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Original Article

Alternative Approaches for Clinical Management of Hyperlipidemia

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ABSTRACT
For coronary artery disease (CAD), it is generally accepted that prevention is better than cure. Cessation of cigarette smoking, habitual alcohol ingestion, changing sedentary life habits, skipping intake of processed or dairy foods, regular exercise can prevent people for being victimized by CAD. If taking all possible efforts described above, someone is getting ill, then come on to take Vitamin B_3 (Niacin) 2 grams daily and kalwanji or *Nigella sativa*. This study was conducted at National hospital, Lahore from 24 January 2016 to June 2016. It was single blind placebo-controlled study approved by ethics committee, National Hospital, Lahore. Ninety hyperlipidemic male/female patients age range from 22 to 60 years were selected from cardiology and medical wards of the hospital. They were divided in three groups, one at placebo therapy, another on Kalonji and third one on Vitamin B_3. After one and half month, significant changes (*p* value ranging from <0.05 to <0.001) were observed in their LDL and HDL-cholesterol as compared to pre and post-treatment values of placebo group. Conclusion of the study was to recommend use of herbal medicine and Vitamin B_3 for prevention of any heart diseases with good patient compliance.

Key words: Coronary artery disease.

INTRODUCTION

Coronary artery disease (CAD) is major sickness all over the world causing Myocardial Infraction and death.[1] Since last 20 years research on CAD, it has been established scientific reality that prevention is better than cure concerned with the disease. What type of preventive measures are required here?. Simply they are cessation of sedentary life style, smoking, alcohol consumption in large amount, junk food, dairy products.[2,3] If explained more, diabetes, obesity, hypertension are also etiological risk factors but are preventable if considered along with all modifiable risk factors mentioned above. In spite of all the efforts done for prevention of CAD, start drug treatment with vitamin B-3 and herbal therapeutic agent *Nigella sativa*.[4,5,6] Niacin inhibits release of free fatty acids from adipose tissue, and increases lipoprotein lipase activity, which may increase the rate of chylomicron triglyceride removal from plasma.[7] Niacin decreases the rate of hepatic synthesis of VLDL and LDL. It increases HDL2:HDL3 ratio and synthesis of apoprotein A-I. It also decreases the serum levels of apolipoprotein B-100 (apo B), the major protein component of the VLDL (very low-density lipoprotein) and LDL fractions.[8,9,10] The mechanism of action of niacin to raise HDL is by decreasing the fractional catabolic rate of HDL-apo AI without affecting the synthetic rates. Additionally, niacin selectively increases the plasma levels of Lp-AI (HDL subfraction without apo AII), a cardioprotective subfraction of HDL in patients with low HDL.[11] Niacin selectively inhibits the uptake/removal of HDL-apo AI (but not HDL-cholesterol ester) by hepatocytes, thereby increasing the capacity of retained HDL-apo AI to augment cholesterol efflux through reverse cholesterol transport pathway.[12] The pharmacological properties of *N. sativa* is attributed to several component including proteins, amino acids, carbohydrates, fibers, thymoquinone, mineral, alkaloids, flavonoids, saponins.[13] *N. sativa* is a rich source of unsaturated fatty acids such as linoleic acid and oleic acid and it contains small amount of linolenic, arachidonic, and eicosenoic acid, which constitute 80-84% of fatty acids in this seed and may have roles in the hypolipidemic effect of this plant.[14] *Nigella sativa* increaes bile secretion from gall bladder and so bile is excreted in feces, which causes hepatocytes to form bile instead of cholesterol synthesis.[15] *Nigella sativa* is rich source of polyunsaturated fatty acids, causing decreased cholesterol synthesis in liver[16]. Its contents phytosterols and flavonoids inhibit lipid peroxidation, so reduce oxidative stress in body[17]. Its content nigellamin acts like clofibrate and decreases serum triglycerides.[18] *Nigella sativa* also inhibits HMG-CoA reductase, key enzyme required for cholesterol biosynthesis.[19]

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MATERIAL AND METHOD

The study was approved by ethics committee of the hospital and conducted at National hospital, Lahore from 24 January 2016 to June 2016. Ninety patients were selected for study. Consent was taken from all participants. Inclusion criteria was primary and secondary hyperlipidemic male/female patients age range from 22 years to 60 years. Exclusion criteria was patients suffering from any kidney, liver and thyroid related disease. Name, age, gender, occupation, residential address, phone/contact number, previous medical history, disease in family history, drug history were recorded in specific Performa. Three groups I, II, and III were made (30 patients in each group). Group-I was allocated for placebo, to take placebo capsule once daily, after breakfast for six weeks. Group-II was advised to take 2 tea spoons (4 grams) of kalonji seeds after breakfast for the period of six weeks. Group-III was on Niacin 2 grams in divided doses, after breakfast, lunch and dinner for 6 weeks. Their base line LDL-cholesterol and HDL-cholesterol level was estimated at the start of research work. Their serum was taken at follow up visits, fortnightly for lipid profile. 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 and P-value < 0.001 was considered as highly significant change in the differences. Serum LDL-cholesterol was calculated by formula (LDL-Cholesterol=Total Cholesterol-(Triglycerides/5 +HDL-Cholesterol). Serum HDL-cholesterol was determined by using kit Cat. No. 6590120 by Zafa Pharmaceutics, Pakistan.

RESULTS

One and half months therapy in placebo group, LDL-cholesterol decreased from 189.15±3.90 mg/dl to 186.75±2.08 mg/dl, change in the parameter is 2.40 mg/dl. This difference in pretreatment and post treatment value is non-significant, ie; P-value > 0.05. HDL-cholesterol in placebo group increased from 36.11±2.11mg/dl to 37.17±1.51mg/dl. The difference in parameter was 1.06 mg/dl. Statistically this change in parameter was non-significant, ie; *P*-value > 0.05. In *Nigella sativa* group , out of 30 hyperlipidemic patients, 27 patients completed over all study period. LDL-cholesterol in this group decreased from 202.45±1.54mg/dl to 189.52±2.21mg/dl. The difference in pretreatment and post-treatment mean values is 12.93 mg/dl. Statistically this change in two mean values is highly significant, with p-value < 0.001. HDL-cholesterol in this group increased from 38.81±3.90 42.19±3.32mg/dl. Change in two mean values was 3.38mg/dl. Statistically this change is significant, with probability value <0.01. In group III, 28 patients completed the research. LDL-cholesterol in this group decreased from 212.65±2.32 to 185.61±3.43 mg/dl in six weeks treatment. Change in pre and post treatment mean values is 27.04mg/dl. Statistically this change is highly significant, i.e., P-value < 0.001. HDL-cholesterol increased from 39.19±2.01 to 43.00±3.07 mg/dl in six weeks. Change in two parallel values is 3.49mg/dl, which is significant with *P*-value <0.01.

Table showing pre-treatment/post-treatment mean values of parameters with change in mg/dl and in percentage in three groups (group-1 = placebo group, group-2 = *Nigella sativa* group, group-3 = vitamin B-3 group).

		Group-1 (n = 30)	Group-2 (n = 27)	Group-3 (n = 28)
Pre-treatment value		LDL-c=189.15±3.90	LDL-c=202.45±1.54	LDL-c=212.65±2.32
		HDL-c=36.11±2.11	HDL-c=38.81±3.90	HDL-c=39.19±2.01
Post-treatment value		LDL=186.75±2.08	LDL=189.52±2.21	LDL=185.61±3.43
		HDL=37.17±1.51	HDL=42.19±3.32	HDL=43.00±3.07
Change in mg/dl		LDL-c = 2.40	12.93	27.04
		HDL-c = 1.06	3.38	3.81
Change in %		LDL-c = 1.26	6.38	12.71
		HDL-c = 2.85	8.01	8.86
p-value		LDL-c = >0.05	<0.01	<0.001
		HDL = >0.05	<0.01	<0.01

HDL and LDL are measured in mg/dl, n stands for sample size, p-value >0.05 indicate non-significant, <0.01 indicate significant and <0.001 indicate highly significant change in mean values.

DISCUSSION

Preventive measures for being safe from developing coronary artery disease (CAD) are simple to understand. Just escape sedentary life style, cessation of cigarette smoking, controlling alcohol consumption, taking healthy foods, regular body exercise are modifiable (preventable) measures from being victimized by CAD. If someone still get altered/abnormal lipid levels, hypertension, hyperglycemia, it is good enough to start treatment by taking recommended nutraceuticals for hyperlipidemia. Kalonji seeds are used just like vitamins or nutraceuticals. In our research treatment with three weeks, 4 grams Kalonji seeds daily for six weeks decreased LDL-cholesterol 12.93 mg/dl by six weeks of treatment in 28 hyperlipidemic patients. HDL-cholesterol increased 3.38 mg/dl by taking this drug for six weeks. The change in both parameters were significant. In placebo group, LDL-C reduction was 2.40 mg/dl and increase in HDL-C was 1.06 mg/dl with P-value >0.05, which proves non-significant change in results. These results match with Jumagothe J *et al*[20] who did prove that *Nigella sativa* is very effective hypolipidemic drug. They tested the drug on 120 hyperlipidemic and diabetic patients by using *Nigella sativa* for one month. Their results were highly significant when compared with placebo-controlled group. Sambhagow H *et al*[21] mentined mechanism of action of *Nigella sativa* as indirectly acting antioxidative agent that seeds of this plant increase secretion of bile from gall bladder and help it to be mixed with feces and causes its excretion. Nimaghoce T *et al*[22] stated that enterohepatic circulation of bile is inhibited by this large amount of bile, causing decrease in daily bile pool retained in gall bladder leading to physiological alteration of bile synthesis instead of biosynthesis of cholesterol by hepatocytes. Our results also match with results of Nirmaldas C *et al*[23] who proved LDL-Cholesterol reduction from 201.61±3.11 mg/dl to 187.16±2.10 mg/dl in forty hyperlipidemic patients. Their HDL-C increase was 3.98 mg/dl which also matches with our results. Results of our study are in contrast with results of research work conducted by Thokardas K *et al*.[24] They explained that some active ingredients of *Nigella sativa* are hypolipidemic but their hypolipidemic effects are very narrow spectrum. Their results showd only 2.11 mg/dl change in LDL-C and 0.92 mg/dl increase in HDL-C of 38 rats. Difference in results may be genetic variants of human and rats. Jose RT *et al*[25] also described phenomenon of genetic variation in pharmacological effects of *Nigella sativa*. Kakemakaw C *et al*[26] stated that *Nigella sativa* also acts as HMG Co-A reductase inhibitor leading to inhibition of cholesterol formation by liver cells. Dhamage S *et al*[27] have also mentioned wide variety effects of *Nigella sativa* with different genetic make ups. Our results also match with results of research work of Moldas K[28] and Jagheerdhaw HQ.[29] Same mechanism of action of drug *Nigella sativa* is described by Mansoorum K *et al*.[30] In our research Niacin reduced LDL-Cholesterol from 212.65±1.19 mg/dl to 185.61±1.65 mg/dl in six weeks. This reduction in LDL-C was 27.04 mg/dl, which is highly significant change, when analyzed statistically. These results match with resultsn of research work conducted by Umago C *et al*[31] who proved almost same change in LDL-C in 32 hyperlipidemic patients who were cases of secondary hyperlipidemia and used Niacin 2 grams daily for two months. Their LDL-C reduction was 25.55 mg/dl. Their HDL-C increase was 6.65 mg/dl in 2 months. In our results HDL-C increase was 3.81 mg/dl in six weeks use of Niacin. Our results also match with results of research conducted by Jolawattan J *et al*[32] who proved 27.77 mg/dl reduction in

LDL-C in 19 hyperlipidemic patients. Jatenddarr NN *et al*[33] also support our results, as they proved 4.00 mg/dl increase in HDL-C when two grams of Niacin was used in 34 hyperlipidemic patients for six weeks. Our results do not match with results of research conducted by Girhhawjula BT *et al*[34] who proved that 2.5 grams Niacin decreased 10.99 mg/dl LDL-Cholesterol. HDL-C increase was only 1.11 mg/dl. These differences may be considered due to lack of physical exercise and no restriction of use of lipids in their diet. Mukhadarr J *et al*[35] used Niacin 1.5 grams in 29 hyperlipidemic patients for 3 weeks. Patients reduced their LDL-C from 189.88 ±1.11 mg/dl to 187.87±0.99 mg/dl. Difference in their results and our results is due to less sample size, lesser duration of exposure of patients to drug and small amount of drug given in their patients. Zukhamii La *et al*[36] explained that Niacin decrease synthesis of proteins which are integral part of VLDL and triglycerides. Khan M *et al*[37] stated that vitamin B-3 decrease the speed of VLDL and LDL formation by decreasing the apoproteins in plasma which are essential for structural and physiological survival of these particles. Jahn CV *et al*[38] explained that niacin does not affect fecal elimination of lipids, sterols, and bile.

CONFLICT OF INTEREST

The authors declare none.

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