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ROLE OF HERBAL FORMULATION OF GARLIC ON LIPID PROFILE IN PATIENTS WITH TYPE 2 DIABETES RELATED DYSLIPIDEMIA

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Contribution
NAS conceived the idea, planned the study and drafted the manuscript. SH,MMR helped in acquisition of data and did statical analysis. TP drafted and critically revised manuscript. All authors contributed significantly to the submitted manuscript

All authors declare no conflict of interest.

ABSTRACT

Objective: To evaluate the role and side effects of garlic on lipid profile in diabetic dyslipidemic patients along with their lipid lowering efficacy.

Methodology: This cross sectional study was carried out at Surgeon Munawar Memorial Hospital Bahadurabad Karachi. The study period consisted of 8 weeks from 1st February 2015 to 31st March 2015. Patients with age between 30 and 60 years of either gender with diabetic dyslipidemia were included . The exclusion criteria included pregnant/lactating females, liver, renal and established coronary artery disease or ischemic heart disease.

Results: Total of 30 diabetic dyslipidemic patients with abnormal lipid profile were included. Patients were orally administered with local herbal product of garlic (300 mg/day) for 8 weeks. Serum levels of cholesterol, high density lipoprotein (HDL), triglyceride (TG), and low density lipoprotein (LDL) were estimated in patients before and after treatment with local herbal product of garlic (300 mg/day). After the treatment of garlic, serum cholesterol and low density lipoprotein were significantly decreased but there was no effect on triglyceride levels (p > 0.05).

Conclusion: On the basis of this study we concluded that herbal products like garlic significantly decreases cholesterol, low density lipoprotein (LDL) and increases high density lipoprotein (HDL).

Key Words: Lipid profile, dyslipidemia, herbal product, garlic

INTRODUCTION

The ratio of cardiovascular disease (CVD) in Pakistan is high as compared to western world and is one of the chief reasons of disability around the world. When CVD is diagnosed, following preventive measures should be taken including regular exercise, proper diet, weight control and lipid reducing drugs to overcome the risk of morbidity or mortality.[1]

Cardiovascular heart disease is more common in diabetic people than in non diabetic people, and 50% of diabetics have evidence of cardiovascular heart disease at the time of their diagnosis. Dyslipidemia plays an important role for provocation of cardiovascular disease (CVD) due to diabetes.[2] Cardiovascular disease is a primary reason of disability and the number of patients is increasing gradually around the world.[3] Greater than 220 million people have diabetes and by the year of 2030 this number is likely to be more than double.[1]

In patients with risk of coronary heart disease due to diabetes or with high levels of total cholesterol or LDL cholesterol, drug therapy should be initiated at an early stage.[4] The frequency of coronary artery disease in Pakistan is soaring as in western part of world.[5] CVD is now observed subsequent cause of death in Karachi, a metropolitan city of Pakistan.[6] Sophisticated and urbanized style of life is supposed to be the major contributing element of coronary artery disease morbidity and mortality in Pakistan.[7]

A large number of plants have been evaluated for their effects on various CVD risk factors including hyperlipidemia but very few has given conclusive answer specially related to suitable dosage and duration of therapy required for maximum improvement in cardiovascular risk factors.[8] Garlic is a natural substance which has its own positive effects for the deterrence of various macro-vascular risk factors.[9] Garlic has long been known to provide beneficial effects for various disorders and is known to possess high quantity of organo-sulfur compounds such as S-allylcysteine, which is known to possess potent antioxidant activity.[10] Allium sativum or garlic ought to have more attention as cost-effective, safe contender for delaying or preventing complications of diabetes.[11] Garlic constituents were reported to act by inhibiting human squalene monooxygenase and 3-hydroxy-3-methyl-glutaryl-coenzymeA ((HMG-CoA) reductase, which are key enzymes involved in cholesterol biosynthesis.[12,13] Research has suggested that garlic protect against cardiovascular diseases.[14,15] Garlic can cause a direct antiatherogenic effect by avoidance of intracellular lipid accumulation and other atherogenic manifestations at the vascular cell level. All the major manifestations of atherosclerosis (lipidosis, fibrosis, and proliferation) show a propensity toward decrease by garlic.[16] Garlic decreases a large number of risk factors which play an influential part in the origin and succession of atherosclerosis.[17,18]

The aim of this study was to assess the local herbal product for their effectiveness in the treatment of diabetes related dyslipidemia.

METHODOLOGY

This cross sectional study was carried out at Surgeon Munawar Memorial Hospital Bahadurabad Karachi. The population under study was representative of Pakistani population with diabetic dyslipidemia The study period consisted of 8 weeks, from 1st February 2015 to 31st March 2015. Blood pressure, body weight and height of subjects were assessed. The patients answered the questionnaire on health complaints, smoking, social role, drug usage, family history and dietary pattern. Patients were asked to fill a consent form before starting the experiment. The initial inclusion criteria included patients of age between 30 and 60 years old of either sex with diabetic dyslipidemia. The exclusion criteria included pregnant or lactating mothers, patients with liver diseases, renal diseases, established coronary artery diseases or ischemic heart disease. Detailed medical history and physical examination of all patients were carried out.

Serum lipid profile was done before and after the treatment. Patients were orally administered with herbal product of garlic (300 mg/day) for 8 weeks. After 8 weeks, blood samples were collected again for the estimation of lipid profile. The blood sample was drawn using 5ml syringe and centrifuged at 3000 rpm for 10 minutes. Serum was separated and collected in clean and dry Eppendorfs and was stored at -70 C till further analysis.

The serum levels of total cholesterol, TG, and HDL were determined enzymatically on microlab using commercially available (Randox laboratories limited, UK) kits. LDL was calculated using Friedwald formula. The data was analyzed statistically using SPSS version-11.

RESULTS

About thirty patients were selected for the study. Patients were investigated for the lipid lowering activity of the local herbal product of garlic. Table 1 represents the variation of serum lipids including cholesterol, high density lipoprotein (HDL), triglyceride (TG) and low density lipoprotein (LDL) in diabetic dyslipidemia before and after 8 weeks of treatment with local herbal product of garlic.

Patients who have been given garlic at a dose of 300mg/day showed a reduction in total cholesterol from baseline value of 225.86 to $\pm$ 4.22 mg/dl to 207.96 to $\pm$ 4.19 mg/dl at week 8 (p < 0.05). Patients who have been given garlic at a dose of 300mg/day showed baseline value of serum triglyceride from 191.10 to $\pm$ 6.92 mg/dl to 194.30 to $\pm$ 7.20 mg/dl at week 8. This was not significant when

compared from before and after treatment. Patients who have been given garlic at a dose of 300mg/day showed an increase in serum high density lipoprotein (HDL) from baseline value of 35.46 to ± 0.59 mg/dl to 38.00 to ± 0.57 mg/dl at week 8 (p < 0.05). Patients who have been given garlic at a dose of 300mg/day showed a reduction in serum low density lipoprotein (LDL) from baseline value of 158.30 to ± 3.22 mg/dl to 138.63 to ± 3.10 mg/dl at week 8 (p < 0.05).

Figure 1, 2, 3 represents the correlation of serum lipids including cholesterol, high density lipoprotein, triglyceride and low density lipoprotein in diabetic dyslipidemia before and after eight weeks of treatment with local herbal product of garlic. Figure 1 shows positive correlation (r = 0.947) of total cholesterol when compared from before and after treatment.

Figure 2 also shows the positive correlation (r = 0.900) of high density lipoprotein (HDL), while figure 3 shows the modified correlation (r = 0.767) of low density lipoprotein (LDL).

Mean ± SD was used for continues variables. Categorical variables were observed using frequencies and percentages.

Figure 1: Correlation of Cholesterol with before and after Garlic Treatment with Diabetic Dyslipidemic Patients
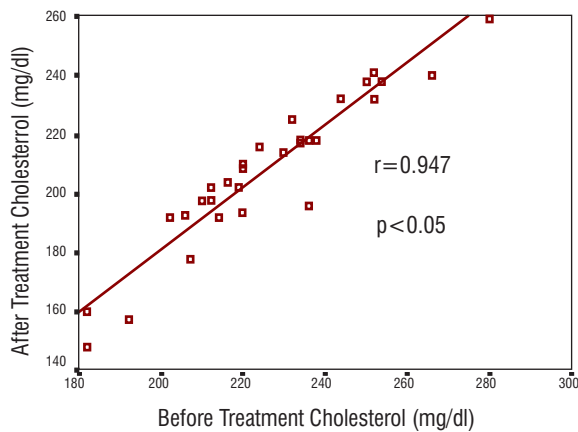

Figure 2: Correlation of High Density Lipoprotein (HDL) with before and after Garlic Treatment with Diabetic Dyslipidemic Patients
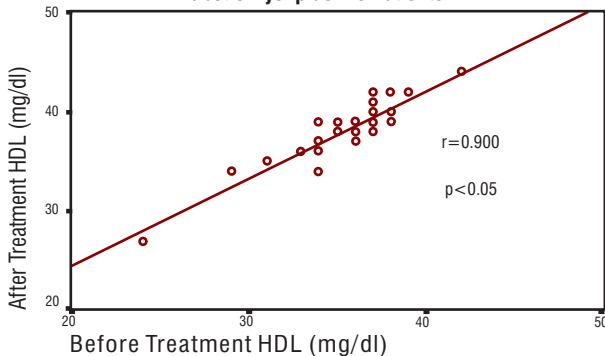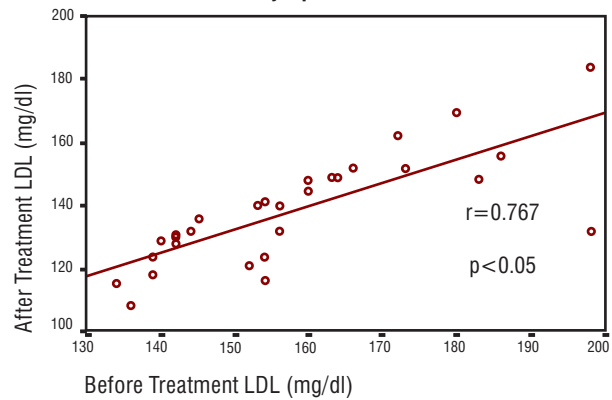

Figure 3: Correlation of Low Density Lipoprotein (LDL) with before and after Garlic Treatment with Diabetic Dyslipidemic Patients

DISCUSSION

Cardiovascular disease (CVD) is the most common and most preventable cause of death of the chronic non-communicable diseases impacting global mortality.[19] Managing and diagnosing dyslipidemia as a way to prevent CVD is a common activity for primary care physicians.[20] Cardiovascular disease is projected to be for most public health and clinical predicament in Asia and by the year 2020, Asia will have exceptionally higher number of patient suffering from CVD than any other region in the world.[21] Cardiovascular disease (CVD) risk factors, such as hyperlipidemia, diabetes, obesity, hypertension and smoking tend to occur together and are major contributors to high mortality around the globe.[22] Risk factors in Pakistani patients include abdominal obesity, dyslipidemia, diabetes mellitus, hypertension, smoking and physical inactivity.[23] Cardiovascular disease due to dyslipidemia and diabetes is also reported to be the leading cause of mortality in Karachi, the largest cosmopolitan city of Pakistan.[6] Diabetic dyslipidemia is one of the major causes of ischemic heart disease.[24] The uses of herbal medicines have increased considerably over the past few years and are becoming a popular alternative treatment option. The relationship between dyslipidemia and atherosclerosis and risk of adverse events associated with standard anti-hyperlipidemic agents has promoted extensive hunt for plant based compounds that safely and efficiently bring about improvement in lipid profile.[25] Garlic has been used in herbal medicine for past many years for various ailments. Garlic has been the target of serious medical and clinical attention in past few years for the reason of having found beneficial effects on numerous cardiovascular risk factors including dyslipidemia.[26] Research has suggested that garlic protect against cardiovascular disease. Garlic can cause a direct antilipidemic effect by prevention of intracellular lipid accumulation and other atherogenic manifestations at the vascular cell level. Supplementation with garlic alone has also been found to significantly reduce total cholesterol

concentrations and LDL-cholesterol concentrations.[27] Garlic consists of organo-sulfur constituents such as glutamylcysteine, S-allyl cysteine, alliin, allicin and ajoene. Although many of these organosulfur compounds have been identified as inhibitors of cholesterol metabolism, it is believed that allicin is the primary active compound responsible for inhibiting cholesterol biosynthesis.[15,29]

The current study was designed to assess the role of garlic (300mg) on lipid profile in diabetic dyslipidemic patients along with their lipid lowering efficacy. Fasting lipid profile was done at baseline i.e. at week 0 and were repeated after week 8.

These individuals were also treated with herbal product of garlic in diabetic dyslipidemic patients, their serum cholesterol and low density lipoprotein (LDL) were significantly decreased while significant increased has been observed in serum high density lipoprotein (HDL) ($p < 0.05$) levels after treatment as compared to before treated patients but there were no significant effects on triglycerides (Table 1).

Table 1: Role of Garlic on Lipids Profile in Diabetic Dyslipidemic Patients (n=30)

	Cholesterol mg/dl	TG mg/dl	HDL mg/dl	LDL mg/dl
Before treatment Mean ± S.E	225.86 ±4.22	191.10 ±6.92	35.46 ±0.59	158.30 ±3.22
After treatment Mean ± S.E	207.96* ±4.19	194.30 ±7.20	38.00* ±0.57	138.63* ±3.10

*$p < 0.05$ significant difference by t-test as compared to respective control

Current analyses conducted by Zeng et al clearly illustrated that garlic therapy is more effective if used for a long term with higher baseline total cholesterol levels. It is also reported that garlic was more effective in reducing serum total cholesterol levels and was more effective in lowering serum triglycerides levels.[30,31] The results of few meta-analyses indicate that garlic supplementation results in modest reductions in serum total cholesterol, low density lipoprotein, and triglyceride levels compared to placebo.[32] The present study is in accordance with a study of Javad et al, who noted significant reduction in total cholesterol; low density lipoprotein (LDL) and increase in high density lipoprotein (HDL) levels but triglycerides were not statistically significant. Garlic improves lipid profile in diabetic dyslipidemic patients.[33] The lower level of total cholesterol observed with garlic is believed to be largely due to a reduction in LDL-C, which may be due to an inhibition of hepatic -cholesterol biosynthesis as reported earlier. Garlic contains a number of organosulfur constituents such as glutamylcysteine, S-allyl cysteine, alliin, allicin which were reported to inhibit cholesterol synthesis. Although many of these organo-sulfur compounds have been identified as inhibitors of cholesterol metabolism, it is

believed that allicin is the primary active compound responsible for inhibiting biosynthesis of cholesterol.[34,35]

CONCLUSION

Garlic could improve lipid profile and its beneficial effects on cardiovascular risk factors are widely known but have not been evaluated specially in Pakistan. In conclusion it is observed that garlic reduces total cholesterol, low density lipoprotein cholesterol (LDL-C) and increase high density lipoprotein cholesterol (HDL-C) without producing adverse effects. It is therefore, suggested that garlic can be use as the first choice for the treatment of diabetic dyslipidemia. However further studies are needed to affirm the safety and quality of the plants to be used by clinicians as therapeutic agents.

REFERENCES

1. Ramahi TM. Cardiovascular disease in the Asia Middle East Region: global trends and local implications. Asia Pac J Public Health 2010;22:83S-9.

2. Vaverkova H, Farnier M, Averna M, Missault L, Viigimaa M, Dong Q, et al. Lipid-altering efficacy of ezetimibe/simvastatin 10/20 mg compared to rosuvastatin 10 mg in high-risk patients with and without type 2 diabetes mellitus inadequately controlled despite prior statin monotherapy. Cardiovasc Ther 2012;30:61-74.

3. Hamed A, Alobaidi A. Effect of Nigella sativa and Allium sativum coadminstered with simvastatin in dyslipidemia patients: a prospective, randomized, double-blind trial. Antiinflamm Antiallergy Agents Med Chem 2014;13:68-74.

4. Ahmed KAA, Muniandy S, Ismail IS, Ali RS, Al-Hamodi ZH. Evaluation of N-(carboxymethyl) lysine and lipid peroxidation in multiethnic Malaysian subjects with type 2 diabetes mellitus. Sci Res Essays 2011;6:1957-62.

5. Eckel R, Daniel J, Rader MD. Preventive cardiology, University of Colorado, Denver. N Engl J Med 2011;13.

6. Bhurgri A, Bhurgri Y, Khan Y, Sharih U, Naqvi F, Soomro IB. Mortality statistics in South Karachi. J Pak Med Assoc 2001;51:446-9.

7. Hakeem R, Thomas J, Badruddin SH. Urbanisation and coronary heart disease risk factors in South Asian children. J Pak Med Assoc 2001;51:22-8.

8. Karira KA, Shah SM, Salahuddin, Qasim R, Soomro MS, Rehman K. Incidence of lipid disorders in offspring of patients with premature myocardial infarction. Med Channel 2000;6:9-12.

9. Mahmood ZA, Sualeh M, Mahmood SBZ, Karim MA.

Herbal treatment for cardiovascular disease the evidence based therapy. Pak J Pharm Sci 2010;23:119-24.

10. Rahman K. Garlic and aging, new insights into an old remedy. Ageing Res Rev 2003;2:39-56.

11. Imai J, Ide N, Nagae S, Moriguchi T, Matsuura H, Itakura Y. Antioxidant and radical scavenging effects of aged garlic extract and its constituents. Planta Med 1994;60:417-20.

12. Ahmad MS, Ahmed N. Antiglycation properties of aged garlic extract: possible role in prevention of diabetic complications. J Nutr 2006;136:796S-9.

13. Gupta N, Porter TD. Garlic and garlic derived compounds inhibit human squalene monooxygenase. J Nutr 2001;131:1662-7.

14. Augusti KT, Chackery J, Jacob J, Kuriakose S, George S, Nair SS. Beneficial effects of a polar fraction of garlic (Allium sativum Linn) oil in rats fed with two different high fat diets. Indian J Exp Biol 2005;43:76-83.

15. Craig WJ. Health promoting properties of common herbs. Am J Clin Nutr 1999;70:491-9.

16. Grogler KB, Ling M, Boudoulas H, Belz GG. Protective effects of chronic garlic intake on elastic properties of aorta in the elderly. Circulation 1997;96:2649-55.

17. Orekhov AN, Grunwald J. Effect of garlic on atherosclerosis. Nutrition 1997;13:656-63.

18. Siegel G, Walter A, Engel S, Walper A, Michel F. Pleotropic effects of garlic. Wien Med Wochenschr 1999;149:217-24.

19. Santos OS, Grunwald J. Effect of garlic powder tablets on blood lipids and blood pressure: a six month placebo controlled double blind study. Br J Clin Res 1993;4:37-44.

20. Saposnik G. The missing ethnicity in primary cardiovascular trials. QJM 2011;104:551-2.

21. Nelson RH. Hyperlipidemia as a risk factor for cardiovascular disease. Prim Care 2013;40:195-211.

22. Prasad DS, Kabir Z, Dash AK, Das BC. Cardiovascular risk factors in developing countries: a review of clinico-epidemiological evidence. CVD Prev Control 2010;5:115-23.

23. Brindis R, Gray HH. The ACC looks globally to tackle cardiovascular disease. J Am Coll Cardiol 2011;57:631-3.

24. Kayani AM, Bakht N, Munir R, Abid I. The mosaic of CVD risk factors: a study on 10,000 Pakistani cardiac patients. CVD Prev Control 2011;6:1-7.

25. Bianchi C, Miccoli R, Penno G, Del Prato S. Primary prevention of cardiovascular disease in people with dysglycemia. Diabetes Care 2008;31:S208-14.

26. Thompson Coon JS, Ernst E. Herbs for serum cholesterol reduction: a systematic view. J Fam Pract 2003;52:468-78.

27. Tattelman E. Health effects of garlic. Am Fam Physician 2005;72:103-6.

28. McRae MP. A review of studies of garlic (Allium sativum) on serum lipids and blood pressure before and after 1994: does the amount of allicin released from garlic powder tablets play a role? J Chiropr Med 2005;4:182-90.

29. Zeng T, Guo FF, Zhang CL, Song FY, Zhao XL, Xie KQ. A meta-analysis of randomized, double-blind, placebo-controlled trials for the effects of garlic on serum lipid profiles. J Sci Food Agric 2012;92:1892-902.

30. Siddiqui NA, Perveen T, Kazmi SAJ, Khanum A, Ambreen. Differences in lipoid profile with international product of simvastatin and local product in patient with primary hyperlipidemia. World J Pharm Pharm Sci 2014;3:2207-15.

31. Alder R, Lookinland S, Berry JA, Williams M. A systematic review of the effectiveness of garlic as an anti-hyperlipidemic agent. J Am Acad Nurse Pract 2003;15:120-9.

32. Kojuri J, Vosoughi AR, Akrami M. Effects of anethum graveolens and garlic on lipid profile in hyperlipidemic patients. Lipids Health Dis 2007;6:5.

33. Siddiqui NA, Perveen T, Ambreen, Akhtar A, Sehar A. Effects of HMG-COA reductase inhibitors (simvastatin and herbal formulation of allium sativum) on liver function test in patients with type 2 diabetes mellitus related dyslipidemia. World J Pharm Pharm Sci 2014;3:1791-9.

34. Lawson LD. Garlic: a review of its medicinal effects and indicated active compounds. In: Lawson LD, Bauer R, editors. Phytomedicines of Europe: chemistry and biological activity. Washington DC: American Chemical Society: 1998. p. 177-209.