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COMPARISON OF LIPID LOWERING EFFECTS OF NIGELLA SATIVA AND GEMFIBROZIL

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ABSTRACT
Increased amount of body fats, hypertension and diabetes mellitus are major problems for clinicians and researchers due to remarkable morbidity and mortality rates in human beings all over the world. There are many drug groups to lower body fats, like statins, Fibrates, niacin, resins, frequently used in allopathy. New dimensions are being explored by researchers for treating many diseases by herbal medicine. We have tried to compare effects of conventional allotherapeutics with herbal therapy by using Fibrates and Nigella sativa in hyperlipidemic patients. It was single blind placebo-controlled study, conducted at Jinnah Hospital Lahore, Pakistan. Seventy five hyperlipidemic patients were enrolled and divided in three groups, 25 patients in each group. One group was on placebo as control and another group was on Nigella sativa two spoons daily for six months. Twenty five patients were on Gemfibrozil 600 mg twice daily for six months. When results compiled and analyzed statistically by using paired "t" test, change in all major parameters of lipid profile were highly significant with probability value < 0.001. We concluded from this research work that Nigella sativa is more effective than allotherapeutics drug Gemfibrozil in hyperlipidemia.

Key words: lipids, low density lipoprotein, high density lipoprotein, Nigella sativa, Fibrates.

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INTRODUCTION

In the context of coronary artery disease (CAD) and in particular atherosclerosis, blood lipids and total cholesterol and LDL cholesterol in particular, have over the years achieved a near dominant position, and what was merely a hypothesis has progressed to a universally accepted truth on a par with the laws of Newton or thermodynamics. A corollary to this hypothesis is that LDL levels are directly related to the risk of atherosclerosis and its

progression.[1-5]One of several factors linked with increased risk of heart disease is high blood levels of cholesterol, a fatty substance which forms part of a biological group called sterols.[6,7]Apart from handling risk factors for coronary heart disease, drug treatment is important part of managing the disease. statins, fibrates, bile acid binding resins and nicotinic acid are approved and specific drugs to lower various types of serum lipids, which are root causes of developing CHD. It has been known for several years that fibrates induce peroxisome proliferation in rodents. This process is linked to the induction of transcription of genes involved in peroxisomal ß-oxidation and is mediated by specific transcription factors, therefore termed peroxisome proliferator-activated receptors (PPARs).[8]The hypotriglyceridemic action of fibrates involves combined effects on LPL and apoC-III expression, resulting in increased lipolysis. The induction of LPL expression occurs at the transcriptional level and is mediated by PPAR. The latter binds to a PPRE that is present both in the human and the mouse LPL gene promoters.[9-13] In contrast to LPL, transcription of the apoC-III gene is inhibited by fibrates, resulting in decreased production of apoC-III in the liver. The repression of apoC-III gene expression by fibrates is mediated via PPAR-α. Consistent with the repression of apoC-III expression, turnover studies in humans indicate that fibrates reduce apoC-III synthesis, leading to enhanced LPL-mediated catabolism of VLDL particles. Moreover, fibrates also decrease apoB and VLDL production. As a consequence, a reduced secretion of VLDL particles, together with the enhanced catabolism of triglyceride-rich particles, most likely accounts for the hypolipidemic effect of fibrates.[14]Nigella sativa seeds are the common drug used in Ayurvedic system of medicine throughout the world. In a clinical trial planned to evaluate the hypercholesterolemic activity of the Baraka oil (kalonji oil) in hypercholesterolemic patients.[15-17]Nigella sativa is a pretty herb, seeds of which are commonly known as kalonji.[7] Its chemical composition is moisture 7.43%, ash 4.14%, fixed oil 37%, volatile oil 1.64%, albumin 8.2%, mucilage1.9%, organic acid precipitated by copper 0.38%,metarabin 1.36%, melanthin 1.4%, cellulose 8.32%, sugar 2.75%, arabic acid 3.41% and other substances dissolved by soda 9.38%.[18]The scientific community has been well aware about hypolipidemic effects of Nigella Sativa and clinics around the world have done extensive studies on both humans and animals including gall bladder, bile and liver functions since these are all part of the cholesterol metabolism. The major mechanism this seems to be effective is simply by preventing the dietary cholesterol from being absorbed in the intestines where fat is digested. Another way this seems to work is by increasing the flow of bile acids, which binds the cholesterol in the digestive track and excretes it in the feces.[19] Kalonji is an easily available and acceptable remedy to treat dyslipidemia and at a low cost. It contains Beta-sisterol which reduces cholesterol levels.[20]

MATERIAL & METHOD

The research work was conducted at Jinnah Hospital, Lahore from February 2011 to July 2011. Seventy five hyperlipidemic patients were enrolled for research work titled “Comparison of hypolipidemic effects of Nigella Sativa (Kalonji) and Fibrates”. Well explained written consent was taken from all patients and approved from ETHICAL COMMITTEE FOR HUMAN RESEARCH, JINNAH HOSPITAL, LAHORE. Specific Performa was designed for the research work. Biological, ethical and legislative vital data like name, age, gender, occupation, residential address, phone/contact number, previous medical history, any genetic variation/disease in family history, drugs taken recently, drug/substance addiction history. 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

Kalonji, 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 Gemfibrozil 600 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[21] (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 change in the results when pre and post-treatment values were compared.

RESULTS

When results compiled and statistically analyzed by using SPSS it was observed that Nigella sativa reduced serum total cholesterol from 231.21±1.12 mg/dl to 200.90±3.11 mg/dl, in eight weeks. This change is significant statistically (P < 0.01). Triglycerides reduced from 178.90±3.11 to 141.10±1.09 mg/dl, LDL-cholesterol reduced from 191.14±3.45 to 159.40±2.99 mg/dl. These changes are highly significant statistically (P < 0.001). High density lipoprotein cholesterol (HDL-C) increased from 36.48±2.11 to 41.17±1.88 mg/dl, which is highly significant change (P-value < 0.001). When changes in drug and placebo-controlled groups compared, in percentage, the difference was -14.81 %, -9.90 %, and -16.78 %, in serum total cholesterol, triglycerides, and LDL-cholesterol respectively. In HDL-cholesterol it was +21.42 %. Mean baseline value of serum total cholesterol in 25 hyperlipidemic patients of fibrate group was 240.92±2.21 mg/dl. It reduced to 197.31±1.00 mg/dl in eight weeks, which is highly significant change statistically (P <0.001). Triglycerides and LDL-cholesterol in this group reduced from 204.31±1.26, and 197.77±3.91 mg/dl to 170.14±2.93 and 159.62±2.20 mg/dl respectively. These changes are highly significant statistically (P <0.001). HDL-cholesterol in this group increased from 32.97±3.10 to 40.45±2.22 mg/dl, which is also highly significant change (P <0.001). In percentage, difference in change as compared to placebo group was -20.42 % in serum total cholesterol, -23.07 % in triglycerides, and -27.10 % in LDL-cholesterol. HDL-cholesterol increased 17.91 %, when compared with placebo group. Change in all parameters in both groups are shown in table # 1.

TABLE # 1, showing mean and ± standard error of mean values of two groups before and after treatment, their P-value and their percentage comparison with control group

Lipid parameter & patient group	Baseline value	Value after 8 weeks	P-value	Difference b/w drug & placebo/control group
T-C (gp-A)	231.21±1.12	200.90±3.11	< 0.01	-14.81 %
TG (gp-A)	178.90±3.01	141.10±1.01	< 0.001	-9.90 %
LDL-C (gp-A)	191.14±3.45	159.40±2.98	< 0.001	-16.78 %
HDL-C (gp-A)	36.48±2.11	41.17±1.88	< 0.001	+21.42 %

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T-C (gp-B)	240.92±2.21	197.31±1.00	< 0.001	-20.42 %
TG (gp-B)	204.31±1.26	170.14±2.93	< 0.001	-23.07 %
LDL-C (gp-B)	197.77±3.91	159.62±2.20	< 0.001	-27.10 %
HDL-C (gp-B)	32.97±3.10	40.45±2.22	< 0.001	+17.91 %

KEY: All values are measured in mg/dl. gp-A stands for group-A (NIGELLA SATIVA GROUP) and gp-B stands for group-B (FIBRATE GROUP). T-C= serum total cholesterol, TG= serum triglycerides, LDL-C= low density lipoprotein cholesterol, HDL-C= high density lipoprotein cholesterol, gp stands for group, all parameters are measured in mg/dl, P-value <0.01 stands for significant change, P-value <0.001 stands for highly significant change. All values are mean and ± stands for standard error of mean.

DISCUSSION

Cholesterol is a waxy, fatlike substance that the body needs to function normally. Cholesterol is naturally present in cell membranes everywhere in the body, including the brain, nerves, muscles, skin, liver, intestines, and heart. Several drugs and diseases can bring about serum high cholesterol, but for most people, a high-fat diet, obesity, a sedentary lifestyle, smoking, excessive alcohol consumption, or inherited risk factors are the main causes. If a person has too much cholesterol in their bloodstream, the excess may be deposited in arteries, which leads to atherosclerosis (commonly called hardening of the arteries), ultimately to develop coronary heart disease (CHD). In this research we compared lipid lowering effects of Nigella sativa and Fibrates, when used in 25 hyperlipidemic patients for eight weeks. Changes in all parameters of lipid profile (i.e.; serum cholesterol, triglycerides, LDL-cholesterol and HDL-cholesterol) were highly significant in two drug groups when they compared with placebo-controlled group, except change in serum total cholesterol in Nigella sativa group, which is significant with probability value <0.01. Our results regarding lipid lowering effects of Nigella sativa match with results of research work conducted by Hossein H et al[22] match with research study conducted by , who did see reduction of serum total cholesterol 13.01 %, triglycerides 9.1 % and 17.89 %. HDL-cholesterol increased 23.62 %. Ghoneim MT et al[23] proved highly significant changes in lipid parameters of hyperlipidemic rats when they used one teaspoon of Nigella sativa oil twice daily for 3 weeks. These results match with results of our work. Rahman A et al[24] conducted research on hyperlipidemic patients and proved 12.76, 8 % , 15 % decrese in serum cholesterol, triglycerides, and LDL-cholesterol in 19 days when they used kalongi oil. They have explained marked protective action of Nigella sativa against ischemic reperfusion-induced gastric mucosal lesions, an effect that was mediated by suppression in the level of lipid peroxide and lactic dehydrogenase and an increase in those in glutathione and superoxide dismutase. The results of research work conducted by Burits M and Mand Bucar F[25] do not match with our results who observed 10.11 %, 12.51 %, 12.45 % reduction in total cholesterol, triglycerides, and LDL-cholesterol when they used kalongi oil for two months in hyperlipidemic patients. This difference in results may be guessed due to large difference in sample size of tested group individuals. Keech AC et al[26] observed much higher quantity of reduction in LDL-Cholesterol (-30.11 %) when they used two spoons of Nigella sativa in 1000 hyperlipidemic patients for the period of 6 months. This difference is surely due to large sample size in their study and duration of research study. Our results are in contrast with research work results of Rajmani K et al[27] who observed(10 %) increase in HDL-cholesterol with use of Kalonji for 3 weeks in 39 hyperlipidemic patients.

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