

Metformin and Garlic Preparations for Hyperglycemia

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ABSTRACT

Background: Diabetes is a chronic disorder of carbohydrate, fat and protein metabolism characterized by increased fasting and post prandial blood sugar levels. The global prevalence of diabetes is estimated to increase, from 4% in 1995 to 5.4% by the year 2025. WHO has predicted that the major burden will occur in developing countries. Drugs used in treatment of diabetes mellitus type II include sulfonylureas, biguanides, meglitinides, thiazolidinediones, dipeptidyl peptidase IV inhibitors, and α -glucosidase inhibitors. Due to low compliance of allopathic medicines patients are in search of medicinal herbs to treat their hyperglycemic state. Garlic is one of those herbs whose hypoglycemic effects are remarkable and accepted by cardiologists. **Methods:** We compared hypoglycemic potential of herbal hypoglycemic herb Garlic with Metformin. It was single blind placebo control research conducted at Jinnah Hospital Lahore-Pakistan from January 2016 to June 2016. Seventy-five diabetic type-II patients were selected for research. Hospital research counsel-approved and explained consent was taken from all patients. They were divided in three groups, 25 patients in each group. Group-1 patients were advised to take 250 mg Metformin thrice daily for two months. Group-2 patients were advised to take 10 grams of garlic in three divided doses for two months. Group-3 was on placebo therapy. Their base line fasting blood glucose level was taken and kept in record. They were advised to visit the lipid research clinic of the hospital fortnightly. They were also advised to check their fasting plasma glucose level daily at the morning by using Glucometer. **Results:** After two months' trial when results were compiled and statistically analyzed by applying paired 't' test, it was observed that Metformin decreased blood sugar level 28.4 mg/dl in 24 diabetic patients, which is highly significant change biostatistically. Garlic reduced fasting blood sugar 25.5 mg/dl in 22 diabetic patients, which is biostatistically highly significant change with p -value <0.001. **Conclusions:** It was concluded from the study that garlic can decrease blood glucose level highly significantly, near to hypoglycemic effect of Metformin.

Key words: Metformin, Biguanides, Diabetes Mellitus

INTRODUCTION

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Diabetes mellitus has been recognized since antiquity. It currently affects as many as 285 million people worldwide and results in heavy personal and national economic burdens. Considerable progress has been made in orthodox antidiabetic drugs. However, new remedies are still in great demand because of the limited efficacy and undesirable side effects of current orthodox drugs.^[1-3] Drug groups used in treatment of diabetes mellitus type II include sulfonylureas, meglitinides, thiazolidinediones, biguanides, dipeptidyl peptidase IV inhibitors, and α -glucosidase inhibitors.^[4] Metformin is the first-line medication for the treatment of type 2 diabetes. This is mainly used in obese DM type II patients. Main advantage of metformin utilization is that it does not increase weight of the patients.^[5-7] Metformin is taken orally and generally is well

tolerated.^[8] Common side effects include diarrhea, nausea, and abdominal pain.^[9] It has a low risk of developing low blood sugar.^[10] High blood lactic acid levels is a concern if prescribed inappropriately and in overdose.^[11] It should not be used in those with liver disease or kidney problems.^[12] While there is no too much harm if used during pregnancy.^[13] Metformin decreases blood glucose levels by decreasing hepatic glucose production, decreasing intestinal absorption of glucose, and improving insulin sensitivity by increasing peripheral glucose uptake and utilization.^[14] Garlic is one of the earth's greatest health tonics and does indeed have scientifically-proven medicinal properties.^[15] Garlic contains a substance called Allicin, which has anti-bacterial properties.^[16] Garlic contains many sulfur compounds which detoxify the body, boost the immune system, lower blood pressure and improve circulation.^[17] A drug based on a chemical found in garlic can treat diabetes types I and II when taken as a tablet.^[18] In various studies oral intake of garlic reduced blood sugar levels of hyperglycemic patients. The drug is based on vanadium and allixin, a compound found in garlic. The researchers believe that these compound work by activating the insulin signalling cascade which plays an important role in the regulation of glucose metabolism. The compound also appears to stimulate the function of an enzyme known as AMP-activated protein kinase which helps cells to absorb glucose.^[19] If be used Garlic with metformin it is the best combination to treat even the reluctant cases of diabetes mellitus. Garlic bulb is the most powerful tool in this fight.^[20]

METHODS

Proposal of research study was placebo control and was conducted at Jinnah Hospital, Lahore from January 2016 to June 2016. 75 diabetic patients of type-II were selected from Jinnah hospital to conduct research. Inclusion criteria was age limit from 20 to 60 years of both gender, male and female hyperglycemic patients. Hyperglycemic patients with other metabolic disease like hypertriglycemia, hypercholesterolemia, hypo or hyperthyroidism, were excluded. Consent was taken from all enrolled individuals. 75 Patients were divided in three groups. In Group-1, 25 diabetic patients were advised to take 250 mg of Tablet Glucophage 250 mg (Metformin) half an hour before taking meal, thrice daily for two months. In group-2, 25 diabetic patients were advised to take Garlic 10 grams daily in divided doses for two months. Group-3 was on placebo therapy, advised to take one tablet (containing grinded corn flour only) thrice daily ie; one tablet at breakfast, one tablet at lunch time and one tablet at dinner for 2 months. All patient's personal data like age/sex/profession/address was kept in separate folder. Their baseline fasting glucose level was determined by Glucometer (Diabos glucometer provided by Zafa Laboratories-Pakistan with Serial no: 190/8-Y) at Day-0 (start of research work). They were advised to check and keep in record their fasting blood glucose level every day early in the morning. They were advised to take their normal meal without any supplement

or high glucose-contained baked or high glucose containing food/fruits. Fortnightly follow-up visit was advised to all participants. After two months their FBS (fasting blood sugar) was again determined adding their own obtained values of FBS on daily basis, as advised them initially. Data were expressed as the mean \pm SD. Paired "t" test was applied to determine statistical significance as the difference between pre and post-treatment mean values. A probability value (P-value) of <0.01 was considered as significant and $P<0.001$ was considered as highly significant. P-value >0.05 was considered as non-significant change in the parameter.

RESULTS

When results were compiled after two months therapy with metformin in 24 DM type-II patients, it was observed that the drug has reduced patients FBS from 199.00 ± 2.76 mg/dl to 170.56 ± 1.95 mg/dl which is highly significant change. In group-2 twenty-two diabetic patients when treated by Garlic 10 grams daily, their mean FBS reduced from 205.17 ± 1.94 mg/dl to 179.65 ± 2.54 mg/dl, which is also highly significant change in the tested parameter with p-value <0.001 . In placebo group FBS reduced from 188.91 ± 2.22 mg/dl to 185.61 ± 2.81 mg/dl. This change in placebo group is non-significant statistically with p-value >0.05 . When calculated change in FBS in group-1 was 14.3 %. In group-2 percentage change was 12.4 %. In placebo group percentage change was only 1.7 %.

DISCUSSION

Cardiologists suggest metformin as the first-line therapy for patients with type 2 diabetes. Thus far, metformin is the only antidiabetic agent which has shown reduced macrovascular outcomes which is likely explained by its effects beyond glycemic control. A large amount of evidence in literature supports its use even in cases where it would be contra-indicated mainly due to the fear of lactic acidosis which has been over-emphasized as the available data suggest that lactate levels and risk of lactic acidosis do not differ appreciably in patients taking this drug versus other glucose-lowering agents. In our research results Metformin decreased fasting blood sugar (FBS) 28.4 mg/dl in two months therapy. Biostatistically this change in mean values is highly significant which match with results of study conducted by Faure P et al.^[21] They proved that diabetic patients when treated by metformin for two months their blood glucose reduced from 240 mg/dl to 210 mg/dl. Kusaka I et al^[22] explained one mode of action of Metformin that it decreases absorption of carbohydrates from GIT. Masoudi FA et al^[23] suggest that metformin may act in part by both increasing the binding of insulin to its receptor and potentiating insulin action. Our results are in contrast with results of study conducted by Krempf M et al^[24] who proved only 12.90 mg/dl reduction in 22 diabetic male patients when Metformin was used at dose of 250 mg twice daily for three weeks. This contrast in results may be due to less amount of drug used and duration of exposure to drug was only three weeks. Metformin's inhibition of

gluconeogenesis by hepatic cells causes hypoglycemia (Park M *et al.*)^[25] Gottschalk M. *et al.*^[26] proved that metformin is safe and moderately good drug for DM type-2 patients because it does not cause hypoglycemia. Gilbert C *et al.*^[27] stated that Patients with certain types of kidney, liver, and heart disease, and those who drink alcohol excessively should not take metformin. Mannucci E *et al.*^[28] explained that Metformin improves body responds to insulin to reduce high blood sugar levels, if patients take it at start of DM. Bailey CJ *et al.*^[29] suggested that Metformin must started with the evening meal; a second dose may be added one to two weeks later. The dose may be increased everyone to two weeks thereafter. In our research results 10 grams Garlic when used by 22 diabetic patients it reduced FBS level of these patients 25.5 mg/dl, which is highly significant change biostatistically with p-value <0.001. Turner Rc *et al.*^[30] also proved same results and explained that phytochemicals are being studied at China, Germany, India, Bhutan, Pakistan and Denmark due to their good patient compliance. Fantus IG *et al.*^[31] explained that Garlic principle active agent appears to be allicin, a sulfur-containing compound that with its breakdown products gives garlic its characteristic odour. Canal JR *et al.*^[32] stated that most of the clinical studies have observed the effects of garlic on blood glucose in normal healthy individuals but not in diabetic patients, leaving no doubt that the role of garlic in the management of diabetic patients still needs to be confirmed. However, bearing in mind that garlic has been an essential part of our diet for centuries, it is taken for granted that garlic is safe in a wide range of doses. Few non-specific adverse effects were reported in clinical studies using garlic and its preparations and frequently consist of gastrointestinal discomfort and nausea. Mukkerji V *et al.*^[33] described that Allicin is the principal bioactive compound present in the aqueous extract of garlic or raw garlic homogenate. Fenole TY *et al.*^[34] mentioned in conclusion of their study that use of fresh aqueous garlic extract is known to be effective in reducing thromboxane formation by platelets in both in vivo and in vitro animal models of thrombosis.

CONCLUSION

It was concluded from the study that garlic can decrease blood glucose level highly significantly, near to hypoglycemic effect of Metformin.

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