Efficacy of Roghan-e-Kalonji *(Nigella sativa oil)* in the Treatment of Primary Hyperlipidaemia

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Abstract

Hyperlipidaemia is an important factor for the development of atherosclerotic lesion which is responsible for various complications such as ischemic heart diseases, cerebrovascular diseases and hypertension etc. These complications are major cause of mortality and morbidity. The association of Hyperlipidaemia with development of atherosclerotic lesion has prompted the researchers of various field of medicine to develop safe and efficacious drug for the management of Hyperlipidaemia. Although, a number of plant origin hypolipidaemic drugs have been screened for hypolipidaemic activity but none of them offers convincing treatment. In Unani system Medicine a large number of drugs are reported to possess possible treatment for some metabolic diseases particularly obesity (*Saman-e-Mufrat*) and its related complications. Most of these drugs have not been subjected for evaluation on scientific parameters. Keeping these facts in mind, a single blind standard controlled non randomized trial was planned to evaluate the efficacy of a Roghane Kalonji (*Nigella sativa* oil) in the management of primary hyperlipidaemia.

The present study was conducted on 60 diagnosed patients of primary hyperlipidaemia at Ajmal Khan Tibbiya College Hospital, Aligarh Muslim University Aligarh. The patients were allocated in two groups. Group A (Test group) comprising of 40 patients and Group 'B' (Placebo group) comprising of 20 patients. In group 'A' the Roghane Kalonji in the dose of 6 ml twice a day was given whereas in group 'B' Atrovastatin in the dose of 10 mg once a day was administered for 3 months. The subjective and the objective parameters (lipid profile) were assessed on 0, 15th, 30th, 60th, 90th days. The test drug was found to be statistically significant in lowering serum cholesterol and serum triglyceride level in the patients of Hyperlipidaemia ($p<0.05$).

Keywords: Hyperlipidaemia, *Roghan-e-Kalonji*, Lipid profile.

Introduction

Hyperlipidaemia is a major public health problem worldwide. It accounts about 3.2 million visits to a doctor per year. It is characterized by an excess of fatty substances such as cholesterol, triglycerides and lipoproteins in the blood. It is an important risk factor for development of atherosclerosis and ischaemic heart diseases. More than half of the coronary heart diseases are attributed to the abnormalities in lipids and lipoproteins metabolism. It also reflects the adverse impact of the sedentary life style and dietary factors like dietary fat

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intake greater than 40% of the total calories, saturated fat intake greater than 10% of total calories. (Akbar *et al.*, 1930; Biff *et al.,* 2003; Fauci *et al.,*2008; Hongdao, 2006; Joshep, 2003; Jurjani, 1878; Khan *et al.,* 2002, Masson *et al.,* 2003; Rath *et al.,* 1991). In classical Unani text *Shaham* is broadly classified into two types *Samin* and *Riwaj*. It is essential for the nourishment of the body and essential for normal health. According to Unani concept, when the amount of lipid increase in the blood it leads to increased viscosity and stickiness (*ghilzat* and *Lazojat*) of blood that reduces lumen of vessels which results in *Tasallube Sharaeen*. (Maseehi, 1963; Ibne Sena, 1929; Razi, 1999).

As such, there is no direct reference to this disease per se, but hyperlipidemia is usually associated with obesity. The ancient Unani physicians like *Buqrat* (460 BC) and *Ibn-Sina* (980-1037 AD) have described *Saman-e-Mufarat* in their Lexicon. They have mentioned the etiological factors, symptoms complications like paralysis, constriction of vessels, coma and sudden death owing to obesity in their clinical observations. Due to the lack of diagnostic facilities and means of evaluation of lipids in blood, ancient Unani physicians may have considered obesity and hyperlipidaemia as one disease thus describing obesity as a whole not specifying excess of fat in blood (Al-Qamri Mansoori, 1255H; Aqsarai, 1907; Arzani, 1954; Baitar, 1999; Hussain, 1980; Ibnul-Qaf, 1986; Jalinoos, 1903; Majoosi, 1889; Mansoor Ibne Mohammad, 1989; Maseehi, 1963; Razi, 1999; Rushd, 1987; Ibne Sena, 1929).

The association of hyperlipidaemia with development of atherosclerotic lesion has prompted the researchers of various field of medicine to develop safe and efficacious drug for the management of Hyperlipidaemia. Although, a number of plant origin hypolipidaemic drugs have been screened for hypolipidaemic activity but, none of them offers convincing treatment. Even though, in mainstream Medicine Statin (HMG-co Reductase inhibitor) is being used but long term administration is associated with several side effects. (Lazar *et al.,* 2011; Siig *et al.,* 2004; Ziajka, 1998) Therefore, search of safe and effective drug is imperative. In Unani system medicine a large number of drugs are reported to be used for the treatment of obesity (*Saman-e- Mufrat)* and its related complications. Such as *Zanjbeel,* (Rafiquddin, 1985), Muqil (Anonymous, 2001; Tripathi, 1984), Kundur (Anonymous, 2004) etc., among them *Kalonji (Nigella sativa L.)* (Rafiquddin, 1985) is one the important drugs, which is extensively used for the remedy of many diseases. The Holy Prophet said that black seed (*kalonji*) is remedy for all diseases except death. (Ibne-al-Qayyum, 1985) Recent studies revealed that seed oil contains major active constituent Thymoquinone which posses anti inflammatory, antioxidant, anti hypolipidaemic and cardio protective properties. *Nigella sativa* oil contains omega-3 fatty acids and other polyunsaturated and monounsaturated fatty acids in large amount (Ali, 2003).

Consumption of some Omega-3 fatty acids such as Eicosapentaenoic (EPA) and Decosahexaenoic (DHA) acids present in fish oil has shown a preventive action against cardiovascular diseases (Anonymous, 2010).

Some practicing Unani physicians are using *Kalonji* oil in the treatment of cardiovascular diseases and dyslipidaemic with better results, but clinical efficacy of *Kalonji* oil has not been carried out, so far, particularly in relation to hypolipidaemic property. Keeping these facts in view, a single blind standard controlled non randomized clinical trial was planned to evaluate efficacy of a *Roghane Kalonji* in the management of primary hyperlipidaemia.

Materials and Methods

For the assessment of efficacy of the *Roghan-e-kalonji* in the management of primary hyperlipidaemia, patients were selected from Ajmal Khan Tibbiya College Hospital OPD, Aligarh, during the period 2010-2012. In the present study, the patients who attended OPD with the symptoms of palpitation, chest pain, joints pain, obesity, dyspnoea on exertion, xantholesma and were enrolled for the screening of hyperlipidaemia. The patients belonging to the age group of 20-60 years of either sex, ready to participate in the study and whose serum cholesterol, serum triglyceride level was found abnormal, were included in the clinical study. The patients of secondary hyperlipidaemia such as hypothyroidism, diabetes mellitus, nephrotic syndrome and obstructive liver diseases were excluded from the study on the basis of relevant symptoms and investigations. Similarly, the patients using oral contraceptive pills and having history of chronic alcoholism were also excluded from the study. Diagnosis of hyperlipidaemia was confirmed on the basis of history, clinical examination and analysis of Lipid profile markers i.e. S. Cholesterol, Triglyceride, VLDL and HDL.

Study Procedure

After complete physical general, systemic examination and biochemical investigations, patients who fulfilled all the inclusion criteria and signed written consent, were included in the clinical trial. Total 60 patients were selected for the study. The patients were allocated into two groups, i.e. Test group (40 patients- Group A) and control group (20 patients- Group B). In the group A the Test drug was administered in the dose of 6 ml three times a day for a period of 90 days, while in the group B the Atrovastatin was given in the dose of 10 mg once a day for same duration. Assessment was done on 0, 15^{th}, 30^{th}, 60^{th}, 90^{th} day of treatment for subjective and objective parameters. In all patients lipid profile (Serum Cholesterol, Serum Triglyceride, and HDL cholesterol) was carried out before and after treatment. The data was statistically analyzed by using Students t test.

In order to assess toxicity of the drugs, safety parameters like liver function Test (Serum Bilirubin, AST, ALT and Alkaline Phosphate), Kidney Function Test (Blood Urea, Serum Creatinine) and complete Haemogram were also carried out.

Results

In this study out of sixty patients of hyperlipidaemia 19 patients were 25-35 years of age, 19 patients were 36-45 years of age, 12 patients were 46-55 years of age, 07 patients were 56-65 years of age group and 03 patients were >65years of age. The highest prevalence was found in 4th decade. The percentage of female patients is 76.66% was slightly higher than the male patients i.e. 23.33%. The demographic data and other observation are depicted in Table 1.

The effects of test drug on objective parameters i.e. Lipid profile (Serum Cholesterol, Serum Triglyceride, HDL, LDL, and VLDL) and body weight are as follows.

Table 1: Demographic Data of patients in Test and Control group n=60(40+20)

	N	Fp%		N	Fp%
Age group			*Mizaj*		
25-35	19	31.66%	Balghami	46	76.66%
36-45	19	31.66%	Damvi	08	13.33%
46-55	12	20.0%	Safravi	06	10.0%
56-65	07	11.66%	Saudavi	0	0%
>66	03	5.0%			
Gender			Marital Status		
Male	14	23.33%	Married	53	88.88%
Female	46	76.66%	Unmarried	07	11.66%
Religion			Dietary Habit		
Muslim	50	83.33%	Vegetarian	09	15.0%
Hindu	10	16.66%	Mixed Diet	51	85.0%
Occupation			History of		
Students	03	5.0%	Xanthomata	07	11.66%
Service	09	15.0%	Xanthelesma	13	21.66%
Labour	02	3.33%	Arcus cornea	07	11.66%
Business	17	28.33%			
House wife	29	48.33%			
History of IHD			Family History of HLD		
Present	35	58.33%	Present	28	46.66%
Absent	25	41.66%	Absent	32	53.33%

Effect on Serum Cholesterol

In Test group mean serum cholesterol level was 183.32 mg/dl ±31.40 before treatment and at the end of study it was167.60 mg/dl ±26.52, showing mean reduction 15.72 mg/dl ±4.88 and which was found to be significant (P<0.001) (Table 2).

Effect on Serum Triglyceride

In Test group mean serum triglyceride level was 299.07 mg/dl ±97.64 before treatment and at the end of study it was 235.82±82.92 mg/dl, showing mean reduction 63.25 mg/dl ±14.72 and which was found to be significant (P<0.001) (Table 2).

Effect on HDL

In Test group mean HDL level was 33.67 mg/dl ±6.96 before treatment and at the end of study it was 38.08 mg/dl ±6.45, showing mean elevation 4.41 mg/dl ±0.51 and which was found to be significant (P>0.05) (Table 2).

Effect on LDL

In Test group mean LDL level was 89.83 mg/dl ±33.83 before treatment and at the end of study it was 82.35 mg/dl ±29.17, showing mean reduction 7.48 mg/dl ±4.66 and where was found to be significant (P<0.05) (Table 1).

Effect on VLDL

In Test group mean VLDL level was 59.81 mg/dl ±19.52 before treatment and at the end of study it was 47.16 mg/dl ±16.58, showing mean reduction 12.65 mg/dl ±2.94 and which was found to be significant (P<0.001) (Table 2).

Table 2: Effect of Test drug on Objective parameter in Test and control group

S. No.	Parameter	Group-A n=40			Group-B n=20		
		Before Treatment (Base line)	After 90 days	P-Value	Before Treatment (Base line)	After 90 days	P-Value
1	S. Cholesterol	183.32±31.40	167.60 ±26.52	<0.001	185.20 ±29.27	141.60±17.53	<0.001
2	S. Triglyceride	299.07±97.64	235.82±82.92	<0.001	290.40 ±58.41	195.25 ±39.12	<0.001
3	HDL	33.67±6.96	38.08±6.45	>0.05	39.42±6.93	40.15±6.34	>0.05
4	LDL	89.83±33.83	82.35 ±29.17	<0.05	87.69±22.87	62.40 ±17.63	<0.001
5	VLDL	59.81±19.52	47.16±16.58	<0.001	58.08±11.68	39.05±7.82	<0.001
6	Body weight	67.27±4.22	64.45±3.73	<0.001	67.00±4.40	65.20±4.67	<0.001
7	SBP	136.22±10.18	131.30±8.10	<0.001	142.60±6.96	133.4±6.55	<0.001
8	DBP	86.75±6.65	84.25±5.21	<0.001	86.30±6.33	83.40±4.55	<0.05

Effect on Body weight

In Test group mean WHR level was 67.27±4.22 kg before treatment and at the end of study it was 64.45±3.73 kg, showing mean reduction 2.82±0.49 kg and which was found to be significant (P<0.001) (Table 2).

Effect on Safety Parameters

The safety parameters of the test drug like, AST, ALT, Blood Urea, Serum Creatinine, Hb% and ESR were remained within the normal limits before & after treatment, in both groups (Table 3).

Discussion

Hyperlipidaemia is a major risk factor for the development of atherosclerotic heart disease. Reducing plasma cholesterol level particularly LDL cholesterol reduces the risk of coronary heart disease and other associated complications. Indeed, dietary modification plays an important role for the prevention of atherosclerotic diseases but in certain circumstances use of hypolipidaemic drugs are imperative. Although, a large number of drugs are being used in contemporary systems of Medicine but search of new plant origin hypolipidaemic drug is still thrust area of research. The seed of *Nigella sativa* L. (black seed) and its oil have been used since long time for the treatment of many diseases including hyperlipidaemia in traditional system of medicine. The Holy Prophet Muhammad (PBUH) said, "The black seed (*kalonji*) is the remedy for every disease except death" (Ibne-al-Qayyum 751H). Recent experimental studies revealed that this drug possess lipid lowering effects in dyslipidaemic patients. Further studies exhibited that *Nigella sativa* oil (*Roghan-e-Kalonji*) contains

Table 3: Effect of Test drug on Safety parameter in Test and control group

S. No.	Parameter	Group-A n=40		Group-B n=20	
		Before Treatment (Base line)	After 90 days	Before Treatment (Base line)	After 90 days
1	S. Bilirubin	0.98±0.2083	0.94±0.1585	1.053±0.23	1.14±0.17
2	AST	23.13±4.66	23.74±4.23	23.49±3.72	25.35±4.60
3	ALT	21.77±3.87	22.44±3.29	20.56±4.27	23.02±6.59
4	S. Alkaline Phosphates	120.80±15.84	122.07±12.85	122.0±10.57	131.0±13.88
5	Blood Urea	29.22±7.51	26.31±5.91	26.86±5.45	27.84±4.75
6	S. Creatinine	0.95±0.144	0.90±0.108	0.93±0.13	0.94±0.11

chemical constituents such as polyunsaturated fatty acids, Omega-3 Fatty acids, Eicosapentaenoic acid (EPA), Decosahexaenoic acid (DHA) and Alpha Linolenic acid (ALA) (Anonymous, 2010).

Several preclinical studies revealed that Omega-3 fatty acids decrease the triglyceride levels either by decreasing hepatic synthesis or secretion of VLDL particles by inhibiting various enzyme transcription factors or EPA and DHA increase the activity of lipoprotein lipase, leading to an increase in chylomicron clearance. (Harris *et al.,* 2008)

Furthermore, researches on *Nigella sativa* seed oil (*Roghan-e-kalonji*) revealed that the seed oil contains major active constituent Thymoquinone. Much of the biological activity of the seed has been possess due to Thymoquinone, which shows antioxidant, anti-inflammatory, anti-hyperlipidaemia and cardioprotective properties. (Ali, 2003; Badary *et al.,* 2000).

The present study demonstrates that the Test drug (*Nigella sativa* oil) significantly reduces. Serum Cholesterol, Serum Triglyceride, LDL Cholesterol. These findings of the study are in accordance to the previous experimental studies as reported by the Dakha Khani *et al.,* 2000 who revealed that the administration of *Nigella sativa* oil for four weeks duration showed significant decrease in serum Cholesterol, Triglycerides and increases of HDL Cholesterol. Further in other clinical study administration of 2.5ml of *Nigella sativa* oil in morning and evening produce significant hypolipidaemic effects (Dakha Khani *et al.,* 2000).

This drug also exhibited significant effect in reducing Blood pressure and other subjective parameters. The safety parameters like, AST, ALT, Blood Urea, Serum Creatinine, Hb% and ESR were remained within the normal limits before & after treatment, in both groups. This indicates that oral administration of the test formulation is safe for therapeutic use.

The above mentioned effect of Test drug are mainly due to chemical constituent present in the seeds of *Kalonji* particularly Thymoquinone and omega -3 Fatty acid and unsaturated Fatty acids. Further antioxidant, anti-inflammatory, hypolipidaemic and cardioprotective properties facilitate the effect of Test drug in the patients of hyperlipidaemia (Ali, 2003).

Conclusion

In the present study the Test drug was found to be significant in lowering serum cholesterol and serum triglyceride level in the patients of hyperlipidaemia without producing any adverse effect. Therefore, it can be concluded that the Test drug possesses significant hypolipidaemic effect and thus it can be used as a safe and cost effective therapy in the management of hyperlipidaemia.

However, further study is required to explore hidden potential of Test drug on larger population.

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