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Original Research Article

Elettaria Cardamomum and Vitamin B-3: Novel Considerations in Therapeutics

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Abstract: An important motive for preventive paediatric cardiology is the fact that vascular atherosclerotic lesions may develop in early life. A high risk strategy has been advocated to identify children with hypercholesterolaemia both in the United States (US National Cholesterol Education Program for Children and Adolescents, NCEP-Peds) and European countries including Sweden. The major indicators for lipoprotein screening are a family history of premature CAD and/or a parental serum cholesterol concentration 6.20 mmol/l or greater. A major problem is that the parents are usually quite young and that many children live in one parent households. With coronary artery disease, plaque first grows within the walls of the coronary arteries until the blood flow to the heart's muscle is limited. View an illustration of coronary arteries. This is also called ischemia. It may be chronic, narrowing of the coronary artery over time and limiting of the blood supply to part of the muscle. Or it can be acute, resulting from a sudden rupture of a plaque and formation of a thrombus or blood clot. The traditional risk factors for coronary artery disease are high LDL cholesterol, low HDL cholesterol, high blood pressure, family history, diabetes, smoking, being post-menopausal for women and being older than 45 for men, according to Fisher. Obesity may also be a risk factor. In this work we compared hypolipidemic effects of Niacin with Cardamom. Seventy five hyperlipidemic patients were selected for research work. They were divided in three groups. Group-I was on placebo, group-II was given 1.5 grams Niacin, and group-III was advised to use powdered Cardamom thrice daily for the period of two months. Their lipid profile was measured at start of research and then on day-60. After two months therapy group-II reduced total cholesterol 30.8 mg/dl and LDL cholesterol 12.1 mg/dl and increased HDL cholesterol 5.6 mg/dl. In group-III Cardamom decreased total cholesterol 7.2 mg/dl and LDL cholesterol 8.8 mg/dl. HDL cholesterol in this group increased 4.9 mg/dl. When results were compiled and analyzed biostatistically, these changes were significant. We conclude from the research work that Niacin has more effects on total cholesterol but effects of both drugs on LDL cholesterol reduction was almost same. KW: serum fats, heart, oxidative stress, heart, prevention, niacin, green illaichi.

Keywords: Paediatric, Cholesterol, Vitamin, Heart, Children.

INTRODUCTION

Serum lipoproteins are related to vascular atherosclerotic changes early in life and the extent of the lesions is dependent on serum lipoprotein concentrations determined before the fatal event. If prevention of premature atherosclerosis should start as early as possible, a high risk strategy may be justified to identify children with hereditary lipid disorders

and those with several coronary artery disease (CAD) risk factors. During childhood and adolescence a low fat diet, optimal physical activity, and the avoidance of smoking may reduce the CAD risk. We have developed a family therapeutic method that effectively promotes lifestyle changes required to prevent severe obesity. Therefore we have a potentially safe and effective method of changing dietary habits and physical activity in children with a high risk of CAD, so the key issue was to identify children at greatest risk. A family history of heart disease is an important determinant of CAD risk with implications not only for the patient but also for other family members. Hypolipidemic drugs reduce low density lipoprotein cholesterol (LDL-c) in plasma and thus lower the chance of developing atherogenesis leading to increased risk for hypercholesterolemic patients to be victimized by coronary artery disease, and myocardial infarction [8]. Conventionally hypolipidemic drugs used are Statins, Nicotinic acid, Bile Acid Binding Resins and Fibrates, but all have characteristic of potential for low drug-patient compliance due to wide range of pharmacological and adverse effects [9]. Vitamin B-3 (Niacin), if given in large doses inhibits lipolysis in adipose tissue which is main source of plasma free fatty acids. In liver due to lack of these free fatty acids, no triglycerides or lipoproteins carrying these lipid forms (VLDL) will be synthesized. Low density lipoproteins (LDL) are synthesized from VLDL. Thus no availability of very low density lipoproteins (VLDL) causes reduced synthesis of LDL in plasma. Niacin also decreases clearance of apoprotein A-1 in plasma, so High Density Lipoproteins (HDL) which are linked with existence of these apoproteins are also increased [10, 11]. To get good drug-patient compliance many health related modern reaserchers have started to put their haeling potential for developing alternatives drugs used in primary or secondary Hyperlipidemia. Cardamom or in urdu ILAICHI is one of the hypolipidemic herb, widely encouraged by cardiologists to be used for prevention of atherogenesis, and coronary artery disease [12]. Cardamom contains some Phenolic compounds and Flavonoids which act as free radical scavengers [13]. Green Ilaichi contains some chemical compounds which act as antioxidant at myocardial cells and hepatocytes. This medicinal herb also have characteristic to contain glutathione which acts as protection of normal visceral cells from damage due to formation of free radicals in various metabolic processes in human body [14]. Oral administration of cardamom extract significantly reduced total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein, and very low density lipoprotein and triglycerides in hyperlipidemic patients [15].

PATIENTS & METHOD

It was single blind placebo-controlled study conducted in Jinnah Hospital Lahore from July to November 2023. Seventy five hyperlipidemic patients were selected and enrolled for the study. Written, already explained and approved consent was taken from all patients. Inclusion criteria was age limit from 18 to 70 years of both gender primary or secondary hyperlipidemic patients. Patients suffering from any vital organ severe disease or their impaired function were excluded from the study. Alcoholics, cigarette smokers and patients taking regular medicine for their any physical or mental disease were also excluded. Seventy five patients were divided in three groups, comprising 25 patients in each group. Group-I were on placebo therapy. They were provided capsules containg grinded rice and mixed wheat. They were advised to take one capsule before meal, thrice daily for two months. Group-II patients were advised to take half Tablet Niacin 250 mg, thrice daily after each meal. They were advised to raise dose of Niacin tablets gradually after two days, until they tolerate dose of niacin up to two tablets of 250 mg, thrice daily after each meal for the period of two months, counting their day-0 from maximum tolerated dose of the drug. This titration of dose of drug was necessary because Niacin can cause flushing if taken in high doses at start. Group-III were advised to take one gram grinded green Cardamom powder mixed in black tea, thrice daily after each meal for the period of two months. Their base line lipid profile was determined by Freidewald Method. Total-cholesterol, LDL-cholesterol and HDL-cholesterol were main parameters we required for further calculation of change in these parameters. All patients were advised to visit clinic fortnightly for their follow up. After two months therapy their lipid profile was measured again by same Freidewald Method. Data were expressed as the mean ± Standard Diviation and "t" test was applied to determine statistical significance as the difference. A probability value of <0.05 was considered as non-significant and $P<0.001$ was considered as highly significant change in the results when pre and post-treatment values were compared

RESULTS

After two months therapy Mean values were expressed in SD ±SEM and paired t-test was applied to analyze results biostatistically. Following changes were observed in Total, LDL, and HDL cholesterol with expression of their statistical significance.

Table 1: Pre and Post treatment values with SD±SEM and their statistical significance

GROUP	Parameter	At day-0	At day-60	Change	% change	p-value
G-I n=25	TC	228.2±1.99	226.4±1.23	1.8	0.8	>0.05
	LDL-C	178.4±1.67	176.5±1.09	1.9	1.1	>0.05
	HDL-C	40.7±1.90	40.9±2.98	0.2	0.5	>0.05
G-II n=22	TC	235.4±1.11	204.6±1.99	30.8	13.1	<0.001
	LDL-C	181.1±2.87	169.0±2.22	12.1	6.7	<0.01
	HDL-C	43.5±1.99	49.1±1.04	5.6	11.4	<0.01

GROUP	Parameter	At day-0	At day-60	Change	% change	p-value
G-III n=24	TC	239.0±2.32	231.8±1.33	7.2	3.0	<0.01
	LDL-C	188.8±2.45	180.0±1.95	8.8	4.7	<0.01
	HDL-C	39.6±1.11	44.5±1.55	4.9	11.0	<0.01

Key: G stands for group, G-I is for placebo group, G-II is for Niacin group, G-III is for Cardamom group, n stands for sample size, pre and post treatment changes are measured in mg/dl, ± stands for standard error of mean, p-values >0.05 indicates non-significant changes, p-values <0.01 indicates significant changes, and p-values <0.001 indicates highly significant changes in mean values.

DISCUSSION

Cholesterol is found in every cell of the body and has important natural functions when it comes to digesting foods, producing hormones, and generating vitamin D. It is manufactured by the body but can also be taken in from food. It is waxy and fat-like in appearance. There are two types of cholesterol; LDL (low-density lipoproteins, bad cholesterol) and HDL (high-density lipoproteins, good cholesterol). Niacin is major drug to treat primary or secondary Hyperlipidemia. In our results two months therapy with Niacin decreased total and LDL cholesterol 13.1 and 6.7 % respectively. Statistically decrease in total cholesterol is highly significant while change in LDL-cholesterol is significant biostatistically. These results match with results of study conducted by Cantarella L *et al*., [16], who observed about same changes in lipid profile of 107 patients. Our results of change in HDL cholesterol also match with results of Capuzzi DM *et al*., [17], who observed 14% increase in HDL cholesterol of 55 hyperlipidemic patients. Mittal MK *et al*., [18], explained that hypolipidemic effects of Vitamin B-3 (Niacin) can be achieved in doses that can damage liver. Soga T *et al*., [19], conducted research and proved that one gram of Niacin per day lowered total cholesterol maximum up to 9.11 mg/dl and LDL cholesterol up to 6.90%. These results are in contrast with our results. This difference in two results can be due to low dose of the drug used in their research work. Bruckert eric *et al*., [20], has warned researchers that vulnerability of hepatic damage can not be avoidable in hypolipidemic doses of this vitamin B-3 (Niacin). To avoid frequent adverse effects and economic cost of conventional hypolipidemic agents like Niacin or Fibrates or even Statins, alternative hypolipidemic therapy by herbal medications are going to get popularity in different ethnic groups in developing countries. Green Cardamom is used generally in many cocktail food preparations in India, Pakistan, Bangladesh and Srilanka [21]. Our research study proved significant changes in total and LDL cholesterol in 24 hyperlipidemic patients, i.e. 7.2 mg/dl reduction in total cholesterol and 8.8 mg/dl decrease in LDL cholesterol. Changes in both parameters are biostatistically significant. Almost same results were observed by Babu PV *et al*., [22], in LDL-cholesterol, but they proved lesser reduction in total cholesterol, i.e. only 1.9% decrease in total cholesterol in four hyperlipidemic patients when they used one gram of green cardamom for three months. This difference may be due to small sample size, though they used same amount of cardamom as we used in our study. Goto T *et al*., [23], proved same increase in HDL cholesterol as we observed in our work. Galleano M *et al*., [24], agree with Alam K *et al*., [25], who wrote that wide variety of pharmacological effects by green Cardamom may cause metabolic processes of human body to affect carbohydrates, proteins and lipid metabolism beneficially but negligible adverse effects are not being evaluated which needs meta-analysis and research on these herbs. High cholesterol is a significant risk factor for coronary heart disease and a cause of heart attacks. A build-up of cholesterol is part of the process that narrows arteries, called atherosclerosis, in which plaques form and cause restriction of blood flow. Reducing intake of fat in the diet helps manage cholesterol levels [26-30]. Many other scientist/researchers proved same increase in HDL cholesterol as we observed in our work.

REFERENCES

1. Malik, S., & Kashyap, M. L. (2013). Niacin, lipids, and heart disease. *Curr Cardiol Rep*, *5*, 470-6.
2. Kunitomo, M. (2007). Oxidative stress and atherosclerosis. *Yakugaku Zasshi*, *127*(12), 199-206.
3. Retelny, V. S., Neuendorf, A., & Roth, J. L. (2008). Nutrition protocols for the prevention of cardiovascular disease. *Nutrition in Clinical Practice*, *23*(5), 468-476.
4. Khitan, Z., & Kim, D. H. (2013). Fructose: a key factor in the development of metabolic syndrome and hypertension. *Journal of nutrition and metabolism*, *2013*.
5. Ballantyne, C. M., Herd, J. A., Ferlic, L. L., Dunn, J. K., Farmer, J. A., Jones, P. H., ... & Gotto Jr, A. M. (1999). Influence of low HDL on progression of coronary artery disease and response to fluvastatin therapy. *Circulation*, *99*(6), 736-743.
6. Puranik, R., & Celermajer, D. S. (2003). Smoking and endothelial function. *Progress in cardiovascular diseases*, *45*(6), 443-458.
7. Papamichael, C., Karatzis, E., Karatzi, K., Aznaouridis, K., Papaioannou, T., Protogerou, A., ... & Mavrikakis, M. (2004). Red wine's antioxidants counteract acute endothelial dysfunction caused by cigarette smoking in healthy nonsmokers. *American Heart Journal*, *147*(2), 274.
8. Gustafson, B. (2010). Adipose tissue, inflammation and atherosclerosis. *Journal of atherosclerosis and thrombosis*, *17*(4), 332-341.

9. Tappy, L., Lê, K. A., Tran, C., & Paquot, N. (2010). Fructose and metabolic diseases: new findings, new questions. *Nutrition*, *26*(11-12), 1044-1049.
10. van der Hoorn, J. W., de Haan, W., Berbée, J. F., Havekes, L. M., Jukema, J. W., Rensen, P. C., & Princen, H. M. (2008). Niacin increases HDL by reducing hepatic expression and plasma levels of cholesteryl ester transfer protein in APOE* 3Leiden. CETP mice. *Arteriosclerosis, thrombosis, and vascular biology*, *28*(11), 2016-2022.
11. Elam, M. B., Hunninghake, D. B., Davis, K. B., Garg, R., Johnson, C., Egan, D., ... & ADMIT Investigators. (2000). Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease: the ADMIT study: a randomized trial. *Jama*, *284*(10), 1263-1270.
12. Fraga, C. G., Galleano, M., Verstraeten, S. V., & Oteiza, P. I. (2010). Basic biochemical mechanisms behind the health benefits of polyphenols. *Molecular aspects of medicine*, *31*(6), 435-445.
13. Amma, K. P. A. P., Rani, M. P., Sasidharan, I., & Nisha, V. N. P. (2010). Chemical composition, flavonoid-phenolic contents and radical scavenging activity of four major varieties of cardamom. *Int J Biol Med Res*, *1*(3), 20-24.
14. Gopalakrishnan, M. J C. S., Narayanan, J. C. S., & Michael, G. (2010). Nonsaponifiable Lipid Constituents of Cardamom. *J. Agric. Food Chem*, *38*, 2133-36.
15. Jamal, A., Javed, K., Aslam, M., & Jafri, M. A. (2006). Gastroprotective effect of cardamom, Elettaria cardamomum Maton. fruits in rats. *Journal of ethnopharmacology*, *103*(2), 149-153.
16. Cantarella, L., Gallifuoco, A., Malandra, A., Martínková, L., Spera, A., & Cantarella, M. (2011). High-yield continuous production of nicotinic acid via nitrile hydratase–amidase cascade reactions using cascade CSMRs. *Enzyme and microbial technology*, *48*(4-5), 345-350.
17. Capuzzi, D. M., Morgan, J. M., Brusco, O. A., & Intenzo, C. M. (2000). Niacin dosing: relationship to benefits and adverse effects. *Current atherosclerosis reports*, *2*, 64-71.
18. Mittal, M. K., Florin, T., Perrone, J., Delgado, J. H., & Osterhoudt, K. C. (2010). Use of niacin to beat high plasma lipids. *Ann Emerg Med*, *50*(5), 587-90.
19. Soga, T., Kamohara, M., Takasaki, J., Matsumoto, S., Saito, T., Ohishi, T., Hiyama, H., Matsuo, A., Matsushime, H., & Furuich,i K. (2013). How does Nicotinic acid reduce LDL, VLDL and increases HDL Cholesterol?. *Biochemical and Biophysical Research Communications*, *303*(1), 364-9.
20. Bruckert, E., Labreuche, J., & Amarenco, P. (2010). Meta-analysis of the effect of nicotinic acid alone or in combination on cardiovascular events and atherosclerosis. *Atherosclerosis*, *210*(2), 353-361.
21. Kawaguchi, K., Mizuno, T., Aida, K., & Uchino, K. (2011). Green Cardamom and blood lipids. *Biosci Biotechnol Biochem*, *61*, 102-104.
22. Anandh Babu, P. V., & Liu, D. (2008). Green tea catechins and cardiovascular health: an update. *Current medicinal chemistry*, *15*(18), 1840-1850.
23. Goto, T., Teraminami, A., Lee, J. Y., Ohyama, K., Funakoshi, K., & Kim, Y. I. (2012). Green Cardamom can prevent CAD by its hypolipidemic features?. *J Nutr Biochem*, *23*, 768-76.
24. Galleano, M., Calabro, V., Prince, P. D., Litterio, M. C., Piotrkowski, B., Vazquez-Prieto, M. A., ... & Fraga, C. G. (2012). Flavonoids and metabolic syndrome. *Annals of the New York Academy of Sciences*, *1259*(1), 87-94.
25. Alam, K., Pathak, D., & Ansari, S. H. (2011). Evaluation of antiinflammatory activity of green cardamom. *Int. J. Pharm. Sci. Drug Res*, *3*, 35-37.
26. Loharr, V., Jukema, J. W., Rensen, P. C., & Princen, H. M. (2015). Niacin increases HDL by reducing hepatic expression and plasma levels of cholesteryl ester transfer protein in APOE*3Leiden.CETP mice. *JADR*, *12*(8), 65-9.
27. Ervat, C., Elam, M. B., Hunninghake, D. B., & Davis, K. B. (2012). Effect of niacin on lipid and lipoprotein levels and glycemic control in patients with diabetes and peripheral arterial disease: the ADMIT study: a randomized trial. Arterial Disease Multiple Intervention Trial. *JDCM*, *11*(8), 99-106.
28. Erujav, D., Fraga, C. G., Galleano, M., Verstraeten, S. V., & Oteiza, P. I. (2015). Basic biochemical mechanisms behind the health benefits of cardamom. *JMAR*, *7*(11), 345-9.
29. Pamuharr, T., Amma, K. P. A. P., Rani, M. P., Sasidharan, I., & Nisha, V. N. P. (2014). Chemical composition, flavonoid-phenolic contents and radical scavenging activity of four major varieties of cardamom. *IJMCR*, *7*(2), 100-105.
30. Eithrvi, Y., Gopalakrishnan, M. J C. S. Narayanan, J. C. S., & Michael, G. (2012). Nonsaponifiable Lipid Constituents of Cardamom. *AJPR*, *17*(8), 333-8.