EFFECTS OF GARLIC ON DYSLIPIDEMIA IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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Background: Garlic (Allium Sativum) has been used in herbal medicine for centuries for various ailments. In recent years garlic has been the focus of serious medical and clinical attention because of beneficial effects on several cardiovascular risk factors like reduction of serum lipids, blood pressure and plasma viscosity. There is also wide spread belief among general public that garlic has beneficial effects on cardiovascular system. The purpose of present study was to evaluate the effects of garlic on one of the major cardiovascular risk factors i.e. dyslipidemia in patients with type 2 diabetes mellitus. **Method:** This 12 week randomized, single-blind, placebo controlled study was conducted on Type 2 diabetic patients with newly diagnosed dyslipidemia (n=70). Patients were selected from Diabetic OPD of Jinnah Post Graduate Medical Centre, Karachi and were divided into two groups each comprising of 35 patients, they were given tablet garlic (Garlex–Bosch Pharmaceuticals) 300 mg (containing 1.3 % allicin) twice daily and identical placebo tablets respectively. Both groups were given diet and exercise plan. **Results:** After 12 weeks the garlic treated group (n = 33) had a significant reduction in total cholesterol (-28 mg/dl, -12.03 % P= <0.001), LDL – C (-30 mg/dl, - 17.99 % P=<0.001) while the placebo treated group (n=32) had a non significant decrease in total cholesterol (– 2 mg/dl, - 0.9 % p= ns) and LDL-C (-3 mg/dl, -1.6 % p=ns). HDL cholesterol was significantly increased in patients treated with garlic (3.35 mg/dl, 8.81% P= <0.05) compared with placebo group (0.62, 1.6 % P= n.s) but there was no significant difference in triglyceride was observed between two groups. **Conclusion:** This study suggests possible small short term benefits of garlic on dyslipidemia in type 2 diabetic patients. Garlic significantly reduced serum total cholesterol and LDL cholesterol and moderately raised HDL cholesterol as compared to placebo. Controlled Clinical Trials of longer duration are needed to assess the long term benefit of garlic on vascular and circulatory disease processes.

KEY WORDS: dyslipidemia, Type 2 diabetes mellitus, Garlic

INTRODUCTION

Patients with type 2 diabetes have a two fold to fourfold excess risk of coronary artery disease as compared to non-diabetic patients[1] and many of the primary risk factors for coronary artery disease frequently coexisting in this patient population. High blood cholesterol is one of the major modifiable risk factor for coronary heart disease.[2,3]

Lipid lowering drugs used for treating high-risk persons include 3 hydroxy-3-methylglutaryl CoA reductase inhibitors (statins, bile acid binding sequestrants, fibrates and nicotinates. None of these pharmacological options are free of adverse effects and some have been associated with potential carcinogenicity. A harmless yet effective therapy for lowering cholesterol levels would therefore be of considerable interest.[4]

There has been an increasing recognition that certain natural substances have the potential to reduce the detrimental effect of a number of cardiovascular risk factors. The use of natural substances has become more widespread over the past few years, driven undoubtedly by the belief that natural substances may have fewer side effects than do pharmaceuticals and by their ready availability to the public without prescriptions or visits to the health providers. Garlic and various forms of extracts prepared from it represent an example of such natural substances that have been claimed to possess beneficial effects for the presentation of various aspects of cardiovascular disease.[5]

Garlic was known to be effective in decreasing cholesterol,[4,6] and can inhibit LDL-Oxidation.[7,8] Over 40 clinical trials have been conducted to determine the lipid-lowering effects of fresh garlic (Allium Sativum) and garlic supplements.[9]

Though many clinical trials showed a positive effect of garlic on hyperlipidemia, atherosclerosis, thrombosis, hypertension and diabetes,[4,7,10-13] however a number of negative studies[14-18] have cast doubt on the efficacy of garlic specially its cholesterol lowering effect.

Garlic principle active agent appears to be allicin, a sulfur-containing compound that with its breakdown products gives garlic its characteristic odor. Allicin is formed enzymatically from an odorless precursor, alliin, when garlic cloves are mechanically disrupted. Since the alliin content of natural garlic may vary 10-fold, the quantity of allicin

released can be influenced by specific extraction methods. Formulation of garlic supplements could therefore be a critical factor. A dried garlic powder tablet, standardized to provide 1.3 % alliin equivalent to 0.6% allicin, has been available in Germany as over the counter to improve cardiovascular risk factors.[19] Recently these garlic tablets become available in Pakistan.

As previous clinical trials have cast doubt on the proposed lipid lowering effects of garlic and there is no previous trial showing the effects or benefits of garlic on hyperlipidemia in patients with diabetes and also keeping in mind the incidence of hyperlipidemia that is quite high in Pakistan[20] and a wide spread belief among general public that garlic has beneficial effects on cardiovascular system., we designed a study to evaluate the hypolipidemic effects of garlic in patients with type 2 diabetes mellitus.

MATERIAL AND METHODS

We conducted a 12 weeks randomized, single-blind, placebo controlled study comparing the effects of dried garlic powder tablet 300 mg (standardized to provide 1.3 % alliin equivalent to 0.6% allicin (Garlex, Bosch Pharmaceuticals Pakistan) twice daily with that of placebo on serum lipids in type 2 diabetic patients with abnormal lipid profile.

Study was conducted in the Department of Pharmacology and Therapeutics, Basic Medical Science Institute (BMSI), Jinnah Post Graduate Medical Centre, Karachi. Type 2 diabetic patients with newly diagnosed dyslipidemia (n=70) were initially enrolled in this study after taking informed and written consent and were divided randomly into 2 groups each comprised of 35 patients and were given tablet garlic 300 mg twice daily and identical placebo tablets with same dosing schedule respectively. Both groups were advised same diet and exercise plan and were advised not to change their dietary habits or physical activity during the course of the study. All patients in the study were selected according to following criteria.

Inclusion criteria for the selection of patients were: Patients with Type 2 diabetes mellitus of either sex with newly diagnosed dyslipidemia, Patients aged between 25-70 years, Serum LDL >130mg/dl, Serum triglyceride >150 mg/dl, Serum total cholesterol > 200mg/dl, Serum HDL < 40 mg/dl. Exclusion criteria were: History of allergy to Garlic, Pregnant or lactating women, History of myocardial infarction, proven coronary artery disease, unstable angina, Hepatic dysfunction, Impaired renal function. Lipid profile was done at day of inclusion i.e. week 0 and repeated at week 6 and week 12.

All laboratory analyses were done in the central laboratory of Jinnah Postgraduate Medical Centre Karachi. The serum total cholesterol (TC) and serum triglycerides (TG) and HDL were measured by using analyzers (Selectra-II, MICROLAB Germany). LDL-C was calculated by the Friedwald equation, LDL-C = TC-HDL-C + TG/5.

All data was fed in SPSS version10.0 and analyzed. Descriptive statistics were calculated. Mean ± SEM of each category of lipid profile for each group was calculated. Paired t test was used to compare the mean values of lipid parameters at various points in time (0 week, 6 week and 12 week) for each group separately. P value of less than 0.05 was considered statistically significant.

RESULTS

The demographic characteristics of the study population are shown in table 1. The two treatment groups are fairly comparable for the listed variables. The patients were male (45%) and females (55%). The mean age was 59 years (range 25-70 years) (table 1). Out of 70 patients enrolled in study, 65 patients were associated through out the study period. Out of remaining 5 patients, 2 patients were dropped out in garlic group, 1 due to heart burn in the first week of study refused to take the treatment and 1 has not come for follow up due to unknown reason, 3 patients were dropped in placebo group, 2 has not come for follow-up due to unknown reason while 1 patient has refused to follow the exercise and diet plan and was excluded from the study.

Table-1: Demographic Data of Garlic and Placebo Group

	Garlic (n=35)	Placebo(n=35)
Men	15	17
Women	20	18
Age (years)	60 ± 5.04	58± 5.80
Body weight (Kg)	62.2 ± 10.45	63 ± 9.80
Height (cm)	165.2 ± 8.8	167.60 ± 9.20

Blood lipids were measured at week 0, 6 and 12 (table 2). At the end of 12 week it was found that changes in total cholesterol, HDL-cholesterol, and LDL-cholesterol were significantly different between the garlic and placebo groups though no significant difference in the triglyceride concentration was seen between garlic and placebo groups. The garlic treated group had a significant reduction in mean total cholesterol (-28 mg/dl, -12.28 %, P= <0.001), LDL – C (-30 mg/dl, -17.99 % P=<0.001) while the placebo treated group had a non significant decrease in total cholesterol (–2 mg/dl, - 0.9 % P= n.s) and LDL - C (-3 mg/dl, -1.6 % P= n.s). HDL cholesterol was significantly increased in patients treated with garlic (3.35 mg/dl, 8.81% P= <0.05) compared with placebo group (0.62, 1.6 % P= n.s) but this increase in HDL-

cholesterol was appeared to be time dependent as there was no significant increase observed between week 0 and week 6. There was a very small non significant increase in triglyceride concentration in garlic grouping comparison to placebo group which showed a small non significant decrease in triglyceride concentration.

DISCUSSION

We evaluated the efficacy of garlic on hyperlipidemia in patients with type 2 diabetes mellitus in comparison to placebo. In our study treatment with garlic powder preparation significantly effected plasma lipid levels while in the placebo group small but non-significant changes in all lipid parameters were observed which might be explained by the diet and exercise advice given to patients at the time of initiation of study. The other reason could be that there were more women in both the groups. It is considered that generally women are more experienced and motivated to follow dietary advice.
The onset of hypolipidemic effects was evident as early as 6 weeks and become more progressive and greater with time.

Tohidi and Rhahbani[7] showed that taking 1200 mg garlic powder for 4 weeks reduced total cholesterol (9%), triglyceride (11%), and LDL-C (15%). This study coincides with that of our study with the exception of that of triglyceride concentration.

The changes in lipid parameters observed in present study are in accordance with the previous clinical trials.[4,10,11] reported that ingestion of garlic by chewing or crushed garlic can reduce cholesterol, triglyceride systolic and diastolic blood pressure even in the presence of increasing fat intake but undamaged garlic (swallowed) had no significant effect on serum lipids (TG, T.Cholesterol, LDL-C, HDL-C).

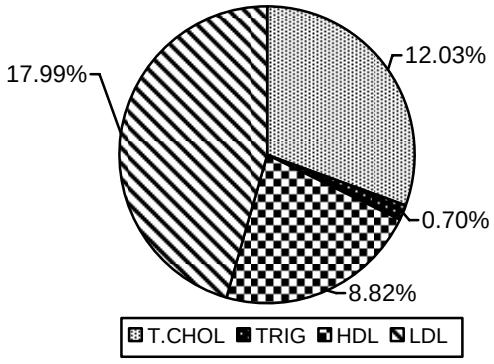

Figure-1: Percentage Changes with Garlic From Week 0 to Week 12 On Lipid Profile in Patients With Type 2 Diabetes Mellitus

Table-2: Changes in lipid parameters from week 0 to week 6 & week 12 of treatment with garlic and placebo in patients with type 2 diabetes mellitus (Values are given as Mean ±SEM)

Lipid profile	Drugs	Week 0 (mg/dl)	Week 6 (mg/dl)	P Value Week 0 -6	Week12 (mg/dl)	P Value Week 0-12
T. Chol	DR1	228.23 ± 4.54 (n=35)	209. 3 ± 4.95 (n=33)	<0.001	200.77 ± 5.07 (n=33)	<0.001
	DR2	220.45 ± 2.25 (n=35)	218.64 ± 2.30 (n=32)	N.S	218.34 ± 3.05 (n=32)	N.S
TG	DR1	202.03 ± 8.59 (n=35)	203.88 ± 8.93 (n=33)	N.S	203.45 ± 8.81 (n=33)	N.S
	DR2	200.6 ± 5.05 (n=35)	199.42 ± 5.58 (n=32)	N.S	198.58 ± 5.25 (n=32)	N.S
HDL	DR1	38 ± 1.73 (n=35)	39.85 ± 1.44 (n=33)	N.S	41.35 ± 1.31 (n=33)	<0.05
	DR2	36.58 ± 3.45 (n=35)	36.6 ± 3.20 (n=32)	N.S	37.2 ± 3.86 (n=32)	N.S
LDL	DR1	163.57 ± 4.66 (n=35)	143.42 ± 4.61 (n=33)	<0.001	133.42 ± 4.61 (n=33)	<0.001
	DR2	167 ± 3.37 (n=35)	165.2 ± 3.45 (n=32)	N.S	164.3 ± 3.56 (n=32)	N.S

DR1 = Garlic group, DR2 = Placebo group, Chol. = Total Cholesterol, TG. = Triglyceride, HDL = High Density lipoprotein, LDL = Low Density Lipoprotein, ± indicates Standard Error of mean, All observations were measured in mg/dl. Figures in Parenthesis indicates number of patients.

Siegel et al[12] studied the effects of garlic on genesis and progression of arteriosclerosis but also reported a decrease in total cholesterol and LDL cholesterol, increase in HDL cholesterol but contrary

to our study also showed a reduction in serum triglyceride level.

Adler et al[13] reported a reduction of total cholesterol by (12 % by week 12) and LDL-C (14% by week 12) but expected decrease in triglyceride was not seen. The lowering 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 hydroxymethylglutaryl-CoA reductase, by allicin. The active principle of garlic, allicin is not formed until the reaction between alliin and alliinase take place in aqueous solutions when fresh garlic is chopped or when garlic powder is dissolved in the stomach. The active alliin-alliinase system is only present in fresh garlic and in carefully dried garlic powder. The amino acid L- alliin and the enzyme alliinase are currently regarded as the marker substances for fresh garlic and powdered garlic preparations. In fresh garlic they are present in separate compartments, so that no enzymic conversion can take place. The contradiction to demonstrate the hypochloremic effect of the garlic powder tablets in the present study while other failed,[14-18,21] which showed garlic to be ineffective, may be attributed to the high allicin yield of the garlic powder used in our study.

Isaacsohn et al[21] have observed no change in serum cholesterol levels in patients with hypercholesterolemia after 12 weeks of treatment with garlic powder 900 mg per day, while significant reduction in total cholesterol and LDL cholesterol as well as moderate increase in HDL cholesterol but no change in triglyceride levels was observed in our study.

The slight non-significant increase in triglyceride observed in our study is in accordance with that of Jain et al[19] who reported a slight increase in triglyceride in both the placebo and garlic treated groups. The reason for this apparent discrepancy in our triglyceride data as compared with that of other studies is not clear. Voluntary modification of diet may have partly accounted for the changes in triglyceride observed in our study.

CONCLUSION

This study suggests possible small short term benefits of garlic on lipid profile. Treatment with garlic tablets standardized to deliver 0.6% allicin, the active ingredient of garlic, produced a significantly greater reduction in total cholesterol and LDL-cholesterol and moderate increase in HDL cholesterol than that with placebo while it has no significant effect on serum triglyceride levels. Garlic was very well tolerated in patients with type 2 diabetes mellitus. Controlled Clinical Trials of longer duration are needed to assess the long-term benefit of garlic on vascular and circulatory disease processes.

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