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The Effects of *Nigella sativa* (Kalonji) on Lipid Profile in Patients with Stable Coronary Artery Disease in Multan, Pakistan

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Abstract: The present study has been carried out to determine the effects of *Nigella saitva* on the lipid profile in cardiac patients visited at Ch. Pervaiz Elahi Institute of Cardiology, Multan. The age of the subjects was 26-69 years. The eighty subjects were divided into two groups (interventional and non-interventional) through random stratification (n = 40/group) by weight. The interventional group given *Nigella sativa* and statin, non-interventional group given statin daily. Both groups were advised to take the recomended doses regularly for a period of six months and the patients were on usual care. Fasting blood samples were taken before and after two and six month's treatment. In interventional group, cholesterol decreased by (-14.58%), LDL (-23.00%), VLDL (-15.16%) and triglycerides (-15.16%) significantly ($p<0.05$) after the treatment, whereas there was significant increase ($p<0.05$) in HDL cholesterol (3.18%) after six months. In non-interventional group the cholesterol decreased by (+1.17%), LDL (-4.13%), VLDL (-3.10%) and triglycerides (-2.12%) non significantly ($p>0.05$) after the treatment, whereas there was significant increase ($p<0.05$) in HDL (+5.87) after six months. In conclusion, the *Nigella sativa* is effective to change the lipid profile significantly in a way which is beneficial to heart.

Key words: *Nigella sativa*, statin, LDL, VLDL, HDL, cholesterol

INTRODUCTION

Coronary heart disease is a major cause of mortality and morbidity, both in developed and developing countries. It accounts for approximately one-third and one-quarter of all deaths among men and women, respectively (Sacks *et al*., 1996). Increased level of blood cholesterol, low density lipoprotein, triglycerides, smoking and raised blood pressure is established as major modifiable risk factors for coronary heart disease (Stamler *et al*., 1986).

Herbal remedies have been in use by people as a medicine or treatment that relieves or is intended to relieve a disease or disorder. *Nigella* (Kalonji) (*Nigella sativa* L.) belonging to the buttercup family Ranunculaceae, is commonly known as black seeds. *Nigella* seeds have many pharmaceutical uses. The seeds have occupied special place for their medicinal value for centuries in the Middle East and Southeast Asia (Gilani *et al*., 2004). They have been traditionally used in the treatment of a number of ailments including respiratory health, stomach and intestinal health, kidney, hypertension, bladder and liver function, circulatory and immune system support and for general overall well-being (Baser *et al*., 1986; Handa, 1998; Deliorman *et al*., 2002; Malhotra, 2006). Numerous traditional applications of *Nigella* seeds recorded as medicinal and pharmacological activities (Gilani *et al*., 2004; Ramadan, 2007).

N. sativa has been shown to produce multi-systemic beneficial actions (Ali and Blunden, 2003), including hypoglycemic (Bamosa *et al*., 1997), hypocholestermic (Bamosa *et al*., 2002) and antioxidant (Kanter *et al*., 2003) effects. There is some controversy about the cardiovascular actions of *Nigella sativa* or its active ingredients as some investigators reported no effect on blood pressure levels in animals (Mahfouz and El-Dakhakhny, 1960) or humans (Toppozada *et al*., 1965) whereas others reported a dose-dependent decrease in the arterial blood pressure and heart rate in normal (Tahir *et al*., 1993) or spontaneously hypertensive rats (Zaoui *et al*., 2000) respectively. In addition, it has been reported that the seeds with bee honey have protective effects on hepatotoxicity and on the oxidative stress and carcinogenesis (Al-Elyani, 2008). A mixture of seed oil with bee wax can be used for burns, skin infections, moisturizers, joint pain reliever, or an antiwrinkle agent (Ramadan, 2007).

However, with the advent of the pharmaceutical industry early in this century, the popularity of traditional/herbal medicine declined, in spite of the fact that twenty five percent of all prescription drugs still contain ingredients isolated from plants. The resources now do exist which can help and assist for greater understanding of the ways in which herbs can facilitate health and restore balance in disease (Murray, 1995).

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Recent evidence suggests that lipid-lowering therapy reduces cardiovascular morbidity and mortality and causes regression of coronary atherosclerosis (Ridker *et al*., 2008). Serial studies using Intravascular Ultrasound (IVUS) show that regression of coronary atherosclerosis induced by intensive statin therapy is related to the large reduction in low-density lipoprotein cholesterol (Okazaki *et al*., 2004). The benefits of intensive statin therapy may also be due to increased high density lipoprotein cholesterol (Nicholls *et al*., 2007).

The literature shows many previous studies evaluating the *Nigella sativa* possessing a hypoglycemic activity (Lamba *et al*., 2000; Ali *et al*., 2003; El-Saleh *et al*., 2004; Le *et al*., 2004; Dahri, 1996; Qidwai *et al*., 2009). There for this study was carried out to investigate the effect of oral administration of *Nigella sativa* along with statin on serum lipid profile levels in cardiac patients.

MATERIALS AND METHODS

The present study was designed to determine the effects of the *Nigella sativa* seed on lipid profile in patients with stable coronary artery disease, at Ch. Pervaiz Elahi Institute of Cardiology, Multan.

***Nigella sativa* seed:** *N. sativa* seeds of indigenous variety were obtained from a local herbal market Multan, (Pakistan). *N. sativa* seeds were authenticated by Institute of Pure and Applied Biology, (Botany and Pharmacy Division) Faculty of Science, Bahauddin Zakariya University, Multan, Pakistan. Then the seeds were washed, dried and crushed to a powder with an electric microniser. Five hundred milli gram capsules were made by this powder.

Eighty patients of both gender 26-69 years of age with stable coronary artery disease were selected. Data was recorded on a prescribed performa to take information about their age, sex, marital status, tobacco use, family history of heart disease and known history of hypertension, hyperlipidemia and diabetes. Patients were equally divided into two groups, interventional group and non-interventional group. All the patients in interventional group consumed *Nigella sativa* seed powder 500 mg/daily along with statin (10-20 mg) for 180 days. Patients in non-interventional group were taken statin 10-20 mg/daily.

Three fasting blood samples were collected from every subject of each group; the first sample reading was extracted before taking the dose (base line). The second and third sample readings were recorded after taking dose, after two and six months, respectively. After collecting base line lipid profile data, a dose of one month *Nigella sativa* capsules (30 capsules) was given to patients in interventional group along with usual care and were asked to use capsules regularly and take their next dose every month at their visit.

In the mean while patients were inquired fortnightly about their health and of using capsules on daily bases through telecommunication. After the end of one month patients were asked about their body response if any, after using capsules and then next dose was given to them. After two and six months the fasting venous blood samples of two groups were collected for lipid profile test in the same procedure as mentioned above and data was recorded on Performa.

Blood sample: The cardiac patients of both the interventional and non-interventional group were sampled for blood after at least 12 h fast. The blood samples of both groups were subjected for estimation of total cholesterol, triglycerides, HDL and LDL and VLDL using commercial kits (Roche, Germany).

Statistical analysis: The results of the various parameters were analysed by statistical methods. Standard descriptive statistics were used for the calculation using the statistical package of Microsoft Excel. The results were expressed as Percentages and Mean ± SEM. The comparisons of different types of means were made by paired t-test. $P<0.05$ was taken as statistical significance.

RESULTS

The results of the present study showed that lipid profile in the interventional group is shown in Table 1. The Mean±SEM values, at base line, for cholesterol were 190.92±6.63 mg/dl, for LDL, 113.08±5.77 mg/dl, for HDL, 40.85±0.78 mg/dl, for VLDL, 39.20±2.65 mg/dl, for Triglycerides it was 195.77±13.08 mg/dl and after two months, these values for cholesterol, LDL, HDL, VLDL and Triglycerides were 172.15±5.68 mg/dl, 96.08±4.90 mg/dl, 40.8±0.76 mg/dl, 34.78±2.49 mg/dl and 176.08±12.43 mg/dl respectively and after six months, the Mean±SEM values for cholesterol, LDL, HDL, VLDL and Triglycerides were 163.08±5.32 mg/dl, 86.72±5.25 mg/dl, 42.15±0.93 mg/dl, 33.02±2.09 mg/dl and 166.08±10.24 mg/dl respectively. The comparison of Mean±SEM values for cholesterol, LDL, HDL, VLDL and Triglycerides, showed that HDL increased ($p<0.05$) significantly after six months, whereas cholesterol, LDL, VLDL and Triglycerides decreased significantly ($p<0.05$) after treatment. Table 2 represents the lipid profile of non-interventional group. The Mean±SEM values at base line for cholesterol were, 173.77±6.75 mg/dl, for LDL, 105.37±7.43 mg/dl, for HDL, 39.67±0.75 mg/dl, for VLDL, 32.25±2.04 mg/dl and for Triglycerides it was 160.75±9.88 mg/dl and after two months, these values for cholesterol, LDL, HDL, VLDL and Triglycerides were, 173.97±6.32 mg/dl, 100.75±5.92 mg/dl, 40.62±0.75 mg/dl, 31.47±1.64 mg/dl and 158.75±7.92 mg/dl respectively and after six months the Mean±SEM values for cholesterol, LDL, HDL, VLDL and Triglycerides were

Table 1: Mean±SEM of lipid profile in interventional group given *Nigella sativa* and statin

Parameters	Base line	After two months	After six months
Cholesterol (mg/dl)	190.92±6.63[a]	172.15±5.68[b]	163.08±5.32[c]
LDL (mg/dl)	113.08±5.77[a]	96.08±4.90[b]	86.72±5.25[c]
HDL (mg/dl)	40.85±0.78[a]	40.8±0.76[a]	42.15±0.93[b]
VLDL (mg/dl)	39.20±2.65[a]	34.78±2.49[b]	33.02±2.09[b]
Triglycerides (mg/dl)	195.77±13.08[a]	176.08±12.43[b]	166.08±10.24[b]

Values within rows with different superscripts differ significantly ($p<0.05$)

Table 2: Mean±SEM of lipid profile in non-interventional group, given statin for 6 months

Parameters	Base line	After two months	After six months
Cholesterol (mg/dl)	173.77±6.75	173.97±6.32	175.80±7.02
LDL (mg/dl)	105.37±7.43	100.75±5.92	101.02±6.46
HDL (mg/dl)	39.67±0.75[a]	40.62±0.75[a]	42.00±0.82[b]
VLDL (mg/dl)	32.25±2.04	31.47±1.64	31.25±1.39
Triglycerides (mg/dl)	160.75±9.88	158.75±7.92	157.35±6.99

Values within rows with different superscripts differ significantly ($p<0.05$)

Table 3: Comparison of Mean±SEM of lipid profile b/w intervention and non-interventional group after 6 months

Parameters	Interventional group	Non-interventional group
Cholesterol (mg/dl)	163.08±5.32	175.80±7.02
LDL (mg/dl)	86.72±5.25	101.02±6.46
HDL (mg/dl)	42.15±0.93	42.00±0.82
VLDL (mg/dl)	33.02±2.09	31.25±1.39
Triglycerides (mg/dl)	166.08±10.24	157.35±6.99

Table 4: Percentage (%) changes of lipid profile after 6 months in interventional and non-interventional groups

Parameters	Interventional group (%)	Non-interventional group (%)
Cholesterol (mg/dl)	-14.58	+1.17
LDL (mg/dl)	-23.00	-4.13
HDL (mg/dl)	+3.18	+5.87
VLDL (mg/dl)	-15.16	-3.10
Triglycerides (mg/dl)	-15.16	-2.12

- = Decrease and + = increase

175.8±7.02 mg/dl, 101.02±6.46 mg/dl, 42±0.82 mg/dl, 31.25±1.39 mg/dl and 157.35±6.99 mg/dl respectively. The Mean±SEM values for HDL improved ($p<0.05$) significantly after six months, whereas there was no significant effect ($p>0.05$) on cholesterol, LDL, VLDL and Triglycerides.

The results of comparison of Mean±SEM of lipid profile between interventional group, cardiac patients given statin and *Nigella sativa* and non-interventional group cardiac patients given statin after six months are shown in Table 3. The Mean±SEM values for cholesterol, LDL, HDL, VLDL and Triglycerides after six months in non interventional group were 175.8±7.02 mg/dl, 101.02±6.46 mg/dl, 42±0.82 mg/dl, 31.25±1.39 mg/dl and 157.35±6.99 mg/dl respectively, whereas the values for cholesterol, LDL, HDL, VLDL and Triglycerides after six months in interventional group were 163.08±5.32 mg/dl, 86.72±5.25 mg/dl, 42.15±0.93 mg/dl, 33.02±2.09 mg/dl and 166.08±10.24 mg/dl respectively. This comparison of Mean±SEM values for cholesterol, LDL, HDL, VLDL and Triglycerides revealed there was no significant ($p>0.05$) effect on lipid profile after six months.

Table 4 presents percentage (%) changes of lipid profile after six months in interventional and non-interventional group In interventional group cholesterol, LDL, VLDL and Triglycerides decreased by 14.58, 23.00, 15.16 and 15.16% respectively whereas HDL was increased 3.18%. In non-interventional group cholesterol and HDL increased 1.17%, 5.87% respectively whereas LDL, VLDL and Triglycerides decreased by 4.13, 3.10 and 2.12% respectively.

DISCUSSION

The present study was carried out to determine the effects of *Nigella sativa* (black seed) on lipid profile in patients having stable coronary artery disease. The results of the present study revealed that in interventional group cholesterol decreased 14.58%, LDL 23%, triglycerides 15.16% and VLDL 15.16% whereas HDL increased 3.18% significantly ($P<0.05$) after six months. In non-interventional group LDL decreased 4.13%, triglycerides 2.12% and VLDL 3.10% whereas cholesterol and HDL increased 1.17%, 5.87% respectively. Bamosa *et al.* (1997) worked on the effects of oral ingestion of *Nigella sativa* seed on some blood parameters and reported a pattern of decreased levels of glucose and cholesterol (on days 7 and 14) on sixteen second year medical students, treated with 2 gram of *Nigella sativa* capsules twice daily. Nine students took 2 capsules of 500mg *Nigella sativa* twice daily and served as test group. Seven students served as controls and took 2 capsules of 500 mg brown sugar twice daily. In the test group, the parameters, which showed a significant decrease, were glucose ($P<0.05$) and cholesterol ($P=0.05$). However, both levels went up by the end of the treatment but remained below the base line. There was no significant decrease in triglycerides ($P>0.05$).

Tissera *et al.* (1997) reported the effective reduction of serum cholesterol by braka oil (Oil of *Nigella sativa*) in hypercholesterolemic patients. Seventeen hypercholesterolemic patients (40 y - 70 y age group) were included in the study. Patients were administered braka oil in the morning and evening for four weeks.

Before the trial period total cholesterol level in patients blood as 260.8 ± 43.69 mg/dl LDL cholesterol was 149.2 ± 56.03 mg/dl HDL cholesterol was 89.92 ± 27.86 mg/dl and serum Triglecerides was 114.59 ± 25.86 mgkdl. After the trial period total cholesterol level in patient's blood was 208.29 ± 33.05 mg/dl, LDL cholesterol was 118.11 ± 38.53 mg/dl, HDL cholesterol was 73.00 ± 21.84 mg/dl and serum Triglycerides was 102.75 ± 35.65 mg/dl. Total cholesterol fell by 20% to ($p<0.001$) 208.29 ± 73.00 mg/dl, LDL cholesterol levels were reduced to 118.11 ± 38.53 mg/dl, HDL cholesterol levels were reduced to 73.00 ± 21.84 mg/dl after the trial period.

Badary *et al.* (2000) observed the influence of Thymoquinoe (Active ingredient of *Nigella sativa* seeds) on Doxorubicin, which induces hyperlipidemic nephropathy in rats, results showed rats treated with Thymoquinone (10mg/kg/day) for five days scientifically had lowered serum urea, triglycerides and total cholesterol. Hypolipidemic activity of *Nigella sativa* was observed in a study conducted by El-Dakhakhani *et al.* (2000) he used 800 mg/kg *Nigella sativa* oil in rats orally for 4 weeks showing a significant decrease in serum total cholesterol, low density lipoprotein and triglycerides and an elevation of serum high density lipoprotein level. Zaoui *et al.* (2002) studied the effects of *Nigella sativa* fixed oil on blood homeostasis in rats. The effects of the fixed oil of *Nigella sativa* seeds in rats were investigated by monitoring blood homeostasis and body weight as well as toxicity. Animals were treated daily with an oral dose of 1 ml/kg body weight of the *Nigella sativa* seed fixed oil for 12 weeks. Changes in key hepatic enzymes levels were not observed in *Nigella sativa* treated rats after 12 weeks of treatment. The serum cholesterol and triglycerides decreased significantly by 15.5% and 22%. Similarly the effects of *Nigella sativa* seeds on the blood levels of cholesterol, triglycerides, HDL and LDL in white albino rats were studied by Ali *et al.* (2003) a total of 200 rats, 150 experimental and 50 controlled were included in the study. Six doses of *Nigella sativa* were used (50, 100, 200, 300, 400 and 500 mg/day/200g rat). Each dose was given for five durations: 1, 4, 7, 10, and 14 days. Generally all doses of *Nigella sativa* produced significant reduction in the blood level of all parameters studied. There was no linear dose or time dependent effect of *Nigella sativa* on these parameters. The effect of *Nigella sativa* started after 4 days and continued with some swings, for the rest of the duration. The effective dose of *Nigella sativa* seemed to lie between 100-400mg.

Le *et al.* (2004) observed the effects of petroleum ether extract of *Nigella sativa* exert lipid lowering and insulin sensitizing action in rats. At the end of four weeks of treatment *Nigella sativa* treated rats had lowered TGs and higher HDL cholesterol.

A significant activity of *Nigella sativa* in dyslipidemic patients as an add-on therapy was observed by Najmi *et al.* (2008) They worked on the effect of *Nigella sativa* on various clinical and biochemical parameters. The patients were divided into two groups of 30 each. In group I (the standard group), patients were advised tablet atorvastatin 10 mg once a day and tablet metformin 500 mg twice a day for a period of 6 weeks. In group II (the *N. sativa* group), the patients were advised tablet atorvastatin 10 mg once a day, tablet metformin 500 mg twice a day, and *N. sativa* oil 2.5 ml twice daily for a period of 6 weeks. The treatment group showed significant ($P < 0.05$) improvement with reference to total cholesterol, low density lipoprotein cholesterol (LDL-C). Qidwai *et al.* (2009) observed the effectiveness of *Nigella sativa* in dyslipidemia at Agha Khan University In this study one hundred and twenty-three (123) patients were recruited. Half of the respondents received powdered *Nigella sativa* (Kalonji) seed in capsule and the rest received a placebo. Favorable impact of powdered *N. sativa* (Kalonji) seed in capsule was noted on almost all variables, but results were not statistically significant because of small sample size.

Results of the present study are in agreement with results of the studies conducted by Tissera *et al.*, 1997; El-Dakhakhani *et al.*, 2000; Zaoui *et al.*, 2002; Ali *et al.*, 2003; Badary *et al.*, 2003; Le *et al.*, 2004; Najmi *et al.* 2008.

The exact mechanism of action of *Nigella sativa* is not known, however, It has been proved that volatile oil of *Nigella sativa* has two main constituents i.e. Nigellone and thymoquinone which play a key role in heart disease prevention (Gad *et al.*, 1963; Babayan *et al.*, 1978; Abdel-Aal and Attia, 1993). According to Feldman (2001) antioxidants (e.g., vitamins E and C) may lessen the risk of CVD by decreasing oxidized LDL, which is more atherogenic. High blood levels of the amino acid homocysteine (Hcy) are associated with increased atherosclerosis. Active antioxidant components thymoquinone of the traditionally used black seeds of *Nigella sativa* plant protect against the HHcy and its associated state of oxidative stress (El-Saleh *et al.*, 2004). Thymoquinone (TQ) and *ter*-butylhydroquinone (TBHQ) of *Nigella sativa* have strong antioxidant potentials through scavenging ability of different free radicals. Moreover, the data shows that TQ is acting mainly as a potent superoxide anion scavenger (Badary *et al.*, 2003.

Increased levels of LDL are also linked with cardiovascular disease; more specifically, it has been reported that oxidation of LDL particles is likely a key step in the development of atherosclerotic plaques (Luc and Fruchart., 1991). *Nigella sativa* increase bile excretion, which was stimulus, to plan this study to see the effect of *Nigella sativa* on serum cholesterol of albino rats, for El-Dakhakany. The carbonyl fraction of the seed extract has got excellent choleretic activity as shown by El-Dakhakhani (1982). Enhanced expression and activation of LDL-R may cause a rapid clearance of LDL-

C from circulatory lipids pool producing hypercholesterolemia thus reducing the chances of potential atherogenesity (Grundy, 1989). Thus the choleretic characteristics of *Nigella sativa* may effect the body total lipid concentration and help prevent atherosclerosis. It has been observed that *Nigella sativa* is very useful in treatment of thrombosis due to its lipid reducing, blood diluting and anti-oxidant property.

In conclusion the results of the present study show that there is a significant ($P<0.05$) decrease in cholesterol, LDL, VLDL and triglycerides, and significant increase of HDL in interventional group as compared to non interventional group. The *Nigella sativa* has ability to reduce lipid profile which is a major risk factor for coronary artery disease in cardiac patients.

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