure, good cholesterol; i.e. HDL-cholesterol and bad cholesterol; i.e. LDL-cholesterol.

Study Design: A single blind placebo- Randomized controlled research study.

Place and Duration: In the Department of Medicine, Services Hospital Lahore in Collaboration with department of Pharmacology Services Institute of Medical Sciences for three months duration from June 2019 to September 2019.

Methods: Forty men and women with hyperlipidemia were included, 20 of them received a placebo, as a control group and 2.25 grams of niacin per tablet per day were given to 20 subjects over a three-month dose. Patients with diabetes mellitus, peptic ulcer disease, liver disease, kidney disease, alcoholism and hypothyroidism were not included in the study. The patient's blood pressure and body weight were recorded every two weeks on follow-up. LDL cholesterol was checked with the Friedewald formula ($LDL = TC(TG/5 + HDL-C)$) and by a direct method serum HDL cholesterol was calculated, triglycerides and cholesterol were calculated using a colorimetric method. To determine statistical significance of results, Data was stated as the mean \pm SD and "t" test was applied.

Results: In the 3-month treatment with niacin 2.25 grams, HDL cholesterol raised from 36.41 ± 1.96 to 43.70 ± 1.81 mg / dl. This was a major change if statistically analyzed. Niacin reduced LDL cholesterol from 181.98 ± 9.24 mg / dl to 118.18 ± 3.99 mg / dl when compared with the paired t-test and it was highly significant. The total percentage (%) of the changes from 0 days to 90 days was 34.67. The triglycerides were decreased from 170.04 ± 7.59 to 136.85 ± 6.29 mg / dl; this was an important decrease in 3 months (p value <0.001). The blood pressure was also reduced by Niacin. The mean variation between diastolic and systolic blood pressure values was considered significant at days 0 and 90 ($P <0.001$). Body weight was decreased from 66.30 ± 1.93 kg in three months to 64.80 ± 1.81 kg. This variation was major ($P <0.01$).

Conclusion: we conclude that niacin has reduced body weight, LDL cholesterol and blood pressure and increased HDL cholesterol in patients with primary hyperlipidemia.

Key words: Low density lipoprotein, nicotinic acid, cholesterol, high density lipoprotein.

Corresponding author:

Dr. Syed Jahanzaib Naqvi,

University College of Medicine and Dentistry, University of Lahore

QR code



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INTRODUCTION:

Nicotinic acid (niacin) has effect on blood vessels, permitting them to relax and provide improved flow of blood to all parts of the body, together with the feet and hands. Inositol hexacnic acid is a form of niacin that can have a similar effect on the circulatory system¹. As associated with the (RDA) recommended daily allowance, nicotinic acid (niacin) in very high doses are beneficial to stop the atherosclerosis development and to decrease repeated problems such as myocardial infarction, peripheral vascular disease and heart attacks². Circulatory disorders are painful and often debilitating problems. Intermittent claudication is a pathology of the circulation characterized by painful cramps that occur in the calf area, usually while walking³. Another aggravating disorder due to poor circulation is Raynaud's disease, which causes pain and numbness in the extremities when exposed to cold⁴. The mixture of a cholesterol-lowering drug called simvastatin and niacin (a class known as HMG-CoA reductase statins or inhibitors) decreases dramatically, reducing the heart attack risk. Niacin is widely used to reduce high levels of serum triglycerides and LDL cholesterol and is much beneficial in maintaining HDL cholesterol high levels⁵. In the blood, LDL high level can mean that in the liver cell membranes have reduce numbers of LDL receptors due to an increase in the amount of cholesterol in the cell. When cholesterol is utilised by the cell for chemical processes it decreases the LDL receptors number. This allows LDL to increase in the blood⁶. When this occurs, the LDLs accumulate cholesterol in the walls of artery and begin to form thick plaques⁷. In contrast, HDL ("good") acts to transport this liver to eliminate excess cholesterol and eliminate it⁸. High nicotinic acid doses tends to reduce triglycerides and LDL cholesterol and increase HDL cholesterol. Nicotinic acid has been shown to have important benefits in reducing high cholesterol levels, but not nicotinamide. It is particularly beneficial in increasing (HDL) high-density lipoprotein levels, but is less effective in reducing (LDL) low-density lipoprotein levels than other drugs which are helpful in reducing cholesterol⁹. Nicotinic acid is currently used only or in amalgamation with HMG-CoA reductase inhibitors as one of the first-line therapies for hyperlipidemia.

MATERIALS AND METHODS:

This single blind placebo- Randomized controlled research study was held in the Department of Medicine, Services Hospital Lahore in Collaboration with department of Pharmacology Services Institute of Medical Sciences for three months duration from June 2019 to September 2019. The patients were selected from the OPD of medicine department. Primary hyperlipidemic patients with male and female aged 17 to 70 years

were carefully chosen. Patients with hypothyroidism, alcohol dependence, peptic ulcer, diabetes mellitus, liver disease and kidney disease were discarded from the analysis. All participants received written approval. The research analysis was initiated after the research ethics committee approval. The study duration is 3 months with every two weeks follow-up visits. Name, gender, address, age, profession, date of follow-up, previous medications and laboratory research, etc. was recorded in a designed Performa. In the start, a detailed physical examination and clinical history of all subjects was performed. All baseline valuations were done on the inclusion day (day 0) and a same valuation was done on 90th day of the research project. After having met the criteria of inclusion, the patients were divided randomly into 2 groups: In one group Drug 1 (2.25 g Niacin tablet) and Drug 2 (placebo capsules having an equal amount of partially grinded wheat). In 1st drug group patients were recommended to increase the dose of Tab: niacin (250 mg) T.I.D, after meal for 2 days and then one tablet for 2 days after meals, then two tablets, T.D.S after meals for two days, then until the end of working time, ie up to 90 days, 3 tablets of 3 tablets 3 times a day. The dose of the drug (called niacin titration) has been given because the adverse effects that occur when starting with higher doses of niacin are avoided. Every 2 weeks, patients were asked to moitor the weight, blood pressure, heart beat and the individual general appearance. During each clinical visit, compliance with drug therapy was verified through counselling. Data were analysed as mean \pm standard deviation and for statistical significance determination as a difference the "t" test was applied. $P > 0.05$ was used for non-significant results and significant results were obtained in the study with $p < 0.01$ and < 0.001 . Using the Friedwald formula (LDL cholesterol = total cholesterol (triglycerides / 5 + HDL cholesterol) Serum LDL cholesterol was calculated.

RESULTS:

Three patients stopped taking the drug in group 1 (niacin group) due to side effects such as rash, temperature and headache. Therefore, thirty of the forty patients finished the three-month study duration. The table showing the basic conditions and values after the treatment is self-explanatory. When the outcomes were summarized and the comparison of test parameters was done, the LDL cholesterol decreased from 181.98 ± 9.24 mg / dl to 118.18 ± 3.99 mg / dl after three months of treatment with niacin and this was quite important ($P < 0.001$). The total percentage (%) of the changes from 0 days to 90 days was 34.67. The level of LDL cholesterol in the placebo group at day 0 was 149.74 ± 2.66 mg / dl and decreased to 148.50 ± 2.27 mg / dl, which was not noteworthy ($P > 0.05$). The 1.29 mg/dl was the overall decrease in parameters. The variation

between the mean values between the niacin group and placebo group is 33.5, which is quite important (<0.001) as given in Table I.

The Group of Placebo (n=20)				The Drugs given Group (n=17)			
Parameter	Pre-treatment	Post-treatment	P-Value	Pre-Treatment	Post-treatment	P-Value	Variation in Groups
Systolic BP	122.75±219	120.75±2.18	<0.01	125.89 ± 3.49	120.01 ± 3.14	<0.001	3.28%
Diastolic BP	84.25±1.99	82.00±1.82	<0.01	89.25 ± 1.92	84.70 ± 1.74	<0.001	2.27%
TG	148.45±4.8	146.20±4.20	>0.05	170.04 ± 7.59	136.85 ± 6.29	<0.001	17.52%
LDL-C(mg/dl)	149.74 ± 2.66	148.50 ± 2.27	>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	36.51 ± 1.95	44.71 ± 1.79	<0.001	19.32%
Body weight	69.35±1.76	69.17±1.68	>0.05	66.30 ± 1.93	64.80 ± 1.81	<0.001	2.01%

HDL cholesterol increases from 36.51 ± 1.95 to 44.71 ± 1.79 mg / dl after taking Niacin, which is a very vast variation (p value <0.001). There is a 20.02% increase in percentage. The triglycerides were reduced from 170.04 ± 7.59 to 136.85 ± 6.29 mg / dl; this was a major decrease in 90days (p value <0.001). Systolic blood pressure was reduced from 125.89 ± 3.49 mm Hg to 120.01 ± 3.14 mm Hg at three months. During this treatment, diastolic pressure was decreased with niacin 2.25 grams to 84.70 ± 1.74 mm Hg from 89.25 ± 1.92 . These variations in diastolic and systolic blood pressure were very important (P <0.001). Body weight was decreased from 66.30 ± 1.93 kg in three months to 64.80 ± 1.81 kg, which is quite significant compared to the placebo group (P <0.001).

DISCUSSION:

Three patients stopped the treatment because of side effects such as redness, hives and a feeling of warmth. The other subjects were persuaded to continue taking the 250 mg aspirin before start the first dose of niacin in the morning¹⁰. There are different groups of drugs used as lipid-lowering agents but niacin increase HDL and reduce LDL and is best lipid-lowering drug. In our study, HDL cholesterol increases from 36.51 ± 1.95 to 44.71 ± 1.79 mg / dl and 34.66% decrease in LDL cholesterol levels in males and females treated with niacin 2.25 grams. 2.26% was the mean decrease in body weight. The 4.90% reduction in Systolic blood pressure was observed and 4.94% in diastolic blood pressure within 3 months of using niacin in the same dose as the dose reduce LDL and increase HDL. The triglycerides were reduced from 170.04 ± 7.59 to 136.85 ± 6.29 mg / dl; this was a major decline in three months (p value <0.001)¹¹. These results coincide with the results of the study by J. M. S. Lee et al., Who noted almost the similar differences in body weight, blood pressure and LDL cholesterol. HDL cholesterol does not increase as much as in this study. His study showed an increase in HDL cholesterol of only 11.09%. In the study, the primary dyslipidemic patient with decreased LDL-C 29.75 47% 90% 2.89% systolic BP, diastolic pressure and body weight 3.98% 2.94% with three grams of niacin therapy. The results of the study by Allen J. Taylor et al coincide with the results of our analysis¹². In the results, 31.98% reduction in LDL cholesterol, 3.87% in systolic blood pressure and 3.87% in DBP and 2.91% body weight. When niacin

was used for two months, 15 hyperlipidemic patients had a significant increase in HDL cholesterol for 4 months. Guyton JR noted that niacin was much beneficial among all lipid-lowering agents that could lower LDL cholesterol and significantly rise HDL cholesterol¹³. When 20% of the 3 grams of niacin was used, it showed a 30.12% decrease in LDL cholesterol, triglycerides reduction of 17% and HDL cholesterol rise about 20.56%. These results also overlap with our results with respect to HDL and LDL cholesterol. Results from a research study accompanied by SE Bays ME and McGovern show that in a dyslipidemic patient for a period of three months, three grams of niacin were reduced by only 12.99%. Diastolic and Systolic blood pressure decreased by 2.51% and 0.19% respectively. 2.90% reduction in body weight was observed¹⁴. These results do not coincide with our results, with the exception of body weight. The reason for the variation could be due to the environmental factors and small sample size. His patients took absolutely no drugs and followed the Step-I diet. Taylor AJ et al showed a 24.3% decrease in LDL cholesterol concentration, 10.32% decrease in serum triglycerides and an increase of 11.87% in HDL cholesterol¹⁵. This observations probably contradict our results and opinion due to the small sample size in our study and the drug which is used in low dose. They used niacin 4.4 grams in 87 hyperlipidemic patients for 8 months duration.

CONCLUSION:

We concluded that niacin reduced body weight, LDL cholesterol and blood pressure and increased

HDL cholesterol in patients with primary hyperlipidemia.

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