RESEARCH ARTICLE

PLACEBO-CONTROLLED STUDY ON COMPARISON OF TWO HERBAL HYPOLIPIDEMIC AGENTS

[1]**Niaz Khalid,** [2]**Qudoos Abdul,** [3]**Fatima Ajaz,** [4]**Moeen-ud-din Hafiz,** [5]**Murad Shah,**

[1]Assistant Professor of Pharmacology, IMDC, Islamabad, Pakistan

[2]AP, Pharmacology at FMDC, Islamabad, Pakistan

[3]AP, Pharmacology, IMDC, Islamabad, Pakistan

[4]Assistant Professor, AIMC, Islamabad, Pakistan

[5]Professor of Pharmacology, IMDC, Islamabad, Pakistan

ABSTRACT

Introduction: Hyperlipidemia, either primary or secondary causes atherogenetic abnormalities leading to coronary artery disease, cardiac arrest and arrhythmias. Herbal therapy for prevention or cure of Hyperlipidemia is replacing allopathic medicine due to their bioequivalence and good compliance features. This study was conducted to compare hypolipidemic effects of Garlic and Nigella sativa.

Place of Study: Study was conducted at Jinnah Hospital Lahore from July 2013 to December 2013. Seventy five hyperlipidemic patients were enrolled after getting written consent which was approved by Ethics committee of the hospital.

Grouping: They were divided in three equal groups comprising 25 patients in each group. Group-A was treated by Nigella Sativa, Group-B was advised to take Garlic 10 grams twice daily for two months. Group-C was on placebo.

Results: After two months therapy it was observed by statistical analysis that Nigella sativa decreased total cholesterol 12.4 mg/dl, triglycerides 16.7 mg/dl, and LDL cholesterol 27.3 mg/dl. HDL rise was 5.2 mg/dl. Garlic decreased total cholesterol 17.9 mg/dl, triglycerides 19.9 mg/dl and LDL cholesterol 14.8 mg/dl. HDL cholesterol rise was 8.0 mg/dl.

Conclusion: It was concluded from this study that there is little difference between hypolipidemic effects of two important and famous herbal medicines ie, Nigella sativa and Garlic.

*For Correspondence:
Dr. Khalid Niaz, Pharmacology Deptt:
IM&DC, Main Murree road, Islamabad, Pakistan
drkhalid.niaz@gmail.com CELL: 0333-5150629

INTRODUCTION

Coronary artery disease (CAD) and atherosclerosis are the leading causes of morbidity and mortality in the western as well as in developing countries of the world. Lowering cholesterol levels is known to be an effective preventive measure of atherosclerosis, reducing both coronary and all-cause mortality in patients with established coronary artery disease[1]. The effect of hypocholesterolemic therapy on primary prevention of atherosclerosis is still primary focus by researchers. So hypolipidemic drugs are still under research. Patient and doctor compliance of allopathic drugs is still major problem among various ethnic populations. Some cardiologists prefer allopathic hypolipidemic drugs and

some are trying herbal hypolipidemic medications. Herbal medicines Garlic and Nigella sativa are getting popularity in western world as well as in east, due to their lesser adverse effects[2]. Garlic has been found to lower serum and liver cholesterol, inhibit platelet growth and reduce oxidative stress. The cholesterol-lowering effect of garlic is attributed to the bioavailability of allicin and its derivatives[3]. Garlic is one of the most popular herbal remedies and is steadily gaining interest in complementary and alternative medicine practice. There is a general belief that garlic is an effective and harmless mode of lowering cholesterol. This effect has not been linked to inhibition of HMG

CoA reductase and is presumably due to a different mechanism of action. Garlic has also been attributed with other protective cardiovascular effects like antihypertensive, anti-inflammatory, beneficial effects on blood rheology and coagulability, some of which may be independent of its cholesterol-lowering effect[4-7]. Nigella sativa is a pretty herb, seeds of which are commonly known as kalonji. 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%.[8] Nigella sativa seeds used as a herbal medicine has many effects including cholerectic activity. Kalonji seeds also help in lowering blood cholesterol, blood pressure. It increases bile excretion which may play as hypolipidemic role in primary and secondary Hyperlipidemia[9]. Its different fractions (extracts) were used to observe its effects in whole blood clotting and plasma clot time. In vitro it significantly shortened both and bleeding time, partial thromboplastin time, prothrombin time and thrombin time in vivo it shortened bleeding time and partial thromboplastin time but prothrombin time and thrombin time remained unaffected.[10] Seeds of Nigella sativa are given with butter and milk to cure obstinate hiccup. Seeds are employed as a purgative. They are also useful in indigestion, loss of appetite, fever, diarrhea, and puerperal disease etc[7,8,11]

PATIENTS & METHOD

Research Design, duration, sample size and place of work: The research work was single blind placebo-controlled, conducted at Jinnah Hospital, Lahore from July 2013 to December 2013. Seventy five hyperlipidemic patients were selected for research work. Written consent was taken from all patients. Specific Performa was designed for the research work.

Selection of patients with Inclusion and Exclusion Criteria: 75 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.

Division/grouping of patients: 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. Twenty five patients of group-A were advised to take one tea spoon of Nigella sativa (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 Garlic 10 grams twice daily. Twenty five patients of group-C 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. All participants were called every 2 weeks for follow up.

Method for measurement of lipid profile: Serum lipid profile (total cholesterol, HDL-cholesterol, triglyceride) as well as other biochemical parameters were determined after a 12 hour overnight fast by standard methods. LDL-cholesterol level was calculated according to the Friedewald's formula. Psychological status was determined at the first and last visit by the following self report questionnaires, all of which are considered sensitive and reliable.

Biostatistical analysis: Data were expressed as the mean ± Standard Diviation and "t" test was applied to determine statistical significance as the difference. A probability value of <0.05 was considered as non-significant and P<0.001 was considered as highly significant change in the results when pre and post-treatment values were compared.

RESULTS

When results were compiled and statistically analyzed by using SPSS New Version 5, it was observed that Nigella sativa and Garlic decreased total-cholesterol, LDL-cholesterol, triglycerides significantly and increased HDL-cholesterol significantly as compared to placebo treatment. Pre and post-treatment values/results are shown in table 1, 2 and 3.

Table 1: Showing parameters values before & after treatment with their statistical significance in group A (Nigella Sativa)

TC before treat: 269.13.72	**After Treat: 256.77±2.41**	**Difference 12.4 %**	**P-value= <0.001**
TG before treat: 208.68±2.81	After Treat: 191.94±2.90	16.7 %	P-value= <0.001
LDL-C before treat:177.64±2.76	After Treat: 150.32±1.46	27.3 %	P-value= <0.001
HDL-C before treat: 33.83±1.00	After Treat: 39.00±2.38	5.2 %	P-value= <0.001

Table 2: Showing parameters values before and after treatment with their statistical significance in group B (Garlic)

TC before treat: 287.33±1.30	**After Treat: 269.44±2.70**	**Difference 17.9 %**	**P-value= <0.001**
TG before treat: 221.65±2.06	After Treat: 201.72±1.47	19.9 %	P-value= <0.001
LDL-C before treat:203.17±2.01	After Treat: 188.42±1.00	14.8 %	P-value= <0.001
HDL-C before treat: 33.17±2.91	After Treat: 41.15±1.98	8.0 %	P-value= <0.001

Table 3: Showing parameters values before and after treatment with their statistical significance in group C (Placebo)

TC before treat: 254.61±1.02	After Treat:252.81±3.78	Difference 1.8 %	P-value= >0.05
TG before treat: 240.80±3.01	After Treat:241.70±2.44	0.9 %	P-value= >0.05
LDL-C before treat:170.55±2.65	After Treat:170.10±1.77	0.5 %	P-value= >0.05
HDL-C before treat: 34.43±2.87	After Treat:35.14±1.55	0.7 %	P-value= >0.05

KEY: P-value <0.01 stands for significant change, P-value >0.05 stands for non-significant change. All values are in mean and ± stands for standard error of mean. T-C= serum total cholesterol, TG= serum triglycerides, LDL-C= low density lipoprotein cholesterol, HDL-C= high density lipoprotein cholesterol. Treat: stands for treatment. All parameters pre and post-treatment are measured in mg/dl.

DISCUSSION

Among numerous genetic and lifestyle parameters, dyslipidemia is one of the most prominent risk factors for CAD. In the past decade, lowering LDL cholesterol (LDL-c), serum total cholesterol, serum triglycerides and increasing high density lipoprotein cholesterol (HDL-c) has been the major target in cardiovascular protection strategies. This approach has proven to be beneficial and effective in both primary and secondary prevention of cardiovascular disease (CVD). When analyzed biostatistically in this study the serum total cholesterol, triglycerides and serum low density lipoprotein cholesterol were decreased and high density lipoprotein cholesterol was increased significantly when compared with placebo group. These results suggest that nigella sativa and Garlic has a protective role in atherosclerosis and that is due to their hypolipidemic activity by different mechanisms. In our observations two months therapy by Nigella sativa decreased total cholesterol 12.4 %, triglycerides 16.7 %, LDL-cholesterol 27.3 % and increased HDL-cholesterol 5.2 % when pre and post treatment values were compared. All these changes are highly significant when analyzed statistically. These results match with results of study conducted by Cross DE et al.[12] They observed 10.11 %, 15.00 %, 22.90 % decreased in total cholesterol, triglycerides and LDL-cholesterol respectively. They proved 7.91 % increase in HDL-cholesterol. Their results support our results. Botsoglou NA et al[13] described that herbal medications have more than one or two mechanism to balance plasma lipids in hyperlipidemic patients. LE PM et al[14] have explained one important mechanism of action of Nigella sativa that oil of these seeds inhibits enterohepatic circulation causing biosynthesis of bile acids instead of cholesterol by hepatocytes. EI Dakhakhani M et al15 observed that Nigella sativa reduces LDL-cholesterol lesser than HMG CoA-reductase inhibitors statins. They proved reduction in LDL-cholesterol only 10.75 % when one tea spoon of Nigella sativa oil was used in 16 hyperlipidemic patients for four months. Their results are in contrast with our results. Reason for this mismatch in results may be less concentration of NS oil used in small number of patients, although they used it for four months. In our results Garlic reduced 17.9 %, 19.9 %, 14.8 % total cholesterol, Triglycerides and LDL-cholesterol respectively. HDL-cholesterol increased from 33.17±2.91mg/dl to 41.15±1.98 mg/dl. In percentage it was 8.0 % increase. These results match with results of research work conducted by Raeesi M et al[16] who proved almost same change in serum total cholesterol, triglycerides and HDL-cholesterol but in their results LDL-cholesterol reduction was much less than our results ie; only 7.3 %. They explained that LDL-cholesterol is important for consideration of development of atherosclerosis, CAD leading to cardiac arrhythmias and heart attack. Our results for reduction in LDL-cholesterol and boosting of HDL-cholesterol matches with results obtained by Islam MS and Choi H[17] who proved 13.00 % reduction in LDL-cholesterol and 7.81 % increase in HDL-cholesterol by Garlic use for 3 months in 26 hyperlipidemic patients. Kim YJ et al[18] proved no significant change in HDL-cholesterol when 5 grams of Garlic was used in 10 secondary hyperlipidemic patients for 10 days. So much change in results may be due to less amount of Garlic, lesser sample size and duration of intake of the selected herbal medication used in their research work.

CONCLUSION AND RECOMMONDATION

It was concluded from this research study that when hypolipidemic features of herbal medications are compared, their results are usually same. Patient compliance of herbal medications is good in our ethnic background. We recommend that research on hypolipidemic herbs/plants should be expanded and be supported by concerned government departments in our country.

REFERENCES

1. Badary OA, Abdel Nain AB, Abdel Wahab MH, Hamada FM. Induced hyperlipidermic nephropathy in rats: Toxicology 2000;143(3):219-26.

2. A. Wertelecki, T. and Skorupinska, J. The influence of phytogenic extracts on performance, nutrient digestibility, carcass characteristics, and gut microbial status in broiler chickens. Journal of Animal and Feed Sciences 2003;12:583-596.

3. Iji, P.A., Saki, A. and Tivey, D.R. Body and intestinal growth of broiler chicks on a commercial starter diet. 1. Intestinal weight and mucosal development. British Poultry Science2001; 42:505-513.

4. Hernandez, F., Madrid, J., Garcia, V., Orengo, J. and Megías, M.D. Influence of two plant extracts on broilers performance, digestibility, and digestive organ size. Poultry Science 2004;83:169-174.

5. Demir, E., Sarica, S., Ozcan M.A. and Suicmez, M. The use of natural feed additives as alternatives for an antibiotic growth promoter in broiler diets. British Poultry Science2003; 44:S44-S45.

6. Lewis, M.R., Rose, S.P., Mackenzie, A.M. and Tucker, L.A. Effects of dietary inclusion of plant extracts on the growth performance of male broiler chickens. British Poultry Science2003; 44:S43-S44.

7. Bampidis, V.A., Christodoulou, V., Florou-Paneri, P., Christaki, E., Chatzopoulou, P.S., Tsiligianni, T. and Spais, A.B. Effect of dietary dried oregano leaves on growth performance, carcase characteristics and serum cho-lesterol of female early maturing turkeys. British Poultry Science 2005; 46:595-606. Park K. Parks text book of preventive and social medicine. 24th ed. Jabalpur India: Banarasi Das Bhanot, 2004: 272 – 73.

8. Amooz Mehr, A. and Dastar, B. (2009) Effects of alcoholic extract of two herbs (garlic and thymus) on the per-formance and blood lipids of broiler chickens. Journal of Agri-cultural Sciences and Natural Resources 2009;16:61-72.

9. Sivam, G.P. Protection against helicobacter pylori and other bacterial infections by garlic. Journal of Nutrition 2001; 131:1106S-1108S.

10. Sarica, S., Ciftci, A., Demir, E., Kilinc, K. and Yildirim, Y. (2005) Use of an antibiotic growth promoter and two herbal natural feed additives with and without exogenous enzymes in wheat based broiler diets. South African Journal of Animal Science 2005; 35:61-72.

11. Freitas, R., Fonseca, J.B., Soares, R.T., Rostagno, H.S. and Soares, P.R. Utilization of garlic (Allium sati-vum L.) as hypolipidemic agent. Revista Brasileira de Zootecnia 2001;30:761-765.

12. Cross, D.E., Acamovic, T., Deans, S.G. and McDevitt, R.M. The effect of dietary inclusion of herbs and their volatile oils on the Hyperlipidemia. British Poultry Science 2002;43: 533-535.

13. Botsoglou, N.A., Christaki, E., Florou-Paneri, P., Giannenas, I., Papageor-giou, G., and Spais, A.B. The effectof a mixture of herbal essential oils or α-tocopheryl acetate on performance parameters and oxidation of body lipid. South African Journal of Animal Science 2004;34: 52-61.

14. Le PM,Benhaddou-Andaloussi A, Settaf A, Cherrah Y, Haddad PS. The petroleum ether extract of Nigella sativa exerts lipid lowering effect. J Ethanopharmacol. 2004:94(2-3): 251-9.

15.EI DakhaKhani M, Mady NL, Halim MA. Nigella sativa L. oil protects against induced hepatotoxicity and improves serum lipid profile. Arzneimittel for schunge 2010; 5(9):832-36

16.Raeesi, M., Hoe-ini-Aliabad, S.A., Roofchaee, A., Zare Shahneh, A. and Pirali, S. Effect of periodically use of garlic (Allium sativum) on hyperpatients. World Academy of Science, Engineering and Technology 2010;68:1213- 1219.

17.Islam, M.S. and Choi, H. Comparative effects of dietary ginger (Zingiber officinale) and garlic (Allium sativum) investigated in Hyperlipidemia. Journal of Medicinal Food 2008;11:152-159.

18. Kim, Y.J., Jin, S.K. and Yang, H.S. Effect of dietary garlic bulb and husk on hyperlipidemia. Poultry Science 2009; 88:398-405