ORIGINAL ARTICLE

EFFECT OF INSULIN VERSES METFORMIN ON HYPER-GLYCEMIA AND DYSLIPIDEMIA IN TYPE-II DIABETIC PATIENTS

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ABSTRACT

Objective: To compare the anti-hyperglycemic and anti-dyslipidemia effects of insulin verses metformin in diabetic human subjects.

Material and Methods: Total of 240 blood samples were collected (120 from male and female) for all the three groups i.e. Group-I serve as non-diabetic individuals, Group-II included diabetic patients treated with insulin and Group-III included diabetic patients treated with metformin. The study period was from January 2018 to September 2018. Fasting-serum-glucose, lipid profile, triglyceride, AST and ALT analysis were done with serum samples. Body mass index was also measured for each subject.

Results: A significant weight gain was recorded in metformin treated group than insulin treated group. Insulin showed more significant anti-hyperglycemic effects than metformin treated group. Insulin therapy showed more significant reduction for total-cholesterol and very low density-lipoprotein both in male and female groups. For low-density-lipoprotein a significant reduction and for high-density-lipoprotein a significant increase was found only in male insulin treated group. Insulin also showed significant increase for alanine aminotransferase, aspartate aminotransferase only in male group.

Conclusion: Insulin showed stronger anti-hyperglycemic, anti-hypercholesterolemia activities than metformin. Insulin showed more significant improvement in lipid profile.

Key words: Diabetes mellitus, Dyslipidemia,Hyper-glycemia, Insulin, Metformin.

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INTRODUCTION

Diabetes is a metabolic disorder associated with hyper-glycemia. Abnormal lipid profile is the leading reason of cardiac problems in diabetic patient. Type-II diabetes mellitus (DM) is a group of chronic metabolic disorders of carbohydrate, lipid and protein, characterized by hyper-glycemia[1]. Diabetes is considered as a global health issue, since mortality rate due to this metabolic disorder increased greatly in both developed and underdeveloped countries and it is estimated to reach about 300 million patients by almost a decade[2]. DM is caused by insufficient insulin secretion, mechanism or both which leads to insulin resistance[3,4]. Chronic hyper-glycemia in diabetes is associated with certain health complications such as cardiac infarction, dyslipidemia, hyper-cholesterolemia, oxidative stress, nephropathy, neuropathy, foot amputation, micro and macro-vascular disorder[5,6]. Beside heredity many factors like obesity, gender, lack of physical activities, hypertension, high blood pressure, improper diet and socioeconomic status are also involved in diabetic development[7]. Diabetes is associated with disturbance in serum lipids profile and decrease HDL subsequently increase the risk of cardiovascular disease[8]. Lipid abnormalities are dominant in diabetes due to insulin resistance, which in turn affects the enzymatic pathways of lipid metabolism[9]. Hyperglycemia in diabetes is associated with dyslipidemia characterized by lipoprotein irregularities i.e increased very low density lipoprotein-cholesterol (VLDL-c), low density lipoprotein-cholesterol(LDL-c) and triglyceride (TG), decreased in high density lipoprotein-cholesterol (HDL-c) in blood

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concentrations[1,10]. In Pakistan nearly 6.9 million individuals are suffering with diabetes. Type-II diabetes is the leading health problem both among urban and rural population of Pakistan[7]. This high prevalence of diabetes in Pakistan is might be due to lack of awareness and proper education regarding this chronic disease. To regulate the blood glucose concentration is the main task in diabetes, however it is not easy to achieve this goal without proper diet, regular exercises and proper health management[11]. For diabetic treatment many oral drugs e.g sulfonylurea, biguanides and thiazolidinediones, metformin along with insulin are available.Both insulin[3,12]. And metformin[13] are the most commonly used anti-hyperglycemic agents. Insulin and metformin are the most recommended therapies in type-II diabetes, however in the absence of comparative study it is difficult to know which of the given drug is more effective in controlling hyper-glycemia and dyslipidemia. Therefore, this study provides a clear comparison between insulin and metformin in controlling hyperglycemia, dyslipidemia and hyper-cholesterolemia. These findings would be useful for the further research to optimize the diabetic treatment protocol to improve the quality of diabetic patient's life. However, as the number of subjects were limited in this study toconduct well-planned disease management approach for providing reasonable suggestions to the clinicians and practitioners. Furthermore, the dietary habit, life style, treatment and physical activities vary from individual to individual and people do not have the awareness regarding genetic diseases.

MATERIALS AND METHODS

Experimental Deign: Multiple visits were done in different Government hospitals of the Quetta city, from January 2018 to September 2018. A total 240 subjects were randomly selected. We collected blood samples from fourth subjects in all groups (control group, insulin treated diabetic group and metformin treated group) for both genders. Body mass index (BMI) were measured (kg/m2). Patients having type II diabetes between the age 25-60 years were included in the study. Both long and short term insulin therapy were considered. Complete history of all the participants were taken from the physician. Dietary habit and physical activities were also asked from the patients. Individuals having cardiac problem, taking any hormonal therapy, hepatic problem, alcoholic, smokers, pregnant women or having any other genetic disease were excluded from the study. Before blood collection the pulse rate and blood pressure of each individual was recorded. Blood was collected by following the WHO, guideline.14. Blood samples were collected after overnight fasting condition (5-7 cc) and serum were separated immediately for further biochemical analysis. The biochemical analyses of fasting serum glucose (FSG), ALT (alanine aminotransferase), AST (Asparatate aminotransferase), serum total cholesterol (TC), Very low density lipoprotein-cholesterol (VLDL-c), low density lipoprotein-cholesterol (LDL-c), high density lipoprotein-cholesterol (HDL-c) and triglycerides (TG) were perform using commercially available kits (Randox, UK). Results were presented as Mean ± S.E.M. Two-way repeated measure analysis of variance (ANOVA) followed by post hoc Tukey's test by using GraphPad Prism (version 06)were performed for all the biochemical and physiological parameters between control and treated subjects. Differences were considered significant at $P < 0.05$.

RESULTS

Body Mass Index (BMI): We found significant weight gain in diabetic male ($P<0.05$) and female ($P<0.001$) than normal individuals. More significant weight gain was found in metformin treated ($P<0.05$ for males and $P<0.001$ for female) group in comparison to insulin treated group (Fig-1).

Fasting Serum Glucose (FSG): A highly significant increase for FSG was found in both male group II ($P<0.001$) and female group-II ($P<0.0001$) diabetic groups in comparison with group-I. However, more significant increase was found in female diabetic group as compare to male diabetic group. Insulin therapy showed significant decrease for FSG in male ($P<0.05$) as compare to metformin group, but non-significant change was found in female among both treated groups (Fig-2).

Serum lipid profile: Serum lipid profile (TC, VLDL-c, LDL-c, HDL-c) and TG was also measured for all the studied groups (Table 1). A significant decrease was found for TC both in male ($P<0.0001$) and female ($P<0.001$) insulin treated subjects verses metformin. Our study showed a significant decrease for VLDL-c in insulin therapy group verses metformin group in both genders. For LDL-c a significant decrease was found only in male insulin group female showed non-significant difference between two treated groups. However, a significant improvement was found for HDL-c only in male insulin treated group than metformin group. Whereas, in case of TG no significant reduction was found to be occur between the two treated groups

Biochemical parameters: Table-1 showed the results for AST and ALT. Both for AST and ALT a significant increase was found in male insulin treated group verses metformin group. Female group showed no significant difference for AST and ALT between the two treated groups.

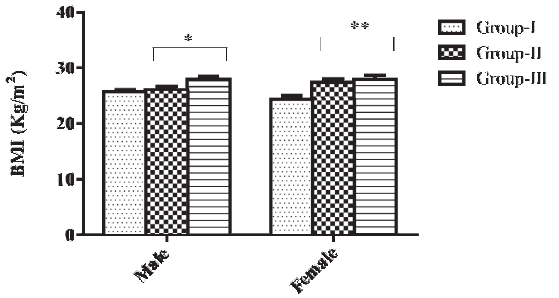

Fig 1: Body mass index (Kg/m2) of diabetic male and female patients.Group-I (Control group), group-II (Insulin treated group), group-III= (Metformin treated group). Results represented as Mean ± S.E.M.* represent P<0.05 & ** represent 0.001.

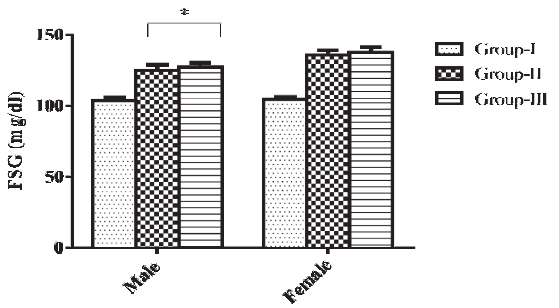

Fig 2: Fasting serum glucose (mg/dl) of diabetic male and female patients. Group-I= (Control group), group-II(Insulin treated group), group-III (Metformin treated group). Results represented as mean ± S.E.M. * represent P<0.05.

DISCUSSION

The ability of β-cells to secrete insulin is crucial to manage diabetes, preventing diabetic complications and delaying onset of cardiovascular disease[13]. Weight control is always a challenging issue for diabetic patients. We found that metformin is more associated with weight gain than insulin and the results are in according to other researchers[1,13,15]. Obesity in diabetes is associated with inequity energy intake and energy consumption[16]. Insulin therapy leads to insulinisation in hepatic cells and reduced peripheral hyperinsulinaemia, helpful to reduce bodyweight gain and the risk of hypoglycaemia[12]. Body weight control in insulin treatment may be attributed because improvement in blood glucose level and lipid metabolism. In the patients with type-II diabetes, when intensively treated with insulin therapy showed marked improvement in glycemic state along with insulin secretion and its action[15]. Our results showed a high significant decrease in fasting serum glucose in insulin therapy group than metformin. Since insulin is well known to control the hyper-glycemia in diabetes. Numerous studies provide the fact that early and intensive insulin therapy improve the β-cell function,even short-term insulin therapy can successful reduces the hyperglycemia[15,17]. In another study it was demonstrated that insulin along with metformin showed more successful long-term protection of β-cell function[18]. However, metformin is well known effective oral antihyperglycemic drug[13,17]. Long-lasting hyperglycemia is associated with failure of certain vital organs of the body like hepatic, cardiac and renal failure etc[6]. thus to control and to maintain blood glucose level

Table 1: Serum Lipid profile, AST and ALT in male and female diabetic patients of Quetta city treated with insulin and metformin (N=240)

Parameters	Male			Female			
	Group-I	Group-II	Group-III	Group-I	Group-II	Group-III	P Value
TC	139.70±3.26	166.17±6.57***	204.55±8.47	142.62±2.86	174.90±6.41**	214.52±7.74	0.0009
VLDL-c	17.10±0.81	34.85±1.77**	42.45±1.95	18.22±0.85	35.77±1.85***	45.02±2.16	0.0029
LDL-c	101.17±1.94	114.62±3.79**	128.25±5.05	102.87±1.39	119.52±4.25	120.07±4.20	0.0001
HDL-c	62.67±1.01	41.10±1.34*	39.32±2.01	63.57±1.22	42.27±1.72	42.25±1.84	0.0008
TG	119.87±2.09	128.80±5.54	129.00±5.19	121.70±2.26	139.0±5.53	139.17±6.77	0.0001
AST (μ/L)	27.53±0.67	30.04±1.03***	29.43±1.27	29.91±0.68	32.06±1.22	31.96±1.74	0.0030
ALT (μ/L)	26.50±0.70	27.82±1.17*	28.60±1.28	26.20±0.68	27.57±0.93	27.25±1.22	0.0009

Data represented as Mean ± SEM. Group-I (Control group), group-II (Insulin treated group), group-III(Metformin treated group). * represent P<0.05, ** P<0.001, ***P<0.0001.

Abbreviations: Total cholesterol (TC), Very low density lipoprotein-cholesterol (VLDL-c), low density lipoprotein-cholesterol (LDL-c), high density lipoprotein-cholesterol (HDL-c) and triglycerides (TG), ALT (alanine aminotransferase), AST (Aspartate aminotransferase).

is the primary task in diabetes.

This study showed a significant enhancement in TC, VLDL-c, LDL-c, TG and significant reduction in health friendly lipoprotein HDL-c in diabetic patients. The results are alien with other researchers[1,19]. who also found dyslipidemia in diabetic patients. Insulin showed more efficient results to improve dyslipidemia than metformin therapy. Previously, many studies have been done on anti-hyperglycemia and hyper-cholesterolemia effects of insulin and metformin therapies to regulate blood glucose and hyper- cholesterolemia[3, 20]. Dyslipidemia in diabetes is associated with high risk of cardiovascular disorder (CVD), the primary reason of death in type-II diabetes. To reduce the morbidity and mortality due to CVD it is necessary to decrease blood LDL and TG concentrations[1]. Hyperlipidemia is a major risk factor for CVD and is closely related with development of coronary atherosclerosis and other heart diseases[21]. High concentration of TG and TC are major dyslipidemic feature associated type-II diabetes. Hyper-triacylglycerolemia is the leading factor of CVD and caused due to high VLDL hepatic secretion and delayed in TG rich lipoprotein (VLDL-TG, LDL-TG and HDL-TG) results increase of TG and free fatty acid from adipose tissues into the blood as also the case found in present study[22].

Furthermore, dyslipidemia was more severe in female diabetic group as compare to male diabetic group, might be because of high fatty diet, less physical activities and poor health management in females of this region. It is well known fact that higher lipid concentration plays a pivotal role in diabetic development.The reason for dyslipidemia in type-II diabetes is reducedinsulin secretion which affects the hepaticapolipoproteinassembly and deregulate the enzymatic action oflipoprotein lipase, hepatic lipase and cholesterol ester transport protein[1]. Liver enzymes (AST and ALT) are important bio-marker to identify liver diseases and associated with the development of diabetic complication[23]. Insulin therapy showed a significant reduction in both AST and ALT serum level.

CONCLUSION

Insulin therapy showed more ameliorating influence on hyper-glycemia, hyper cholesterolemia, hyper-triglycemia and weight gain in diabetic patients than metformin group particularly in males. In females the effects of the medication were not prominent because of their imbalanced diet, lack of physical activities and hypertension.

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AUTHOR'S CONTRIBUTION

Following authors have made substantial contributions to the manuscript as under:

Ullah I: Sample Collection and data analysis.

Naseem M: Experimental Design.

Yasinzai MI: Experimental Design.

Kakar AU: Experimental Design.

Ahmed Z: Statistical Analysis.

Ghani AA: Data Analysis.

Ullah Z: Statistical Analysis.

Ullah A: Experimental Design.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.