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Life Science Journal

MARSLAND PRESS
Multidisciplinary Academic Journal Publisher

REPLACING GEMFIBROZIL WITH PLANT SEEDS

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Abstract: Coronary artery disease (CAD) can have long, stable periods, but can also become unstable at any time, typically due to an acute atherothrombotic event caused by plaque rupture or erosion. The disease is chronic, most often progressive, and hence serious, even in clinically apparently silent periods. To evaluate the chest pain patient with suspected coronary disease, the physician has a vast array of noninvasive diagnostic tests from which to choose, including bicycle or exercise treadmill testing, myocardial perfusion imaging, dobutamine stress echocardiography, or coronary computed tomographic angiography, though in many instances, noninvasive testing is inconclusive or nondefinitive in establishing the presence or absence of obstructive disease. In this study we have compared hypolipidemic effects of Fenofibrate 40 mg with Nigella sativa. Seventy five hyperlipidemic patients from National Hospital Lahore were enrolled for study. After getting consent all patients were divided in three groups comprising 25 patients in each group. Group 1 was on Nigella sativa, group 2 was on Gemfibrozil and third group was on placebo therapy. They were advised to take drugs for two months. After completion of study pretreatment and post treatment values of LDL cholesterol were analyzed statistically. In Nigella sativa group LDL cholesterol decreased from 191.14±3.45 to 159.40±2.98 mg/dl, means 31.7 mg/dl LDL reduction was observed when compared with placebo group. In Fenofibrate group of patients LDL cholesterol decreased from 197.77±3.91 mg/dl to 159.62±2.20 mg/dl, means LDL reduction in mean values was 38.2 mg/dl, when compared with placebo group. These changes are highly significant with p-values of <0.001. **CONCLUSION OF RESEARCH WORK:** We concluded from this study that herbal medicine Nigella sativa is as effective as traditionally used hypolipidemic drug Fenofibrate.
[ShahMurad, Professor. **Kalonji, fenofibrates and triglycerides.** *Life Sci J* 2022;19(8)48-51]. ISSN 1097-8135 (print); ISSN2372-613X (online). http://www.lifesciencesite.com. 07 doi:10.7537/marslsj190822.07.

Key Words: Coronary artery disease, hyperlipidemia, mortality, morbidity, blood pressure, hyperlipidemic patients, ICU, Fibrates

INTRODUCTION

A large number of patients who develop CAD have normal or moderately increased lipid levels which demonstrates that, despite the great contribution of dyslipidemias to the development of CAD, other factors also play a role in the progression of atherosclerosis[1-3]. Lp(a) is involved in the pathogenesis and progression of atherosclerosis through different mechanisms. Prospective epidemiological and meta-analysis studies have shown the positive correlation between Lp(a) and CAD[4]. Determination of Lp(a) is an important tool to assess patients with CAD, and is especially useful in the prediction of risk in human population. However, the development and size of lesions from CAD established on angiography and the correlations with serum lipids and Lp(a) are controversial[5]. Hypolipidemic drugs can be used to prevent hyperlidemia, CAD, heart arrhythmias and cardiac arrest. Allopathic drugs used to prevent or cure Hyperlipidemia include Statins, Fibrates, niacin and bile acid binding resins.[6] Fenofibrate increases plasma HDL levels by stimulating their synthesis. Increased transport (turnover) of HDL induced by fenofibrate may be significant in increasing tissue cholesterol removal in hyperlipidemic patients.[7] Furthermore Fibrates treatment results in the formation of LDL with a higher affinity for the LDL receptor, which are thus catabolized more rapidly.[8] Nigella sativa or kalonji

contains conjugated linoleic acid, thymoquinone, melanthin, nigilline,damascenine, and trans-anethole. Thymoquinone (TQ) extracted from Nigella sativa (kalonji) inhibits iron-dependent microsomal lipid peroxidation[9]. Stimulation of polymorphonuclear leukocytes with thymoquinone works as protector against damaging effects of free redicles generated biochemically in human body[10]. The black seed of Nigella sativa (NS), has been used traditionally for centuries in the Middle East, northern Africa, the Far East, and Asia for the treatment of hyperlipidemia[11]. NS contains >30% of a fixed oil and 0.40–0.45% (w/w) of a volatile oil[12]. The volatile oil has been shown to contain 18.4–24% thymoquinone (TQ) and 46% monoterpenes such as p-cymene and α-piene[13-14].

METHOD

This research was single blind placebo-controlled, and was conducted at National Hospital, Lahore from February 2018 to July 2018. Seventy five hyperlipidemic patients were selected for research work. Written consent was taken from all patients. Specific Performa was designed for the research work. Seventy five newly diagnosed primary hyperlipidemic patients were selected with age range from 18 to 70 years. Exclusion criteria were hypothyroidism, diabetes mellitus, alcohol addictive patients, peptic ulcer, any gastrointestinal upset, renal impairment, and any hepatic or cardiac problem. All patients were divided in three groups (group-A, group-B, group-C), 25 in each group. Their baseline experimental data was taken and filed in specifically designed Performa, at start of taking medicine, like lipid profile, blood pressure and pulse rate. The study period was eight weeks. Twenty five patients of group-A were advised to take one tea spoon of Nigella sativa, twice daily, i.e.; one tea spoon after breakfast and one tea spoon after dinner. Twenty five patients of group-B were advised to take Fenofibrate 40 mg tablets, one after breakfast and one after dinner. Twenty five patients were provided placebo capsules, (containing grinded wheat), taking one capsule after breakfast and another before going to bed. All participants were advised to take these medicines for eight weeks. They were also advised for 20 minutes brisk walk at morning or evening time. 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[7] (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. A probability value of <0.05 was considered as non-significancant and P<0.001 was considered as highly significant.

RESULTS

When results were compiled and statistically analyzed, it was observed that Nigella sativa and Fenofibrate 40 mg decreased LDL-cholesterol significantly. Nigella sativa decreased LDL cholesterol from 191.14±3.45 mg/dl to 159.40±2.98 mg/dl. This change in mean values was 31.7 mg/dl with highly significant p-value of <0.001. Fenofibrate decreased LDL cholesterol from 197.77±3.91 mg/dl to 159.62±2.20 mg/dl. In mean values this change was 38.2 mg/dl with highly significant p-value of <0.001. Placebo group showed LDL cholesterol reduction from 163.10±1.45 mg/dl to 159.40±1.77 mg/dl. This change in mean values was 3.7 mg/dl, with non-significant p-value of >0.05.

Table illustrating LDL-cholesterol values before and after treatment with Nigella sativa, Fenofibrate 40 mg and placebo with their p-values

Drug	At day-0	At day-60	Change in mg/dl	p-values
NS group	191.14±3.45	159.40±2.98	31.7	<0.001
Allopathic group	197.77±3.91	159.62±2.20	38.2	<0.001
Placebo group	163.10±1.45	159.40±1.77	3.7	>0.05

KEY; All parameters are measured in mg/dl, P-value <0.01 stands for significant change, P-value >0.05 stands for non-significant change.

DISCUSSION

Coronary heart disease can't be cured but treatment can help manage the symptoms and reduce the chances of problems such as heart attacks. Treatment can include: lifestyle changes, such as regular exercise and stopping smoking, medication, angioplasty - using balloons and stents to treat narrow heart arteries, and surgery. The development of laboratory tests able to identify patients at higher risk of developing CAD is of concern to many researchers and the object of many studies. With base on this type of study it is possible to judge the usefulness of determining a certain parameter in the laboratory to prevent the disease, establish its extent or monitor the efficacy of the treatment adopted. In this study we have compared LDL cholesterol lowering effects of traditional drug Fenofibrate with medicinal herb Nigella sativa. Nigella sativa when used by 25 hyperlipidemic patients for two months, it reduced LDL cholesterol 31.7 mg/dl. Statistically this change is highly significant. Our results match with results of study conducted by Summat BS et al [15] who proved 28.99 mg/dl reduction in LDL cholesterol in 45 hyperlipidemic patients. Their results support our study results. Change in LDL cholesterol in our results are in contrast with results of study conducted by Malaq FG et al[16] who proved much less reduction in LDL cholesterol when Nigella sativa was used in 100 hyperlipidemic patients for one month. Reason for this contrast may be due to their large sample size and less exposure of patients to take Nigella sativa for only four weeks. They have also explained mechanism of action of Nigella sativa that how these agents act as antioxidant. Nigella Sativa oil with its potent free radical scavenging properties, inhibits subarachnoid-haemorrhage-(SAH-) induced lipid peroxidation of the brain tissue against the reactive hydroxyl, peroxyl, and superoxide radicals. This mechanism is also quoted by JH Gurfatv et al[17] In our study fenofibrate decreased LDL cholesterol 38.2 mg/dl which is highly significant change when analyzed statistically. These results match with results of study conducted by Sangatt U et al[18] who observed LDL reduction by 40 mg of Fenofibrate used by 10 patients for 2 weeks. Their results support our results. They explained five mechanisms that how Fibrates make plasma cholesterol levels at normal range. No:1, By induction of lipoprotein lipolysis 2. By induction of hepatic fatty acid (FA) uptake and reduction of hepatic triglyceride production. 3. by increased removal of LDL particles. 4. By reduction in neutral lipid (cholesteryl ester and triglyceride) exchange between VLDL and HDL may result from decreased plasma levels of triglyceride rich lipoproteins (TRL). 5. By increase in HDL production and stimulation of reverse cholesterol transport. Our results do not match with results of study conducted by Beghana JJ et al [19] who proved that LDL reduction by fenofibrate is not significant if used even for three months. Reason for this contrast may be due to lesser dose of Fenofibrate ie; 20 mg once daily for three months. In their results LDL cholesterol reduction was only 18.53 mg/dl. Research conducted by Turtesov T et al[20] stated that Fenofibrate enhances lipolysis and causes elimination of TG-rich lipoproteins from systemic circulation. This mechanism is due to activation of lipoprotein lipase. Jatoi KA et al[21], Mastoi SM et al[22] stated that Fenofibrates also synthesis of apoprotein C-III which is responsible for inhibition of lipoprotein lipase activity. The underlying mechanisms in CAD vary depending on the disease in question. Coronary artery disease, stroke, and peripheral artery disease involve atherosclerosis. This may be caused by high blood pressure, smoking, diabetes, lack of exercise, obesity, high blood cholesterol, poor diet, and excessive alcohol consumption, among others[23]. High blood pressure results in 13% of CVD deaths, while tobacco results in 9%, diabetes 6%, lack of exercise 6% and obesity 5%.Rheumatic heart disease may follow untreated strep throat[24]. It is estimated that 90% of CVD is preventable. Prevention of atherosclerosis involves improving risk factors through: healthy eating, exercise, avoidance of tobacco smoke and limiting alcohol intake[25]. Treating risk factors, such as high blood pressure, blood lipids and diabetes is also beneficial. Treating people who have strep throat with antibiotics can decrease the risk of rheumatic heart disease. The effect of the use of aspirin in people who are otherwise healthy is of unclear benefit[26].

ACKNOWLEDGMENT:

We acknowledge management of National Hospital Lahore, Jinnah Hospital Lahore, Shoukat khanam Hospital Lahore, and Chughtai Lab Lahore for their cooperation in all fields of our research work.

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4/2/2022