Original Article

Effects of Garlic (*Allium sativum*) on Blood Glucose Level in Type 2 Diabetes Mellitus Patients Treated with Metformin

Md. Shefat Jahan Shoshi[1], Hasina Akter[2]
Received: December 14, 2016 Accepted: September 1, 2017
doi: http://dx.doi.org/10.3329/jemc.v7i3.34075

Abstract

Background*: Diabetes mellitus is a heterogeneous group of metabolic disorders with microvascular and macrovascular complications which are the major causes of morbidity and mortality in diabetic patients. Anti-diabetic drugs are available in modern medicine, but prolonged use of these drugs may produce some side effects. Garlic due to some of its active components can improve glycemic status.* ***Objective****: To observe the effect of garlic (Allium sativum) in patients with type 2 diabetes mellitus with obesity.* ***Materials and Methods****: This prospective interventional study was carried out in the Department of Pharmacology & Therapeutics, Sir Salimullah Medical College (SSMC), Dhaka from July 2014 to June 2015. Total 60 type 2 diabetes mellitus with obesity subjects of both sexes in the age range 40 to 60 years were included in this study. They were selected on the basis of inclusion and exclusion criteria from Outpatient Department of Bangladesh Institute of Rehabilitation of Diabetes, Endocrine and Metabolic Disorder (BIRDEM) Hospital, Dhaka. The subjects were divided into two groups by simple random sampling. One was Group A and another was Group B. The subjects (30) of Group A were supplemented only metformin at a dose of 1000 mg per day. The subjects (30) of Group B were supplemented metformin at a dose of 1000 mg and garlic in capsule form at a dose of 500 mg per day. They were studied two times, on day-1 (1st day of metformin treatment, Group A_1), on 12 weeks (after 12 weeks of metformin treatment, Group A_2). Subjects of Group B were also studied two times on day-1 (before supplementation of garlic, Group B_1) and on 12 weeks (after 12 weeks supplementation of garlic and metformin, Group B_2). Fasting blood glucose level and postprandial blood glucose level of all subjects were measured by glucose oxidiase method. Blood HbA1c level of all participants was measured by immunoassay method. The statistical analysis was done by using paired and unpaired sample 't' test.* ***Results****: In this study, the mean FBG and PPBG levels decreased nonsignificantly ($p>0.05$) after 12 weeks treatment of metformin in comparison to 1st day of metformin treatment. Again, the mean FBG and PPBG levels decreased significantly after 12 weeks supplementation of metformin and garlic compared to before supplementation of garlic ($p<0.001$) and after 12 weeks supplementation of metformin ($p<0.05$). Again, blood HbA1c level decreased nonsignificantly ($p>0.05$) after 12 weeks treatment of metformin and metformin and garlic supplementation compared to 1st day of metformin treatment and before supplementation of garlic.* ***Conclusion****: The present study reveals that garlic (Allium sativum) has significant effect on improvement of glycemic status.*

Key words*: Diabetes Mellitus; Garlic; FBG; PPBG; HbA1c*

J Enam Med Col 2017; 7(3): 151–155

Introduction

Diabetes mellitus is defined as chronic or persistent hyperglycemia due to deficiency of insulin secretion or of insulin action, or both.[1] It is the most growing metabolic disease which is characterized by altered carbohydrate, lipid and protein metabolism.[2] According to World Health Organization (WHO) the prevalence of diabetes mellitus in the global population is approximately 9%, of which 90% is type 2 diabetes mellitus. However, the prevalence

1. Assistant Professor, Department of Pharmacology & Therapeutics, Sheikh Sayera Khatun Medical College, Gopalgonj
2. Assistant Professor, Department of Physiology, International Medical College, Gushulia Sataish, Tongi, Gazipur
Correspondence *Md. Shefat Jahan Shoshi, Email: shoshishefat11@gmail.com*

of diabetes mellitus in Bangladesh is approximately 10%. The incidence of diabetes mellitus is increasing day by day, which can be increased from 150 million to 300 million by the year 2025.[3] Characteristic symptoms of diabetes mellitus are thirst, dry mouth, polydipsia, polyuria, tiredness, fatigue, blurring of vision, and weight loss; in its most severe form, symptoms are ketoacidosis, nonketotic hyperosmolar coma and death.[4] The principal laboratory findings of type 2 diabetes mellitus is hyperglycemia, either fasting blood glucose (FBG) level 126 mg/dL or glycosylated hemoglobin (HbA1c) 6.5%.[1]

Type 2 diabetes mellitus is a chronic disorder characterized by chronic hyperglycemia with long term macrovascular and microvascular complications.[5] According to World Health Organization type 2 diabetes constitutes about 85−95% of all diabetes. This increasing trend of type 2 diabetes mellitus is associated with rapidly changing lifestyle such as increasing urbanization, dietary habits, reduced physical activity along with population aging.[3] Type 2 diabetes mellitus most commonly occurs after 40 years.[4]

The general consensus is that the main treatment of type 2 diabetes is lifestyle management, like exercise and weight reduction. Pharmacological agents, including sulfonylureas, biguanides, alpha-glucosidase inhibitors, thiazolidinediones and meglitinide, are also used; however, long-term complications of type 2 diabetes mellitus are unaltered with these agents.[6] Metformin is currently being used in type 2 diabetes as the first choice oral agent, along with appropriate diet control and modification of lifestyle.[7] Metformin acts primarily by reducing the hepatic glucose output and improving insulin sensitivity in the liver and muscle.[8] Metformin has pleiotropic vascular effects that act on endothelial imbalance, probably increasing nitric oxide bioavailability, decreasing atheroma plaque growth, improving the atherogenic lipid profile, and inhibiting lipid incorporation into vessel walls, thereby inhibiting vascular smooth muscle cell proliferation.[9] The American Diabetic Association has recommended metformin as a first line agent for the treatment of type 2 diabetes as metformin helps in weight loss and lowers fasting plasma insulin concentrations, total and low-density lipoprotein cholesterol, and free fatty acids.[10] Metformin is useful in the prevention of type 2 diabetes; the landmark Diabetes Prevention Program concluded that metformin is effective preventing the new onset of type 2 diabetes in middle-aged obese persons with impaired glucose tolerance and fasting hyperglycemia.[11] It is interesting that metformin did not prevent diabetes mellitus in older, leaner prediabetic subjects.[7] However, long-term complications are not altered with metformin therapy. Previous studies have shown mixed results of metformin therapy on C-reactive protein (CRP), but the studies on non-diabetic patients have reported greater inhibitory effects on CRP than the studies on diabetics. Thus, the effect of metformin therapy on CRP needs to be established in type 2 diabetic patients.[12] However, epidemiologic studies suggest that metformin use may dramatically reduce the risk of some cancers.[7] The World Health Organization Expert Committee on diabetes has recommended that traditional medicinal herbs can be further investigated for the treatment of diabetes mellitus. The most commonly used medicinal herbs are *Allium sativum* (garlic), Ginseng species, *Momordica charantia* (bitter melon), *Trigonella foenum-graecum* (fenugreek) and *A. cepa* (onion).[3]

Allium sativum, commonly known as garlic, is widely used around the world with a history of human use of over 7,000 years for culinary and medicinal purpose.[13,14] Recently, garlic has been used in the form of garlic oil, garlic powder and pills for certain therapeutic purposes.[15] Garlic has a reputation in particular because of its widespread health use around the world as a dietary as well as thera¬peutic supplement.[16] Garlic contains a variety of effective compounds, such as allicin, a sulfur-containing compound that exhibits hypocholesterolemic[17], antioxidant[18], hypotensive, anticoagulant and antithrombotic[19] effects. Garlic exhibits a wide range of properties including immunomodulatory and hepatoprotective effect.[20] Garlic extracts are believed to possess beneficial effects for the prevention of cardiovascular diseases.[21] Garlic helps to maintain electrolyte balance, especially sodium and potassium.[22]

It has been observed that consuming 10 gm of raw garlic per day in two meals for six weeks can reduce blood glucose and HbA1c level in patients with diabetes mellitus.[23] Some other researchers showed that daily 40 mg garlic consumption may improve blood HDL-cholesterol levels.[24] In this perspective, we designed this study to observe the effect of garlic in obese type 2 diabetic patients.

Materials and Methods

This prospective interventional study was carried out in the Department of Pharmacology & Therapeutics, Sir Salimullah Medical College (SSMC), Dhaka between 1st July 2014 and 30th June 2015. According to inclusion criteria all the study subjects were selected from Outpatient Department of Bangladesh Institute of Rehabilitation of Diabetes, Endocrine and Metabolic Disorder (BIRDEM) Hospital, Dhaka. After proper counseling, the aim, objectives, risk and the procedure of the study were explained in details to the subjects. Respondents who gave consent were recruited as research participants and were allowed to withdraw themselves from the study even after participation whenever they like. Ethical permission was taken from the Institutional Ethics Committee (IEC) of Sir Salimullah Medical College. Subjects having type 1 diabetes mellitus, hypertension, heart disease, kidney disease, liver disease, thyroid disease, infectious disease etc were excluded from the study.

The subjects were divided into two groups by simple random sampling. One was Group A and another was Group B. The subjects (30) of Group A were supplemented only metformin at a dose of 1000 mg per day. The subjects (30) of Group B were supplemented metformin at a dose of 1000 mg and garlic in capsule form at a dose of 500 mg per day. They were studied two times ─ on day-1(1st day of metformin treatment, Group A_1) and on 12 weeks (after 12 weeks of metformin treatment, Group A_2). Similarly Group B subjects were also studied two times ─ on day-1 (before supplementation of garlic, Group B_1) and on 12 weeks (after 12 weeks supplementation of garlic and metformin, Group B_2). Their general information and data were collected and all the information was recorded in a prefixed questionnaire.

With all aseptic precautions, five mL of venous blood was drawn from median cubital vein by sterile disposable syringe. To assess their glycaemic status FBG and PPBG level were measured by glucose oxidase method and blood HbA1c level measured by immunoassay method in the laboratory of Department of Biochemistry of BSMMU, Dhaka. Data were analyzed by Paired sample 't' test. p value <0.05 was taken as level of significance.

Garlic supplementation

All the subjects of Group B of this study were supplemented with garlic capsule containing 250 mg garlic two times daily for 12 weeks.[13]

Results

Table I shows age, fasting blood glucose (FBG), postprandial blood glucose (PPBG) and HbA1c in different groups of subjects and Table II shows the comparison of FBG, PPBG and HbA1c level in different groups of subjects.

In this study, FBG, postprandial blood glucose (PPBG) and HbA1c levels did not show significant change after 12 weeks of treatment of metformin in comparison to 1st day of metformin treatment. Mean FBG and PPBG levels decreased significantly but HbA1c level decreased nonsignificantly after 12 weeks supplementation of metformin and garlic compared to before supplementation levels.

Table I: Age, fasting blood glucose (FBG), PPBG and HbA1c% in different groups (n=60)

Parameters	Group A_1 (n=30)	Group B_1 (n=30)
Age (years)	48.23 ± 4.59	47.83 ± 4.71
FBG (mmol/L)	8.52 ± 0.29	8.49 ± 0.24
PPBG (mmol/L)	10.69 ± 0.28	10.46 ± 0.24
HbA1c (%)	7.49 ± 0.23	7.44 ±0.12

Independent sample 't' test was done for comparison between the groups. Figures in parentheses indicate ranges. Group A_1: Metformin treated (on day-1); Group B_1: Before supplementation of garlic (on day-1)

Table II: FBG, PPBG and HbA1c level in different groups (n=60)

Groups	FBG (mg/dL)	PPBG (mg/dL)	HbA1c (%)
A1 (n=30)	8.52 ± 0.29 (8.05−9.10)	10.69 ± 0.28 (8.6−11.4)	7.49 ± 0.23 (7.20−1.33)
A2 (n=30)	8.48 ± 0.24 (7.48−8.35)	9.45 ± 0.26 (8.23−9.50)	7.42 ±0.22 (7.20−7.90)
B1 (n=30)	8.49 ± 0.24 (8.20−9.50)	10.46 ± 0.24 (8.55−11.35)	7.44 ±0.12 (7.25−7.78)
B2 (n=30)	6.30 ± 0.18 (5.42−7.23)	7.55 ± 0.21 (6.3−8.78)	7.27 ± 0.05 (7.20−7.35)
		p values	
A_1 vs A_2	1.000^{ns}	1.000^{ns}	1.000^{ns}
A_2 vs B_2	0.05*	0.01**	0.000***
B_1 vs B_2	0.000***	0.000***	0.569^{ns}

Paired-sample t test within the group were performed. Figures in parentheses indicate ranges.
*= Significant at $p < 0.05$; ** = Significant at $p < 0.01$; *** = Significant at $p < 0.001$; ns = Nonsignificant

Discussion

Antidiabetic medications have significant side effects that are not familiar with patients, have limited effectiveness or lack evidence of having impact on the course of the disease. An increasing interest in herbal and complementary medicine has led to a search for effective natural therapies that have significant effects on blood glucose level.

The present study was done to observe the effect of garlic *(Allium sativum)* on type 2 diabetes mellitus subjects with obesity. For this, the levels of fasting blood glucose (FBG), postprandial blood glucose (PPBG) and HbA_1c were measured to assess their glycemic status.

Fasting blood glucose (FBG) level

In this study, FBG level did not decrease significantly ($p>0.05$) after 12 weeks' treatment with metformin in comparison to that of before metformin treatment (on day-1) in Group A. FBG level decreased significantly ($p<0.001$) after 12 weeks' treatment with metformin plus supplementation of garlic compared to that of before supplementation of garlic (on day-1). Moreover, FBG level decreased significantly ($p<0.05$) after 12 weeks treatment of metformin plus supplementation of garlic compared to that of after 12 weeks treatment with metformin only. This finding is consistent with that of some other investigators.[5]

Postprandial blood glucose (PPBG) level

In this study, PPBG level did not decrease significantly ($p>0.05$) after 12 weeks treatment with metformin in comparison to that of before metformin treatment (on day-1) in Group A. PPBG level decreased significantly ($p<0.001$) after 12 weeks treatment with metformin plus supplementation of garlic compared to that of before treatment with metformin plus supplementation of garlic (on day-1). Moreover, PPBG level decreased significantly ($p<0.01$) after 12 weeks of treatment with metformin plus supplementation of garlic compared to that of after 12 weeks treatment with metformin only. This finding is similar with that of some other investigators.

Blood HbA1c level

In this study blood HbA1c level did not decrease significantly ($p>0.05$) after 12 weeks treatment with metformin in comparison to that of before metformin treatment (on day-1) in Group A. Blood HbA1c level was decreased nonsignificantly ($p>0.05$) after 12 weeks treatment with metformin plus supplementation of garlic compared to that of before supplementation of garlic (on day-1). Moreover, blood HbA1c level was decreased significantly ($p<0.01$) after 12 weeks treatment with metformin plus supplementation of garlic compared to that of after 12 weeks treatment of metformin. This finding is consistent with that of Kumar et al.[5]

From this study, it can be concluded that garlic *(Allium sativum)* has got significant effect on improvement of glycemic status with lowering fasting blood glucose level and postprandial blood glucose level.

References

1. Pearson ER, McCrimmon RJ. Diabetes mellitus. In: Walker BR, Colledge NR, Ralston SH, Penman ID (eds). Davidson's principles & practice of medicine. 22nd edn. China. Churchil Livingstone Elsevier, 2014: 797−836.
2. Mutalik S, Sulochana B, Chetana M, Udupa N, Devi UP. Preliminary studies on acute and subacute toxicity of an antidiabetic herbal preparation, Dianex. Indian Journal of Experimental Biology 2003; 41: 316−320.
3. World Health Organization experts committee on status report on diabetes mellitus. 2012 July; 10−22.
4. Field MJ, Burnett L, Sullivan DR, Stewart P. Clinical biochemistery and metabolism. In: Walker BR, Colledge NR, Ralston SH, Penman ID (eds.). Davidson's principles & practice of medicine. 22nd edn. China. Churchil Livingstone Elsevier 2014; 427−460.
5. Kumar R, Chhatwal S, Arora S, Sharma S, Singh J, Singh N et al. Antihyperglycemic, antihyperlipidemic, anti-inflammatory and adenosine deaminase–lowering effects of garlic in patients with type 2 diabetes mellitus with obesity. J of Diabetes, Metabolic Syndrome and Obesity 2013; 6: 49–56.
6. De Fronzo RA. Pharmacologic therapy for type 2 diabetes mellitus. Ann Intern Med 1999; 131(4): 281–303.
7. Matha S, Kennedy N. Pancreatic hormones & antidiabetic drugs. In: Katzung BG, Masters SB, Trevor AJ (eds). Basic & Clinical Pharmacology. 12th edn. India. Tata McGraw-Hill, 2012: 757.
8. Lima LM, Wiernsperger N, Aguiar KLG, Bouskela E. Short-term treatment with metformin improves the cardiovascular risk profile in first-degree relatives of subjects with type 2 diabetes mellitus who have a metabolic syndrome and normal glucose tolerance with¬out changes in C-reactive protein or fibrinogen. Clinics (Sao Paulo) 2009; 64(5): 415–420.
9. Bouskela E, Patel P, Wiernsperger N, Aguiar KLG. Short-term treatment with metformin improves the cardiovascular risk profile in first-degree relatives of subjects with type 2 diabetes mellitus who have a metabolic syndrome and normal glucose tolerance without changes in C-reactive protein or fibrinogen. Clinics (Sao Paulo) 2009; 64(6): 410−415.
10. American Diabetes Association. Standards of medical care in diabetes ─ 2011. Diabetes Care 2011; 34(1): S11–S61.
11. Haffner S, Temprosa M, Crandall J. Diabetes Prevention Program Research Group. Intensive lifestyle intervention or metformin on inflammation and coagulation in participants with impaired glucose tolerance. Diabetes 2005; 54(5): 1566–1572.
12. Caballero AE, Delgado A, Aguilar-Salinas CA, Herrera AN, Castillo JL, Cabaera T. The differential effects of metformin on markers of endothelial activation and inflammation in subjects with impaired glucose tolerance: a placebo-controlled, randomized clinical trial. J Clin Endocrinol Metab 2004; 89(8): 3943–3948.
13. Ensminger AH. Foods and Nutrition Encyclopedia. CRC Press 1994; 1: 750.
14. Simonetti G, Schuler S. Simon and Schuster's guide to herbs and spices. Middle-East J Sci Res 1990; (1): 75.
15. Elkayam A, Mirelman E, Peleg M, Wilcheh T, Miron A, Rabinkov M et al. The effects of allicin on weight in fructose induced hyperinsulinemic, hyperlipidemic, hypertensive rats. Am J Hypertension 2003; 16: 1053−1056.
16. Gorinstein A, Harats D, Rabinkov A, Miron T, Mirelman D, Wilchek M. The antiatherogenic effect of allicin: possible mode of action. Pathobiology 2006; (72): 325–334.
17. Khalid S, Al-Numair. Hypocholesteremic and antioxidant effects of garlic *(Allium sativum L.)* Extract in rats fed high cholesterol diet. Pakistan J of Nutrition 2009; 8(2): 161−166.
18. Drucker A. Growing garlic from true seed. Garlic Analecta 2014; 2: 120−125.
19. Vilela MAL, Alves PC, Akimoto AK, Pereira LC, Guimaraes NKMD, Grisolia CK. The effect of hydrogen peroxide induced oxidative stress on leukocytes depends on age and physical training in healthy human subjects carrying the same genotypes of antioxidant enzymes' gene polymorphisms. American J of Human Biology 2012; 22: 807−812.
20. Tanideh S, Badiei T. Hypocholesteremic and antioxidant effects of garlic *(Allium sativum L.)* Extract in rats fed high cholesterol diet. Pakistan J of Nutrition 2009; 8(2): 161−166.
21. Block E. Garlic and others alliums: the Lore and the Science. In: The Royal society of chemistry. Cambridge: RSC publishing, 2010: 1−32.
22. Sumiyoshi H. New pharmacological activities of garlic and its constituents (Review). Folia Pharmacological Japonica 1997; 110 (1): 93−97.
23. Mahmoodi M, Hosseini ZSM, Hassanshahi GH, Toghroli MA, Khaksari M, Hajizadeh MR et al. The effects of consumption of raw garlic on serum lipid level, blood sugar and a number of effective hormones on lipid and sugar metabolism in hyperglycemic and/or hyperlipidemic individuals. J of Advances in Biological Chemistry 2011; 1: 29−33.
24. Mahesar H, Bhutto MA, Khand AA, Narejo NT. Garlic used as an alternative medicine to control diabetes mellitus in alloxen-induced male rabbits. Pak J Physiol 2010: 6(1): 39-41.