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Research Article

To study the antihyperglycaemic and lipid lowering effect of garlic as an adjunct to metformin in patients of type 2 diabetes mellitus with obesity

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ABSTRACT

Background: Diabetes mellitus is a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia associated with disturbances of carbohydrate, fat and protein metabolism. The treatment constitutes lifestyle management, exercise, weight control and antihyperglycaemic drugs like sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones, and meglitinide. Garlic has shown to have anti-hyperglycaemic and lipid lowering effects in various animal and human studies. Thus, this study was conducted to assess the antihyperglycaemic and lipid-lowering properties of Garlic in type2 diabetes patients with obesity.

Methods: This was an open labelled prospective comparative study conducted on Type 2 diabetes mellitus patients with obesity where a total of 60 patients divided into two groups of 30 each (of either sex) were enrolled. Group 1 was given Tab. metformin 500mg BD/TDS after meals. Group 2 was given Tab. metformin in a dose of 500mg BD/TDS after meals along with Cap. Garlic (Allium sativum) 250mg BD. Patients were routinely investigated for fasting blood sugar, HbA1c and lipid profile i.e. Serum Cholesterol, HDL-C, Triglycerides and LDL-C at the start of the study. Patients were followed up at an interval of two weeks upto 12 weeks. Data obtained at the end of the study was statistically analysed using Student's –t test.

Results: It was observed that both metformin and garlic reduced FBG and HbA1c significantly but percentage reduction in FBG was more with garlic but, change in HbA1c was not significant. Fall in total CHL, TG, LDL and an increase in HDL were more pronounced in patients treated with Garlic when given along with Metformin.

Conclusions: Therefore, garlic showed better results as an antihyperglycaemic and lipid lowering agent.

Keywords: Type 2 diabetes, Allium Sativum, Fasting blood glucose, Lipid profile

INTRODUCTION

Diabetes mellitus is a metabolic disorder of multiple aetiology characterized by chronic hyperglycaemia associated with disturbances of carbohydrate, fat and protein metabolism due to defect in insulin secretion, insulin action, or both. Diabetes mellitus presents typically with characteristic symptoms such as polydipsia, polyuria, blurring of vision and weight loss. In its most severe forms, ketoacidosis or a non-ketotic hyperosmolar state may develop and lead to stupor, coma and, in absence of effective treatment, death.[1] The overall prevalence of diabetes in global population is approximately 6 percent, of which 90 percent is type 2 diabetes.[2] India had 32 million diabetics in 2000 and it is expected to increase to 80 million by 2030.[3]

Diabetes Mellitus is divided into two major categories: type 1 diabetes and type 2 diabetes. The most prominent clinical feature is hyperglycaemia (fasting plasma glucose level >126 mg/dL, or glycosylated hemoglobin A1c (HbA1c) >6.5%).[4] In most patients with type 2 diabetes, the onset is in adulthood, most commonly in obese people over 40 years of age. The long-term complications of Type 2 DM are macrovascular complications (hypertension, dyslipidemia,

myocardial infarction, stroke), microvascular complications (retinopathy, nephropathy, diabetic neuropathy, diarrhoea, neurogenic bladder, impaired cardiovascular reflexes, sexual dysfunction), and diabetic foot disorders.[5]

The general consensus on treatment of type 2 diabetes is lifestyle management like exercise and weight reduction. The Pharmacological therapies include sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones, and meglitinide.

Metformin is being used in the early stage management of type 2 diabetes as the first choice oral agent, along with appropriate diet control and lifestyle advice.[6] It also has a role in preventing people with impaired glucose tolerance (IGT) progressing to type 2 diabetes.[7] Metformin acts by reducing gluconeogenesis (elevated in type 2 diabetes) and improving insulin sensitivity. This is the only biguanide used in clinical practice.

Alternative therapies with anti-diabetic activity have been researched relatively extensively, particularly in India. The World Health Organization Expert Committee on diabetes has recommended that traditional medicinal herbs can be further investigated for the treatment of diabetes.[8]

The following are the most commonly used medicinal herbs - Ginseng species, Momordica charantia (Bitter melon), Trigonella foenum graecum (Fenugreek), Allium cepa (Onion) and Allium sativum (Garlic).

Garlic (Allium sativum) holds a unique position in history and was recognized for its therapeutic potential. Extensive research work has been carried out on the health promoting properties of garlic, often referred to its sulfur containing metabolites i.e. allicin and its derivatives.[9] It also provides cardiovascular protection mediated by lowering of cholesterol, blood pressure, anti-platelet activities, and thromboxane formation thus providing protection against atherosclerosis and associated disorders.

It has been shown to reduce blood sugar and has lipid lowering properties in various animal and clinical studies.

Thus, it can be analysed from various studies that garlic has been shown to demonstrate antihyperglycaemic and lipid lowering effect in patients of diabetes mellitus and obesity.

METHODS

This was an open labeled prospective randomized comparative study which was conducted in Type 2 diabetes mellitus patients with obesity. The patients visiting the Medicine OPD at Sri Guru Ram Das Charitable hospital attached to Sri Guru Ram Das Institute of Medical Sciences and Research, Vallah, Sri Amritsar were enrolled in the study. A total of 60 patients of either sex fulfilling the inclusion criteria were included in the study and were divided randomly into two groups of 30 each. Group 1 was given the control drug metformin in dosage of 500 mg BD/TDS after meals as per the blood sugar profile and tolerance of the drug by the patients.

Each patient was given the test drug i.e. Garlic along with Metformin for a total of 12 weeks duration. The test drug used was Cap. GARLIC (Allium Sativum) available in the brand name of LASUNA of strength 250 mg manufactured by The Himalaya Drug Company, Bangalore. The dosage given was one capsule twice a day after meals. Group 2 were given metformin in dosage of 500 mg BD/TDS as per the blood sugar profile and tolerance of the drug by the patient along with Garlic (Allium sativum) in dosage of 250 mg BD after meals.

Patients were followed up at 2 weekly interval and were routinely investigated for fasting blood sugar (estimated by GOD-POD method)[10] at an interval of 0 day, 2, 4 ,6, 8, 12 weeks and for HbA1c (estimated by Nycocard Reader)[11] and lipid profile i.e. Serum cholesterol, Triglycerides, HDL-C and LDL-C (estimated by CHOD-PAP[12], GPO-Trinder[13] and Phosphotungistic acid[14] methods respectively) and Body Mass Index[15] was also estimated at the beginning and at the end of study. This study was conducted in accordance with the principles of good clinical practices and the Declaration of Helsinki. The approval of Ethics Committee of the institution was obtained prior to the conduct of study. Written Informed consent were sought from all the patients and all the risks and benefits were explained to them in their own language. Patients were advised to undertake diet control and regular exercise as per protocol designed by WHO. The selection of the patients was done on the basis of inclusion and exclusion criteria.

Inclusion criteria:

Male/ Female with type 2 diabetes aged 40-75 years showing FBG >126 mg/dl, HbA1c >6.5%[5] and BMI levels >25 kg/m^2.[15]

Exclusion criteria:

Patients with Type 1 diabetes, patients with past h/o ketoacidosis, bleeding disorders, surgery in the past 6 weeks, hypersensitivity to the test drug, any cardiovascular, hepatic and renal disorder and pregnant females were excluded from the study.

The data obtained were tabulated as mean ± standard deviation (SD) and analyzed using student's t test. The level of significance was determined as its 'p' value with $p > 0.05$ taken as not significant, $p < 0.05$ taken as significant at 5% significance level, $p < 0.01$ taken as significant at 1% significance level and $p < 0.001$ taken as highly significant.

RESULTS

Age of participants varied from 40 - 75 years. Mean age was 53.8 ± 12.2 and 52.8 ± 11.0 years in Groups I and II respectively and this difference was statistically non-significant (p> 0.05).

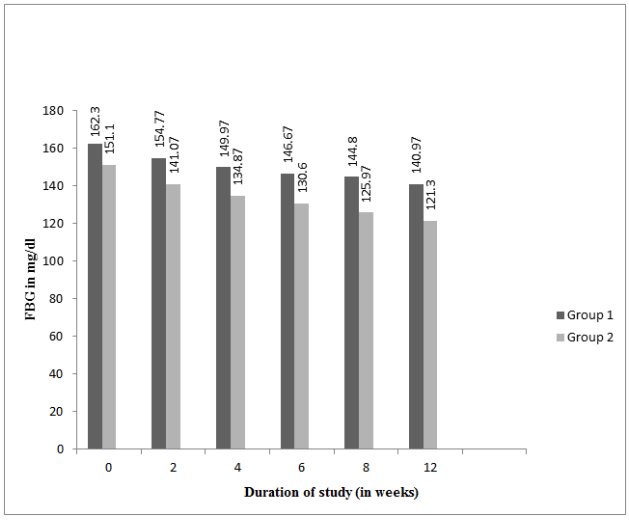

Figure 1: Fasting Blood Glucose (FBG) levels on Day 0 (zero), 2nd, 4th, 6th, 8th and 12th week in Group I and Group II.

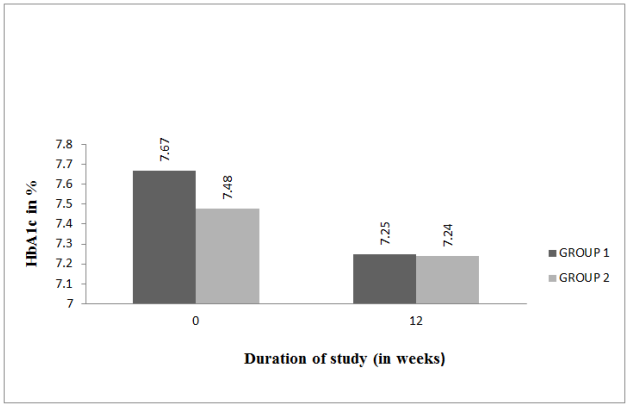

Figure 2: Glycosylated haemoglobin (HbA1c) levels on Day 0 and 12th week in Group I and Group II.

Fall in mean FBG levels was highly significant (p < 0.001) in both the groups i.e. group I on metformin as monotherapy and group II on garlic in addition to metformin at biweekly intervals after the completion of treatment as compared to baseline (Figure 1).

Mean fall in HbA1c levels was highly significant (p < 0.001) from day 0 to the 12th week of study period in both the groups (Figure 2).

There was a highly significant (p<0.001) fall in mean CHL, TGs and LDL-C levels and a highly significant (p <0.001) increase in HDL-C levels from day 0 to the 12th week of study period in both the groups (Figure 3).

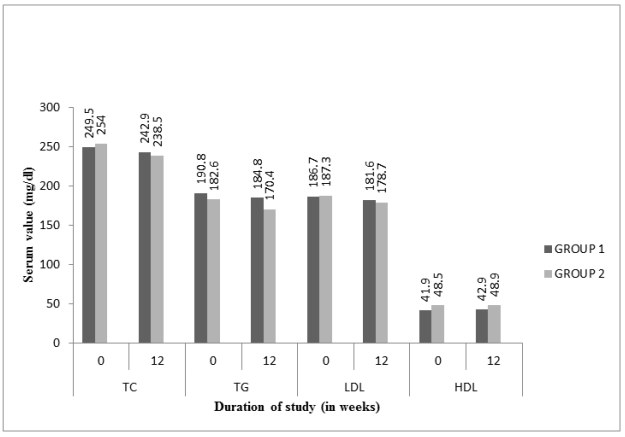

Figure 3: Lipid profile on Day 0 and 12th week in Group I and Group II.

BMI levels also showed a highly significant (p <0.001) fall from day 0 to the 12th week of study period in both the groups (Figure 4).

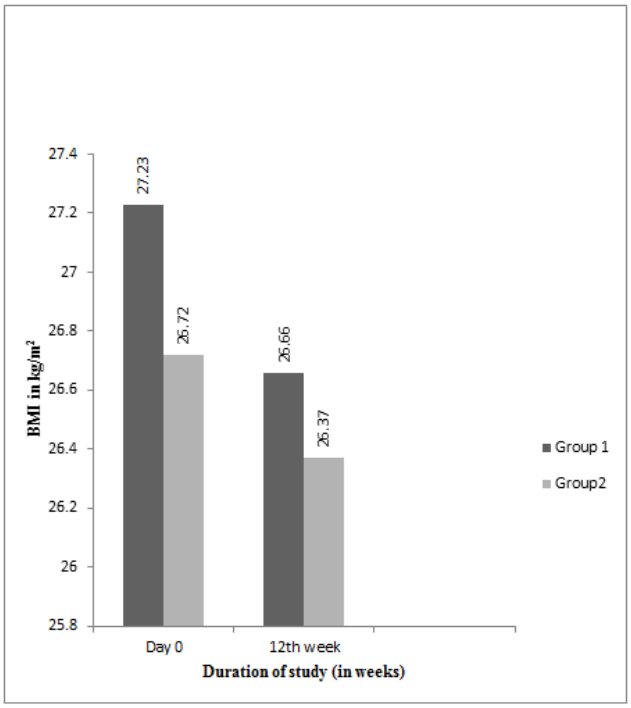

Figure 4: BMI levels on Day 0 and 12th week in Group I and Group II.

DISCUSSION

Glycaemic profile:

In group I, patients received Metformin 500 mg BD after meals for 3 months. The baseline FBG was 162.30 ± 16.73 mg/dl which declined progressively and reached a nadir of 140.97 ± 10.20 mg/dl at the end of 3 months. The mean fall of 21.33 ± 10.53 mg/dl was statistically highly significant (p <0.001). In the present study, the mean HbA1c at the beginning of the study was 7.67 ± 0.97 % and at the end of the study, it decreased to 7.25 ± 0.77 %.

The mean fall was 0.35 ± 0.34 % which was highly significant (p<0.001).

In group II, patients received Metformin 500 mg BD and Garlic 250 mg BD after meals for 3 months. The mean FBG at the baseline was 151.10 ± 13.51 mg/dl and this decreased to 121.30 ± 6.91 mg/dl at the end of 3 months of study period. The mean fall was 29.80 ± 9.11 mg/dl and it was statistically highly significant (p < 0.001).

Also, the HbA1c level was 7.48 ± 0.59 % in the beginning and decreased to 7.24 ± 0.59 % at the end of 3 months. The mean fall in HbA1c level was 0.24 ± 0.27 % which was highly significant (p < 0.001).

Stumvoll M *et al*[16] conducted a study on 10 patients on Metformin which showed highly significant decrease in FBG and HbA1c at the end of study (p < 0.001). Their results were in confirmity with those in the present study in which highly significant decrease in FBG and HbA1c (p< 0.001) were observed**.**

Ashraf R *et al*[17] where conducted a 24 week single blind, placebo controlled study in 210 type 2 DM patients on Garlic treatment which showed a highly significant decrease (p < 0.005) in FBG as well as HbA1c, which was in confirmity to the present study where a decrease in FBG and HbA1c levels were found to be highly significant (p < 0.001) at the end of study in patients treated with garlic as an adjunct to metformin.

Lipid profile:

In the present study in group I, significant difference was observed in the lipid profile i.e. the serum total CHL at the beginning of the study was 249.53 ± 20.44 mg/dl and at the end of 3 months of study period, it was 242.97 ± 20.83 mg/dl. The mean fall was 6.57 ± 3.51 mg/dl which was statistically highly significant (p <0.001). Patients also showed a significant decrease in serum TG and increase in serum HDL levels which were 6.07 ± 4.06 mg/dl (p < 0.001) and 1.03 ± 1.32 mg/dl (p < 0.001) respectively. The serum LDL levels at the beginning of the study were 186.70 ± 26.35 mg/dl and at the end of 3 months these levels decreased to 181.60 ± 25.36 mg/dl which was highly significant (p < 0.001).

Changes in lipid profile were observed in group II i.e. the mean total CHL levels in the beginning were 254.07 ± 16.03 mg/dl, which decreased to 238.50 ± 19.49 mg/dl at the end of 3 months (p < 0.001). The patients also showed a decrease in serum TG levels from 182.60 ± 6.44 mg/dl to 170.47 ± 7.17 mg/dl (p < 0.001) at the end of 3 months. Also, the serum HDL levels showed increase from 48.50 ± 8.96 mg/dl to 48.97 ± 9.14 mg/dl (p < 0.001).

The serum LDL levels decreased from 187.33 ± 36.46 mg/dl to 178.77 ± 34.39 mg/dl (p < 0.001) at the end of 3 months.

Wulfelle *et al*[18] conducted a randomized controlled study for 6 weeks on patients with type 2 DM on metformin which showed a significant decrease in serum CHL, TG and LDL levels (P< 0.05). Whereas, contrary to the above findings in the present study decrease in serum CHL, TG and LDL levels was highly significant (p < 0.001).

In another study conducted by Wu MS *et al*[19] on 12 patients with type 2 DM on metformin therapy a significant decrease (p < 0.05) in FBG, serum TG levels and a significant increase in serum HDL levels at the end of study was found. It was in confirmity to the present study where highly significant (P < 0.001) decrease in FBG and TG levels and significant (p < 0.05) increase in serum HDL levels were observed.

Ashraf R *et al*[20] conducted a 12 week randomized single-blind placebo controlled study on type 2 DM patients on Garlic which showed a highly significant (p < 0.001) decrease in total CHL and serum LDL levels. Serum HDL level also showed a significant (p < 0.05) increase. But, no significant difference was seen in serum TG levels. This was comparable to the present study, where a highly significant (p < 0.001) decrease in total CHL, serum TG and serum LDL levels and highly significant (p < 0.001) increase in serum HDL levels were observed.

In another study conducted by Santen RJ *et al*[21] lipid lowering effect of Garlic in 40 diabetics with hyperlipidemia was studied which showed a highly significant (p < 0.001) decrease in serum TG levels and a significant (p < 0.05) decrease in total CHL levels respectively, which showed comparable difference with the present study where decrease in serum CHL and serum TG levels were highly significant (p< 0.001).

Body Mass Index (BMI):

Also, in the present study in group I BMI level was 27.23 ± 2.77 kg/m^2 in the beginning of study which decreased to 26.66 ± 2.69 kg/m^2 at the end of 3 months.

BMI levels also showed a decrease from 26.72 ± 1.74 kg/m^2 to 26.37 ± 1.70 kg/m^2 from the beginning to the end of study of 3 months in group II.

Hundal RS and Inzucchi S[22] in a study conducted on 150 patients on metformin showed a significant (p < 0.05) decrease in BMI levels at the end of study which was comparable to the present study where highly significant decrease (p < 0.001) in BMI level was observed.

CONCLUSIONS

At the end of 3 months it was observed that both metformin and garlic reduced FBG and HbA1c significantly but the percentage change in FBG was more with garlic whereas, the difference in mean percentage change in HbA1c was not significant.

Metformin and garlic both showed beneficial effect on lipid profile parameters. However, fall in total CHL, TG, LDL and an increase in HDL were more pronounced with garlic.

Conclusively, though metformin and garlic were effective in lowering FBG, HbA1c and lipid profile. Yet garlic showed better results as an antihyperglycaemic and lipid lowering agent as an adjunct to metformin.

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