



Thymoquinone, Lipids and Herbal Medication

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Received: 📅 January 25, 2020

Published: 📅 February 11, 2020

Abstract

Allopathic drugs used as hypolipidemic agents have number of unwanted effects. Herbal therapy for Hyperlipidemia is getting attention due to their less frequent side effects. 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. Consent was taken from all enrolled participants and were divided in three equal numbers i.e. twenty-five 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 25 patients who were on *Nigella sativa*, their LDL cholesterol decreased from 191.14±3.45 to 159.40±2.98 mg/dl. 31.7 mg/dl LDL reduction was observed when compared with placebo group. In 25 patients who were on Fenofibrate 40 mg, their LDL cholesterol decreased from 197.77±3.91 mg/dl to 159.62±2.20 mg/dl. LDL reduction in this group was 38.2 mg/dl. These changes are highly significant with p-values of <0.001. We concluded from this study that hypolipidemic characteristic of *Nigella sativa* is comparable and therapeutically as effective as traditionally used hypolipidemic medication Fenofibrate.

Introduction

In human body free radicals are formed in consequence of various metabolic processes. If there is abundance of low-density lipoprotein particles in plasma, there are chances of risk to develop CAD (coronary artery disease) when free radicals interact with LDL particles. CAD may lead to morbidity and mortality due to cardiac arrest in human population [1-3]. In some cases, atherosclerotic plaques may totally block the blood supply to the myocytes, causing cardiac attack [4]. Atherosclerotic plaque contains calcium, cholesterol, free fatty acids, and macrophages in variable amount. These plaques are of two types i.e. hard and soft. Soft plaques are more vulnerable than hard and can rupture easily as compared to hard one. There are risks for ischemic stroke too if blood supply to neurons ensues [5]. Hypolipidemic drugs can be used to prevent hyperlipidemia, CAD, heart arrhythmias and cardiac arrest. Allopathic drugs used to prevent, or cure Hyperlipidemia

include Statins, Fibrates, niacin and bile acid binding resins [6]. If Fenofibrate is used, there is increased synthesis of high-density lipoprotein particles in plasma. In patients suffering from hyperlipidemia, Fenofibrate enhances turnover of tissue cholesterol, thus reducing lipoprotein particles. Apoproteins in LDL are also changed by Fenofibrates leading to high affinity for the low-density lipoprotein receptors to LDL particles [7,8]. *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. Stimulation of polymorphonuclear leukocytes with thymoquinone works as protector against damaging effects of free radicals generated biochemically in human body [9,10]. Prehistorically *Nigella sativa* is being used to treat, inflammation, high plasma lipids, high blood pressure, asthma,

diabetes mellitus, arthritis, and gastrointestinal problems [11-14]. In this study we tried to compare hypolipidemic potential of *Nigella sativa* with Fenofibrate.

Patients & Method

Design of Research Work: It was single blind placebo-controlled study.

Venue: The research work was conducted at National Hospital Lahore, Pakistan from February to July 2015.

Sample Size and Inclusion Criteria: 75 hyperlipidemic patients were enrolled whose age range was from 18 to 70 years. Well explained, written consent was taken from all participants.

Exclusion Criteria: Hypothyroidism, peptic ulcer, diabetes mellitus type-I and type-2, any major cardiac, renal and hepatic illness.

Grouping and Methodology: Enrolled patients were divided in three equal numbers i.e. 25 patients in Group-1, 25 in Group-2, and 25 patients in Group-3. Baseline LDL -cholesterol of all patients was determined in Biochemistry laboratory of the hospital. Separate folder was designed for each enrolled patient, in which their personal data, medical history, laboratory reports, follow up visit proforma were kept. Their plasma LDL-cholesterol was calculated by Fried wald formula [7] ($LDL-C = Total\ cholesterol - (Triglycerides/5 + HDL-C)$). 25 patients of group-1 were advised to take eight grams of Kalonji (*Nigella sativa*) in two divided doses for two months. 25 patients of group-2 were advised to use 40 mg Fenofibrate tablets twice daily for two months. 25 patients of

group-3 were advised to take Capsule (Placebo capsule containing grinded wheat powder) twice daily for two months. They were advised to take their medication after breakfast and after dinner. All participants were convinced to go for 20 minutes brisk walk at morning or evening time. Fortnight follow up visit was arranged for all participants. After two months research period their lipid profile was determined in same laboratory of the hospital.

Statistical Analysis: Mean values of LDL-cholesterol \pm SEM were analysed statistically by using SPSS 2014 version. Paired t-test was applied to analyse pre-treatment and post treatment values. $p < 0.05$ was minimum probability value to determine statistical significance. $p < 0.05$ was considered as non-significant change in tested parameter. $p > 0.001$ was marked as highly significant change in the tested parameter.

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

Table 1: All Parameters are Measured in Mg/Dl, P-Value < 0.01 Stands for Significant Change, P-Value > 0.05 Stands for Non-Significant Change.

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

Abbreviations: NS: Stands for *Nigella Sativa*; FF: Stands for Fenofibrate; PL: Stands for Placebo Group.

Discussion

Normal plasma lipid levels are required to keep heart healthy. Statins, Fibrates, Bile Acid Binding Resins, and Niacin (Vitamin B3) are used as hypolipidemic medicines in allopathy, but all these have unwanted effects. In Ayurveda discipline of therapeutics, various herbs, fruits and vegetables are used to reduce bad-cholesterol (LDL-C) and to increase good-cholesterol (HDL-C). In various research study results Kalonji is labeled as hypolipidemic therapeutic agent but little research work is done on comparison of its hypolipidemic potential with allopathy related hypolipidemic medicines. This research was targeted to compare its hypolipidemic characteristics with one of the Fibrate i.e. Fenofibrate 40 mg. In our results it was observed that Kalonji or *Nigella sativa* reduced LDL-cholesterol 31.7 mg/dl which is almost 16.58 % reduction in the parameter. This change is highly significant ($p < 0.001$).

Same highly significant change ($p < 0.001$) was observed by using Fenofibrate 40 mg in 25 hyperlipidemic patients. Results of study conducted by Osenda M et al. [15] also support our observation and results. Fandelaki I et al. [16] observed that Kalonji increase HDL-cholesterol, and decrease LDL-cholesterol, triglycerides, and plasma total cholesterol in 4 weeks therapy if brisk walk is added with this medication. Alberti K et al. [17] stated that there are various mechanisms by which seeds of the herb decrease LDL-cholesterol and decrease triglycerides. Duverger A et al. [18] explained that NS inhibit enterohepatic circulation, leading to decreased synthesis of cholesterol by HMG-CoA reductase pathway. Harnandez M et al. [19] observed lesser hypolipidemic effects of Kalonji when used in 15 hyperlipidemic patients for two weeks. They recommended to use herb for prolonged time as lipoproteins and their structural apoproteins take time to be synthesized in hepatic cells. Harnandez M et al. [20] had explained that kalonji is useful for increasing HDL-

cholesterol. Haddad P et al. [21] wrote in their article that kalonji decrease plasma TG (triglycerides) rich lipoproteins (VLDL), thus neutral fat is reduced. Exchange of neutral fats between high density lipoproteins and very low-density lipoproteins in plasma occurs by use of Kalonji [22].

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DOI: 10.32474/TOOAJ.2020.02.000145



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