DOI: https://doi.org/10.53350/pjmhs20221612487

ORIGINAL ARTICLE

Physio Biochemical Effects of Metformin in Association with Non Insulin Dependent Type 2 Diabetic Patients

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ABSTRACT

Introduction: Diabetes happens when your body isn't able to take up sugar (glucose) into its cells and utilize it for energy. This results in a construct up of additional sugar in your bloodstream. Mismanagement of diabetes can lead to serious results, causing harm to a wide run of your body's organs and tissues including your heart, kidneys, eyes and nerves. Sedentary way of life and consistent over-nutrition within the past decades, have led to a disproportionate development in type 2 diabetes making this quiet, however debilitating disease a major health predicament within the 21st century. Diabetes mellitus may be divided into numerous different classes such as type 1, diabetes, type 2 diabetes and gestational diabetes mellitus. With ever growing figures, it is anticipated that by 2030, the overall number of individuals with diabetes will rise to 552 million. It is assessed that in 2007 the United States alone, spent $174 billion for diabetes of which $58 billion were attributable to diabetes-related chronic complications.

Objective: To determine the effects of association between metformin and type 2 diabetic patients

Study design: Open label randomized clinical trial

Settings: Garrison Medical centre Jarrar Garrison, Rawalpindi

Duration: Six months i.e. 1st January 2022 to 30th June 2022

Data Collection procedure: A single-center, open label randomized clinical trial was conducted. Patients were enrolled through medical OPD Jarrar Medical Center Pakistan from 1st January to June 2022. Patients were selected after falling in the criteria: (1) diagnosis of type 2 diabetes mellitus based on American Diabetes Association (ADA) criteria. (2) No history of serious chronic sicknesses of heart, lung, and kidney. (3) No earlier treatment with anti-diabetes medications for either diabetes or conditions related with hyperglycemia (4) No intake of aspirin within the past year. (5) No history of current or past smoking. Ag pre validated questionnaire was used. The total numbers of patients were 50 who participated after taking the informed consent. The Detailed information was given to patient about the current research. Confidentiality of the participants was prioritized.

Results: The total number of patients who participated in the study was 50 in which 30 were males and 20 were females in both groups. There were fifty participants as patients and fifty as control group. There was no gender discrimination in both groups. Baseline characteristics were measured. The others parameters include systolic and diastolic blood pressure, blood sugar fasting, glycemic control and lipid profile was measured.

Practical implication

Conclusion: This clinical trial of the safety and viability of metformin within the subjects with type 2 diabetes mellitus. In outline, metformin is effective and secure for the treatment of type 2 diabetes. The present finding confirms the ADA's suggestion to use metformin in type 2 diabetes mellitus patients.

Keywords: Metformin, Type 2 diabetes, Exercise, HbA1c, Insulin

INTRODUCTION

Diabetes happens when your body isn't able to take up sugar (glucose) into its cells and utilize it for energy. This results in a construct up of additional sugar in your bloodstream. Mismanagement of diabetes can lead to serious results, causing harm to a wide run of your body's organs and tissues including your heart, kidneys, eyes and nerves. Sedentary way of life and consistent over-nutrition within the past decades, have led to a disproportionate development in type 2 diabetes making this quiet, however debilitating disease a major health predicament within the 21st century. Diabetes mellitus may be divided into numerous different classes such as type 1, diabetes, type 2 diabetes and gestational diabetes mellitus[1, 2]. With ever growing figures, it is anticipated that by 2030, the overall number of individuals with diabetes will rise to 552 million. It is assessed that in 2007 the United States alone, spent $174 billion for diabetes of which $58 billion were attributable to diabetes-related chronic complications. Numerous researches concluded by considering diverse studies that 95% type 2 diabetes are shown within the population and larger part of them basic cause is oxidative stress[3, 4]. Diabetes mellitus may be a condition in which the body does not produce sufficient or utilize insulin because it should, lead to unusually high blood glucose levels. Cells become less responsive to the impacts of insulin when biological system has type 2 diabetes, and pancreas is unable to create sufficient insulin to overcome this resistance[5, 6]. Although the exact cause of this is often unknown, it is thought that both hereditary and natural factors contribute to the onset of type 2 diabetes. Type 2 diabetes is exceedingly related with being overweight, but not all individuals with type 2 are obese [7, 8] [9][10, 11]

MATERIAL AND METHODS

A single-center, open label randomized clinical trial was conducted. Patients were enrolled through medical OPD Jarrar Medical Center Pakistan from January to June 2022. Patients were selected after falling in the criteria: (1) diagnosis of type 2 diabetes mellitus based on American Diabetes Association (ADA) criteria. (2) No history of serious chronic sicknesses of heart, lung, and kidney. (3) No earlier treatment with anti-diabetes medications for either diabetes or conditions related with hyperglycemia. (4) No intake of aspirin within the past year. (5) No history of current or past smoking. Ag pre validated questionnaire was used. The total numbers of patients were 50 who participated after taking the informed consent. The Detailed information was given to patient about the current research. Confidentiality of the participants was prioritized.

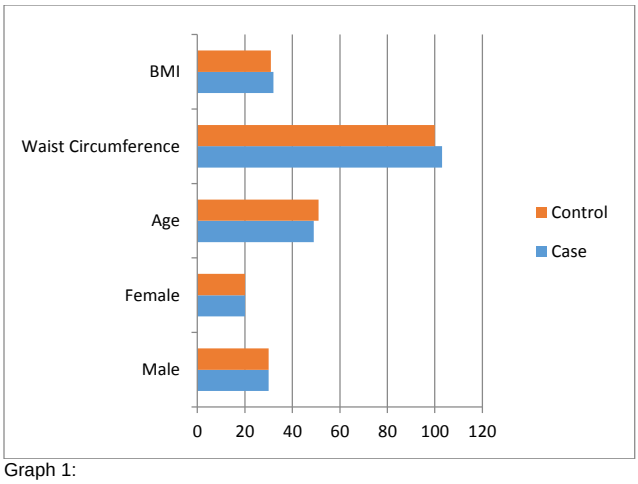
To begin with first group was allocated to the case group and the following was selected as control, this process was continued until each group comprised of 50 patients. Case group received 1000 mg metformin every day furthermore counsel for way of life modification whereas control gather as it were gotten consultation for changing lifestyle. For way of life alteration, patients were

instructed with respect to (1) benefits of slow moderate weight loss in control of hyperglycemia, (2) Focal points of a adjusted eat less (limited utilize of basic carbohydrates, saturated fatty acids, expanded intake of whole grains and dietary fibers, (3) need of a regular exercise plan. Those getting metformin were asked to return if they experienced any noteworthy adverse effects (e.g. severe gastrointestinal discomfort). After 3 months, patients returned for a planned follow-up visit and were met and examined using the same protocol as standard.

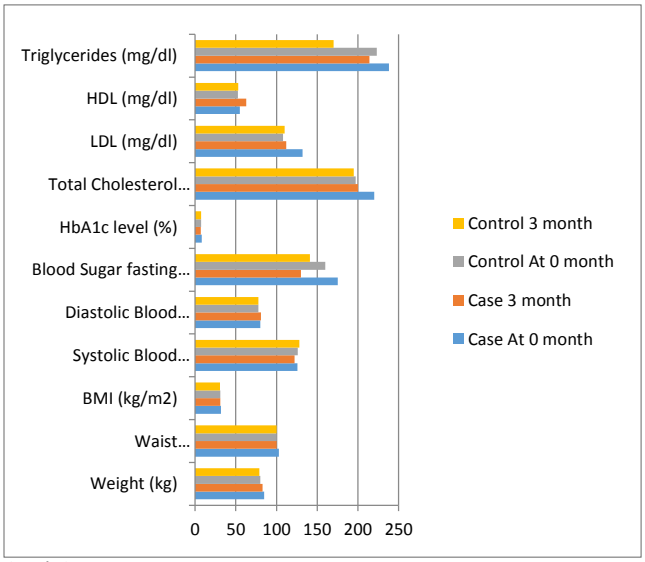
During the introductory visit, patients were met according to a pre-designed questionnaire and experienced a careful physical examination afterward. Blood pressure was measured employing a standard sphygmomanometer. Weight was measured with a digital scale and only light clothing was permitted. Body mass record (BMI) was calculated. Patients were instructed to go on an overnight fasting for atleast 10 hour in both introductory and 3-month follow-up visits. The next morning, 10 mL of venous blood sample was drawn within the hospital laboratory. Fasting plasma glucose (FPG) concentrations were assessed by enzymatic calorimetric method utilizing glucose oxidase test. Percentage of glycated hemoglobin (HbA1c) was determined; serum concentrations of total cholesterol, high density lipoprotein cholesterol (HDL-c), low density lipoprotein cholesterol (LDL-c), and triglycerides were calculated. All the readings were noted. Data was collected and entered into SPSS version 23 and analyzed for results.

RESULTS

The total number of patients who participated in the study was 50 in which 30 were males and 20 were females in both groups. There were fifty participants as patients and fifty as control group. There was no gender discrimination in both groups. Baseline characteristics were measured include weight, waist circumference and body mass index as showed in table 1. The others parameters include systolic and diastolic blood pressure, blood sugar fasting, glycemic control and lipid profile was measured. Systolic blood pressure was little high in control group while diastolic blood pressure as low as compared to control group. Blood sugar fasting was high in cases and low in control group. Glycemic control and lipid profile was also high in case group as compared to control ones. After taking metformin 1000mg in a day patient had follow up after 3 months and all the parameters were checked again. The other control group had received instruction for lifestyle changing and followed up again after 3 month. When we compared the case group regarding parameters systolic blood pressure significantly lowered down after 3 months as 117+10.50 from 120+11.24 and p value 0.089 while diastolic had moderately changed. Blood sugar fasting significantly lowered down after taking three month metformin as 120+20.50 and p value 0.001. HbA1c level lowered down from 7.6 to 6.85 showing good control of diabetes with p value 0.003. Total cholesterol level lowered down to 185 from 205 with p value 0.119. LDL level also decrease while HDL level increased. Lastly triglycerides showed reduction as well. When we compared control group after three month which only received lifestyles modification instruction there were slight changes as before only blood sugar fasting was significantly lowered down along with triglycerides shown in table 2. The significance p value showed against each variable in table 2.



Graph 1:



Graph 2:

Table 1: Demographic profile & Baseline Measures

No.	Variable	Case (n=50)	Control (n=50)	p-value
1	Gender			
	Male	30	30	0.550
	Female	20	20	
2	Age (Years)	45.50 + 7.40	47.30 + 6.45	0.126
3	Weight	79.35 + 10.50	75.45 + 8.75	0.795
4	Waist Circumference (cm)	95.35 + 11.40	96.35 + 7.50	0.710
5	BMI	29.52 + 4.28	28.25 + 4.50	0.739

Table 2: Mean changes of blood pressure, weight, BMI, Lipid profile and glycemic control in cases and control individuals at interval of 0 and 3 month

No.	Variable	Cases		Control		P value
		At 0 month	3-months	At 0 month	3-months	
1	Weight (kg)	79.35 + 10.50	78.40 + 10.11	75.45 + 8.75	75.35 + 8.25	0.252
2	Waist circumference(Cm)	95.35 + 11.40	95.05 + 10.80	96.35 + 7.50	96.35 + 7.50	0.365
3	BMI (kg/m^2)	29.52 + 4.28	29.05 + 3.95	28.25 + 4.50	28.25 + 4.45	0.349
4	Systolic Blood pressure (mmHg)	120 + 11.24	117 + 10.50	122 + 9.35	123 +10.29	0.089
5	Diastolic Blood pressure (mmHg)	77.50 + 5.35	78.10 + 5.95	76.50 + 4.35	75.50 + 6.15	0.797
6	Blood Sugar fasting (mg/dl)	155 + 40.25	120 + 20.50	140 + 40.25	128 + 27.25	0.001
7	HbA1c level (%)	7.60 + 1.45	6.85 + 0.75	7.0 + 0.85	7.0 + 0.95	0.003
8	Total Cholesterol (mg/dl)	205 + 30.53	185 + 33.40	180 + 35.10	178 + 35.25	0.119
9	LDL (mg/dl)	120 + 25.33	105 + 15.19	103 + 11.20	104 + 13.85	0.028
10	HDL (mg/dl)	50 + 11.18	54 + 17.30	48 + 9.15	48 + 10.80	0.075
11	Triglycerides (mg/dl)	190 + 95.36	170 + 88.72	175 + 96.66	150 + 40.55	0.790

DISCUSSIONS

In this study, impacts of metformin treatment on different markers were investigated. Here we showed that addition of metformin to lifestyle modification compared with way of life change alone comes about in a significant reduction in different variables. This study suggests that there may be autonomous benefits of metformin and life style adjustment on glucose control, with the benefits of physical activity being clearer in those not taking metformin. Several pharmaceutical randomized control trials appear evidence of the adequacy of metformin on glycemic by means of decreasing hepatic glucose production[12].

Be that as it may, it is evident that metformin has additional impacts on glycemic control that are not however completely understood. The benefits of exercise on insulin sensitivity are also well described. Whether the benefits of exercise or physical movement are modified in patients utilizing metformin are vague. Consistent with a few previous literatures this study illustrates that the glycemic benefits of physical action are likely attenuated in those people living with type 2 diabetes and as of now utilizing metformin. This may demonstrate a basement impact wherein the useful impacts of metformin on chronic glycemic are not encouraged progressed by physical activity. This may propose a common pathway for metformin and physical movement on making strides glycemic in those with type 2 diabetes. Thus, clinicians maybe should not expect an added substance benefit of physical activity on glycemic control for their patients as of now utilizing metformin [13, 14].

There's literature proposing that physical movement is related with improvements in glucose control that's added substance to the impacts of metformin, or may indeed be related with expanded hepatic glucose generation. These studies are basically intense impacts of exercise on different measures of postprandial glucose control, or other measures of metabolism and in this way may not necessarily translate into chronic glycemic control as reflected by HbA1c[15].

CONCLUSION

This clinical trial of the safety and viability of metformin within the subjects with type 2 diabetes mellitus. The study illustrates that metformin, titrated up to 1,000 mg/day (in expansion to standard dietary management and exercise), and improves glycemic control in subjects with type 2 diabetes. The improvement with metformin was evidenced by noteworthy decreases in BSF and HbA1c levels reported by other studies also.

Normalization of blood glucose has also been related with a less atherogenic lipid profile. In this study, the enhancement in glycemic control with metformin happened without the increase in body weight that's frequently observed with insulin, and it had no adverse impact on the lipid profile. In outline, metformin is effective and secure for the treatment of type 2 diabetes. The present finding confirms the ADA's suggestion to use metformin in type 2 diabetes mellitus patients.

REFERENCES

1. Wang S-B, Lei K-J, Liu J-P, Jia Y-M. Continuous use of metformin can improve survival in type 2 diabetic patients with ovarian cancer: a retrospective study. Medicine. 2017;96(29).
2. Foretz M, Guigas B, Viollet B. Understanding the glucoregulatory mechanisms of metformin in type 2 diabetes mellitus. Nature Reviews Endocrinology. 2019;15(10):569-89.
3. Gao Y, Liu T, Zhong W, Liu R, Zhou H, Huang W, et al. Risk of metformin in patients with type 2 diabetes with COVID-19: a preliminary retrospective report. Clinical and Translational Science. 2020;13(6):1055-9.
4. Griffin SJ, Leaver JK, Irving GJ. Impact of metformin on cardiovascular disease: a meta-analysis of randomised trials among people with type 2 diabetes. Diabetologia. 2017;60(9):1620-9.
5. Schernthaner G, Schernthaner G-H. The right place for metformin today. diabetes research and clinical practice. 2020;159:107946.
6. Kanto K, Ito H, Noso S, Babaya N, Hiromine Y, Taketomo Y, et al. Effects of dosage and dosing frequency on the efficacy and safety of high-dose metformin in Japanese patients with type 2 diabetes mellitus. Journal of diabetes investigation. 2018;9(3):587-93.
7. Zilov AV, Abdelaziz SI, AlShammary A, Al Zahrani A, Amir A, Assaad Khalil SH, et al. Mechanisms of action of metformin with special reference to cardiovascular protection. Diabetes/Metabolism Research and Reviews. 2019;35(7):e3173.
8. Moin T, Schmittdiel JA, Flory JH, Yeh J, Karter AJ, Kruge LE, et al. Review of metformin use for type 2 diabetes prevention. American journal of preventive medicine. 2018;55(4):565-74.
9. Aroda VR, Ratner RE. Metformin and type 2 diabetes prevention. Diabetes Spectrum. 2018;31(4):336-42.
10. Tseng E, Yeh H-C, Maruthur NM. Metformin use in prediabetes among US adults, 2005–2012. Diabetes care. 2017;40(7):887-93.
11. Tseng E, Yeh H-C, Maruthur NM. Erratum. Metformin Use in Prediabetes Among US Adults, 2005–2012. Diabetes Care 2017; 40: 887–893. Diabetes Care. 2018;41(5):1116.
12. Petrie JR, Chaturvedi N, Ford I, Brouwers MC, Greenlaw N, Tillin T, et al. Cardiovascular and metabolic effects of metformin in patients with type 1 diabetes (REMOVAL): a double-blind, randomised, placebo-controlled trial. The lancet Diabetes & endocrinology. 2017;5(8):597-609.
13. Charytan DM, Solomon SD, Ivanovich P, Remuzzi G, Cooper ME, McGill JB, et al. Metformin use and cardiovascular events in patients with type 2 diabetes and chronic kidney disease. Diabetes, Obesity and Metabolism. 2019;21(5):1199-208.
14. Wennberg AM, Hagen CE, Edwards K, Roberts RO, Machulda MM, Knopman DS, et al. Association of antidiabetic medication use, cognitive decline, and risk of cognitive impairment in older people with type 2 diabetes: Results from the population-based Mayo Clinic Study of Aging. International journal of geriatric psychiatry. 2018;33(8):1114-20.
15. Ghomian N, Vahed SHM, Firouz S, Yaghoubi MA, Mohebbi M, Sahebkar A. The efficacy of metformin compared with insulin in regulating blood glucose levels during gestational diabetes mellitus: a randomized clinical trial. Journal of cellular physiology. 2019;234(4):4695-701.