ORIGINAL ARTICLE

Normal Triglycerides and normal Blood Pressure decrease risk of developing Coronary Artery Disease

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ABSTRACT

Background: New research in medicine has proved that high plasma triglycerides could be independent risk factor for coronary artery disease. Increased systolic and diastolic blood pressure with high serum triglycerides increase the risk of developing atherosclerosis, CAD and MI.

Methods: Research study was conducted in Jinnah hospital Lahore, Pakistan. Out of one hundred hyperlipidemic patients, ninety patients completed treatment period of three months. 42 patients were on drug niacin 2 grams daily in three divided doses and 48 were on placebo therapy. Their baseline values of serum TGs and blood pressure were taken at day-0. They were advised to take drug niacin or placebo and were advised to come for follow up at Lipid clinic of the hospital fortnightly. Data regarding parameters of the research work were expressed as the mean values±SD and "t" test was applied to determine statistical difference in results. P-value >0.05 was considered as non-significance, P-value < 0.05 was considered as significant and P-value < 0.001 was considered as highly significant change in the results.

Results: In three months with use of 2 grams Niacin thrice daily, plasma TGs decreased from 169.64±2.00 to 137.35±1.27mg/dl, systolic BP decreased from 125.88±1.65mmHg, to 119.70±1.66mmHg, and diastolic BP decreased from 89.11±1.32mmHg to 84.70±1.22mmHg. Changes in all values when compared with placebo results were found significant.

Conclusion: Standard and recommended Antihyperlipidemic drug therapy includes HMG-CoA reductase inhibitors, niacin, fibrates and bile acid binding resins. Out of these four drug groups, only niacin is the drug which favors the required therapy in sense it normalizes TGs and both fractions of blood pressure. We concluded from the above research that Niacin when used in high doses (as compared to its RDA) reduces TGs, systolic and diastolic blood pressure significantly, so decreases the risk for morbidity or mortality due to atherosclerosis, CAD or heart attack.

Keywords: Triglycerides, blood pressure, coronary artery disease

INTRODUCTION

Newer studies have now established that people with elevated levels of triglycerides are indeed at increased risk of developing coronary artery disease (CAD)[1]. In fact triglycerides are the most common form of fat in the body. In other words, almost all the excess calories consumed by individuals, whether from fats or carbohydrates, are converted to triglycerides and stored in fatty tissues[2]. An elevated level of triglycerides in the blood - a condition referred to as hypertriglyceridemia - is associated with an increased risk of cardiovascular disease in both men and women. Furthermore, people with coronary artery disease and elevated triglycerides have a higher risk of premature death than people with CAD and normal triglyceride levels[3]. High triglyceride levels can be produced by several medical conditions including, obesity, diabetes, metabolic syndrome, hypothyroidism, kidney diseases, and some medicines including estrogen replacement, tamoxifen, and beta blockers[4]. A majority of people with elevated triglyceride levels have metabolic syndrome, which means they have several risk factors for CAD, often including low levels of HDL-cholesterol, increased levels of LDL-cholesterol, hypertension, insulin resistance, obesity, and a tendency for excess blood clotting[5-7]. Niacin -- but not niacinamide -- has been used since long to try to lower elevated LDL cholesterol and triglyceride levels in the blood. However, side effects can be unpleasant and even dangerous. High doses of niacin cause flushing of the skin, stomach upset (which usually subsides within a few weeks), headache, dizziness, and blurred vision. There is an increased risk of liver damage. A time-release form of niacin reduces flushing, but its long-term use is associated with liver damage. In addition, niacin can interact with other cholesterol-lowering drugs[8-10].

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MATERIAL & METHOD

The Research was conducted at Jinnah Hospital, Lahore from June 2007 to December 2007. One hundred male, female patients, age range from 22 to 70 years were enrolled, suffering from primary and secondary hyperlipoproteinemia. Exclusion criteria for patient enrollment were chronic alcoholics, suffering from peptic ulcer, renal impairment, diabetes mellitus, hypothyroidism, hyperthyroidism and impaired liver functions. Specific Performa was designed for patients name, age, sex, occupation, previous medical history, drugs taken in past and written consent from patients.

Two groups were made of these 100 patients. Group-I (50 patients) was on placebo capsules filled with wheat, taken thrice daily after their regular meal, for the period of three months. Group-II (50 patients) was advised to take two grams Niacin in three divided doses, starting with low dose (titration of the drug dose), for the period of three months. Their baseline plasma TGs (triglycerides) levels, systolic and diastolic Blood Pressure were taken, and kept in Performa, designed. Fortnightly clinical visit schedule was advised to all participants, for their treatment follow up. On every visit, their blood pressure and lipid profile test results were noted and kept in their follow up record file. After completion of research study, data were expressed as the mean ± SD and "t" test was applied to determine statistical difference in results. A p-value >0.05 was considered as non-significance, P-value <0.05 was considered as significant and P-value < 0.001 was considered as highly significant change in the results.

RESULTS

Out of fifty hyperlipidemic patients of drug group, 42 patients completed their treatment period of three months. Eight patients discontinued treatment due to non-compliance of drug Niacin. In placebo group, two patients discontinued treatment in between due to their personal reasons. After six months treatment with 2 grams of Niacin when used in 42 hyperlipidemic patients, plasma TGs decreased from 169.64±2.00 to 137.35±1.27mg/dl. In placebo group, this reduction was from 148.45±1.11 to 146.20±1.90 mg/dl. Difference in placebo and drug group in this parameter was 30.00 mg/dl, which is highly significant difference statistically with p-value of <0.001. Mean systolic blood pressure of 42 hyperlipidemic patients at day-0 was 125.88±1.65mmHg, which reduced to 119.70±1.66mmHg after three months. Difference in this result was 6.25mmHg, which is statistically significant with p-value <0.05. In placebo group mean systolic blood pressure of hyperlipidemic patients at day-0 was 122.75±1.38mmHg which reduced to 120.75±2.88 mmHg after three months. Difference between day-0 and day-90 was 2.01mmHg, which is non-significant (p-value >0.05) change statistically as shown in table. Diastolic mean blood pressure of drug group 42 patients at day-0 was 89.11±1.32 mmHg which reduced to 84.70±1.22 mmHg. Difference in results is 4.45 mm of Hg, which is statistically significant (p-value <0.05). In placebo group mean diastolic blood pressure at day-0 was 84.25±1.44 which reduced to 82.00±1.98 mm of Hg after three months, which is non significant change statistically (p-value >0.05)

Table 1: Pretreatment and post-treatment values of plasma TGs, systolic/ diastolic blood pressure with mean, SD and P-values of placebo and drug groups

Pt group	Baseline values (I)	Values after treatment (II)	Difference in values I & II	Statistical significance
On drug (n=42)	TG 169.64±2.00 SBP 125.88±1.65 DBP 89.11±1.32	137.35±1.27 119.70±1.66 84.70±1.22	-19.03 -4.90 -4.94	P= <0.001 P= <0.05 P= <0.05
On placebo (n=48)	148.45±1.11 122.75±1.38 84.25±1.44	146.20±1.90 120.75±2.88 82.00±1.98	-1.51 -1.62 -2.25	P= >0.05 P= >0.05 P= >0.05

KEY: TGs = triglycerides, SBP = systolic blood pressure, DBP = diastolic blood pressure, SD = standard deviation, n = sample size of patients. Plasma triglycerides (TGs) are measured as milligram per dl, and systolic/diastolic blood pressure values are measured in millimeter of mercury.

DISCUSSION

In recent clinical research studies, plasma triglyceride levels and systolic/diastolic blood pressure values are getting focused to be cause of complications involved in coronary artery disease. These two parameters may be considered as independent risk factors for developing atherosclerosis. This research study was started to emphasize on these two parameters to get near normal values/ranges by a so called vitamin B-3 (Niacin or Nicotinic acid) by increasing its dose to get its hypolipidemic effects. In various studies it has been proved that Niacin decreases plasma triglyceride levels, which are statistically significant

changes. This hypolipidemic drug Niacin has another parallel benefit to decrease systolic/diastolic blood pressure, to an extent which is statistically significant. In our research Niacin has decreased 32.29mg/dl of plasma triglycerides (Table 1) in 42 hyperlipidemic patients, when drug was used for the period of three months. These results match with results of study conducted by Goldberg A et al[11] who observed almost same results by using Niacin for the period of four months. They also observed effects of Niacin on HDL and LDL-cholesterol, which effects are already been proved in many studies in past. Our results do not match with results of study conducted by Boden WE et al[12] who observed effects of niacin on blood pressure lesser than our effects. In their study niacin only decreased systolic blood pressure (1.00mmHg), but no effect at all on diastolic BP. This difference may be due to lesser exposure of drug i.e., only for 20 days, where as we used drug for three months in hyperlipidemic patients. Our study results regarding systolic blood pressure match with results of Lukasova M et al[13] and Brown BG et al[14] who observed same effects of niacin on systolic/diastolic blood pressure and on triglycerides, which authenticate our results. These results do not match with results achieved by research study by Bruckert et al[15]. They proved plasma triglyceridesv levels reduced only 12% in hyperlipidemic patients, when one gram of niacin was used for the period of 2 months. In their study systolic BP was reduced up to 2.22mmHg, diastolic BP reduction was 1.90 mm of Hg. These contrast shows dose dependent effects of niacin on blood pressure and TGs. Our study proved 6.25 mm of Hg change in systolic blood pressure, and diastolic blood pressure reduction was only 4.45, which matches with results of study of Sanyals S et al[16]. In their study systolic BP reduction was 5.17mmHg and diastolic blood pressure was reduced up to 4.12mmHg. Match in these results also authenticate our clinical research study. Guyton JR[17] proved 41mg/dl plasma TGs reduction, where as in our results it is 32.29mg/dl reduction. Difference in these results is in contrast. This mismatch in two results may be due to genetic variation, close observation and prolong use of drug by researcher, i.e., he used niacin 3 grams per day in divided doses for the period of six months. He did not include systolic/diastolic BP parameter in the study.

REFERENCES

1. Mittal MK, Florin T, Perrone J, Delgado JH, Osterhoudt KC. Toxicity from the use of niacin to beat urine drug screening. *Ann Emerg Med.* 2007;50(5):587-90.
2. Wan P, Moat S, Anstey A. "Pellagra: A review with emphasis on photosensitivity". The British journal of dermatology 2011;164 (6): 1188–200.
3. Taylor AJ, Lee HJ, Sullenberger LE. "The effect of 24 months of combination statin and extended-release niacin on carotid intima-media thickness: ARBITER 3".Current medical research and opinion 2006;22 (11): 2243–50.
4. Taylor AJ, Villines TC, Stanek EJ, Devine PJ, Griffen L, Miller M, Weissman NJ, Turco M. "Extended-release niacin or ezetimibe and carotid intima-media thickness". The New England Journal of Medicine 2009; 361 (22): 2113–22.
5. Holzhauser E, Albrecht C, Zhou Q, Buttler A, Preusch MR, Blessing E, Katus HA; Bea F. "Nicotinic acid has anti-atherogenic and anti-inflammatory properties on advanced atherosclerotic lesions independent of its lipid-modifying capabilities". Journal of cardiovascular pharmacology 2011;57 (4): 447–50.
6. Chapman MJ, Assmann G, Fruchart JC, Shepherd J, Sirtori C. "Raising high-density lipoprotein cholesterol with reduction of cardiovascular risk: the role of nicotinic acid—a position paper developed by the European Consensus Panel on HDL-C". Curr Med Res Opin 2004;20(8): 1253–68.
7. Papaliodis D, Boucher W, Kempuraj D, Michaelian M, Wolfberg A, House M, Theoharides TC. "Niacin-induced "Flush" Involves Release of Prostaglandin D2 from Mast Cells and Serotonin from Platelets: Evidence from Human Cells in Vitro and an Animal Model". J Pharmacol Exp Ther 2008;327 (3): 665–72.
8. Prakash Ravi, Sachin G, Lokesh KS, Basudeb D, Anuja L."Rapid resolution of delusional parasitosis in pellagra with niacin augmentation therapy". General Hospital Psychiatry 2008;30(6): 581–4.
9. Raja R, Thomas JM, Greenhill-Hopper M, Ley SV, Almeida Paz FA. Facile, one-step production of niacin (vitamin B3) and other nitrogen-containing pharmaceutical chemicals with a single-site heterogeneous catalyst. *Chemistry.*2008;14(8):2340-8.
10. Benjo AM, Maranhao RC, Coimbra SR, Andrade AC, Favarato D, Molina MS, Brandizzi LI, Da Luz PL. "Accumulation of chylomicron remnants and impaired vascular reactivity occur in subjects with isolated low HDL cholesterol: Effects of niacin treatment". Atherosclerosis 2006;187 (1): 116–22.
11. Goldberg A, Alagona P, Capuzzi DM, et al. Multiple-dose efficacy and safety of an extended-release form of niacin in management of hyperlipidemia. Am J Cardiol. 2000;85:1100-1105.
12. Boden W. E, Probstfield J. L, Anderson T, Chaitman B. R, Desvignes-Nickens P, Koprowicz K, McBride R, Teo K, Weintraub W. "Niacin in Patients with Low HDL Cholesterol Levels Receiving Intensive Statin Therapy". New England Journal of Medicine 2011;365 (24): 2255–2267.
13. Lukasova M, Hanson J, Tunaru S, Offermanns S. "Nicotinic acid (niacin): New lipid-independent mechanisms of action and therapeutic potentials". Trends in pharmacological sciences 2011;32 (12): 700–7.
14. Brown BG, Zhao XQ, Chalt A, et al. Simvastatin and niacin, antioxidant vitamins, or the combination for the prevention of coronary disease. N Engl J Med. 2001;345(22):1583-1592.
15. Bruckert E, Labreuche J, Amarenco P. "Meta-analysis of the effect of nicotinic acid alone or in combination on cardiovascular events and atherosclerosis" .Atherosclerosis 2010(2): 353–61.
16. Sanyal S, Karas RH, Kuvin JT. Present-day uses of niacin: effects on lipid and non-lipid parameters. Expert Opin Pharmacother. 2007;8(11):1711-7.
17. Guyton JR. Niacin in cardiovascular prevention: mechanisms, efficacy, and safety. Curr Opin Lipidol. 2007;18(4):415-20.