Original Article

Effects of glibenclamide and metformin on prevalence of metabolic syndrome in type 2 diabetic patients

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ABSTRACT

Objectives: To investigate the effects of glibenclamide or metformin on prevalence of metabolic syndrome in type 2 diabetic patients.

Methodology: One hundred type 2 diabetic patients were divided into 2 groups of equal number (Glibenclamide group and metformin group). Another group consist of 30 newly diagnosed type 2 diabetic patients were also involved as a control group. Metabolic syndrome was diagnosed according to criteria made by the US National Cholesterol Education Program Adult treatment Panel III. Waist circumference in (cm) was determined as the point midway between the costal margin and iliac crest in the mid-axillary's line. Serum glucose concentration, serum triglycerides and HDL-Cholesterol were measured using special Kits.

Results: One hundred thirty patients had metabolic syndrome in three group and the markers of metabolic syndrome were significantly lowered in the metformin group as compared with the glibenclamide group and control group. Females have metabolic syndrome greater than men. Higher age group patients were more prone to develop metabolic syndrome.

Conclusion: Metformin was found to have favorable effects on the frequency of metabolic syndrome and its markers as compared with glibenclamide.

KEY WORDS: Type 2 diabetes mellitus, Metabolic syndrome, Glibenclamide, Metformin.

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INTRODUCTION

The metabolic syndrome (MS), or insulin resistance syndrome accommodates the clustering together of certain cardiovascular risk factors associated with insulin resistance and hyperinsulinemia.[1] It was first identified in 1988 by Gerald Reaven, a Stanford University endocrinologist, in a lecture to the American Diabetes Association.[2] At various times, this syndrome has been called dysmetabolic syndrome, insulin resistance syndrome or syndrome X. Now simply known as metabolic syndrome.[3]

Risk factors for MS according to ATP III[4] include: Abdominal obesity (waist circumferences: Men > 102 cm, Women >88 cm), triglycerides ≥ 150 mg/dl, HDL cholesterol: Men < 40mg/dl, Women < 50mg/dl, BP ≥ 130/ ≥ 85 mmHg, fasting glucose ≥ 110 mg/ dl. When 3 of 5 of the listed characteristics are present, a diagnosis of metabolic syndrome can be made.

Metabolic syndrome is associated with a high risk of coronary heart disease and premature mortality.[5] Besides resulting in macrovascular complications, there is growing evidence that MS, like diabetes mellitus, causes microvascular complications in patients with type 2 diabetes mellitus.[6] Nearly 70-80% of the population with diabetes mellitus is diagnosed with MS.[7]

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Metformin is a biguanide Euglycemic agent, has been approved by the Food and Drug Administration for the treatment of type 2 diabetes mellitus. Although metformin is as effective as sulfonylureas, the drug differ in several respects: Metformin reduces insulin resistance without directly affecting insulin secretion, causes weight loss rather than weight gain, and has lactic acidosis rather than hypoglycemia as its most serious side effect.[8]

Glibenclamide is a second generation sulfonylurea drug. It is at least as effective as the first generation agents and is effective in doses that are considerably less than those needed with first generation sulfonylureas. It is a useful medication for patients with type 2 diabetes whose hyperglycemia is not adequately reduced by dietary management and exercise. It can be used as the initial drug in these patients or as the replacement drug for those with primary or secondary failure during therapy with first generation sulfonylureas. Side effects are minimal, and the most important is hypoglycemia.[9]

The present study was designed to investigate and compare the effects of glibenclamide and metformin on prevalence of MS in type 2 diabetic patients.

METHODOLOGY

One hundred type 2 diabetic patients were included in this study. They were divided into 2 groups of equal number according to the type of hypoglycemic agent used (Glibenclamide group and metformin group). Another group consists of 30 newly diagnosed type 2 diabetic patients according to American Diabetes Association criteria.[10] Patients in control group were on carbohydrate restricted diet or on exercise or both. The study protocol was approved by regional research ethics committees at college of medicine and Mosul Health Administration. The study was a case controlled, comparative trial, performed in Al-Wafaa Diabetic Center in Mosul city during the period between 1/10/2010 and 1/4/2011.

Type 2 diabetic patients on glibenclamide or metformin therapy for a period not less than 6 months were included in the study. All type 1 diabetics were excluded from the study. Patients with renal failure, cushing syndrome or with ascites due to any reason were excluded. Patients with secondary hypertension, hepatobilliary disease and hypothyroidism were excluded from the study after thorough clinical evaluation. Patients taking drugs that may affect the results of the study such as hypolipidemic agents were also excluded.

Metabolic syndrome was diagnosed according to criteria made by the US National Cholesterol Education Program Adult treatment Panel III[4] which require at least three of the following: Waist circumference ≥ 102 cm (male), ≥ 88 cm (female). Triglyceride ≥ 150 mg/ dl, HDL-cholesterol < 40mg/ dl (male), < 50 mg/ dl (female). BP ≥ 110 / ≥ 85 mmHg. Fasting blood glucose ≥ 110mg/dl.

Waist circumference in (cm) was determined with a standard tape measure, as the point midway between the costal margin and iliac crest in the mid-axillary's line, with the subject standing and breathing normally. Blood pressure was measured by sphygmomanometer; measurement was performed after at least five minutes of rest.

Serum glucose concentration was estimated by glucose-oxidase-peroxidase colorimetric method by using a kit supplied by Biocon (Germany). Serum triglycerides and HDL-Cholesterol were measured using special Kits supplied by Biolabo (France).

Statistical Methods: Data were expressed as mean ± SD and %. Unpaired t-test was used to compare data between glibenclamid or metformin and control group, and between glibenclamide and metformin groups. Values ≤ 0.05 were considered significant.

RESULTS

No significant differences were found between the ages and duration of treatment of the glibenclamide and metformin groups (P>0.5). A significant differences were found between the ages of the patients and the control group (P<0.001) (Table-I).

The percentage of patients having MS was lower in the metformin group as compared with the glibenclamide or control group (Table-II). Markers of MS are significantly lowered in the metformin

Table-I: Patient's Characteristics.

Parameters	*Glibenclamide Group (N: 50)*	*Metformin Group (N:50)*	*Control Group (N:30)*
Age (year)	55.30±9.59	52.16±8.87	44.26±7.53
Sex M			
F	23 (46%)	27(54%)	23(46%)
	27(54%)	16(53.3%)	14(46.79%)
Duration of Treatment (year)	4.78±2.4	4.67±1.6	----------

Table-II: Number of patients having metabolic syndrome in the 3 groups.

Parameter	*Glibenclamide Group (N:50)*	*Metformin Group (N:50)*	*Control Group (N:50)*	*Total*
Metabolic Syndrome	39	34	22	95
%	78.0	68.0	73.3	73.1
Non Metabolic Syndrome	11	16	8	35
%	22.0	32.0	26.7	26.9
Total	50	50	30	130
%	100	100	100	100

group as compared with the glibenclamide group or control group (Tables-IVand V). No significant differences were found between markers of MS of the glibenclamide and control groups except for FBS which showed a significant difference (Table-III).

As regards the total number of patients with MS, females have metabolic syndrome greater than men (Table-VI). Higher age group patients were more prone to develop metabolic syndrome (Table-VII).

DISCUSSION

The prevalence of MS in type 2 patients reported in the present study was 68.0-78.0%. Studies conducted in other parts of the world estimated a prevalence of 77% among Pakistan population[11], 75.6% among Chinese population[12], and 76.3% among Indian population.[13] These figures are close to our figures but differ from other reported figure of 85.8% reported by Mohsin et al.[14]

In the present study prevalence and markers of MS in the metformin group were significantly lower than those of the glibenclamide and control groups, indicating that metformin produce a more favorable effects on these parameters. Many studies evaluated the effects of metformin on lipid profile

Table- IV: Comparison of the markers of metabolic syndrome of metformin and control groups.

Markers of MS	*Mean±SD*		*P-value*
	Metformin Group N=34	*Control Group N=22*	
WC(cm)	107.59±8.62	114.82±11.27	0.015(S)
SystolicBP(mmHg)	133.24±14.7	145±5.98	0.000(S)
DiastolicBP(mmHg)	82.35±8.55	90±10.24	0.004(S)
Triglyceride (mg/dl)	210.74±19.77	219.27±9.52	0.036(S)
HDL- cholestrol (mg/dl)	45.65±6.14	38.56±10.42	0.007(S)
FBS(mg/dl)	144.23±17.24	161.77±8.71	0.000(S)

Table-III: Comparison of metabolic syndrome markers of glibenclamide and control groups.

Markers of MS	*Mean±SD*		*P-value*
	Glibenclamide Group N=39	*Control Group N=22*	
WC(cm)	112.59±12.01	114.82±11.27	(NS)
SystolicBP (mmHg)	147.18±9.99	145±5.98	(NS)
DiastolicBP (mmHg)	87.69±8.42	90±10.24	(NS)
Triglyceride (mg/dl)	225.18±17.18	219.27±9.52	(NS)
HDL-cholestrol (mg/dl)	41.73±9.57	38.56±10.42	(NS)
FBS(mg/dl)	156.26±10.06	161.77±8.71	0.030(S)

and blood pressure. Some studies reported reduction of only in triglyceride[15,16], while others reported reduction of total cholesterol and triglycerides with an increase of HDL-cholesterol.[17,18] Metformin in the present study reduce BP significantly in comparison with glibenclamide. This effect of metformin on blood pressure is in agreement with some studies which also found a reduction effect of metformin on BP[19,20] and in contrast with other studies which did not found any effect of metformin on BP.[21,22]

In two previous studies, metformin was found to have favourable effects on serum lipoproteins, body weight, body mass index and blood pressure as compared with glibenclamide.[21,23] In a study done by Mourao Junior et al[24] showed that metformin administered to patients with type 2 diabetes mellitus having markers of MS, resulted in reduced markers of MS significantly including WC, FBS, triglycerides and non significant effects on BP and on HDL-cholesterol.

Table- V: Comparison of the markers of metabolic syndrome of metformin and glibenclamide groups.

Markers of MS	*Mean±SD*		*P-value*
	Glibenclamide Group N=39	*Metformin Group N=34*	
WC(cm)	112.59±12.01	107.59±8.62	0.043(S)
Systolic BP (mmHg)	147.18±9.99	133.24±14.7	0.000(S)
Diastolic BP (mmHg)	87.69±8.42	82.35±8.55	0.009(S)
Triglyceride (mg/dl)	225.18±17.18	210.74±19.77	0.002(S)
HDL-cholesterol (mg/dl)	41.73±9.57	45.65±6.14	0.039(S)
FSG(mg/dl)	156.26±10.06	144.23±17.24	0.001(S)

Table-VI: Sex wise distribution of patients with metabolic syndrome.

Sex	*Glibenclamide Group*	*Metformin Group*	*Control Group*	*Total*
Male	15	17	13	45
%	38.5	50	59.1	
Female	24	17	9	50
%	61.5	50	40.9	
Total	39	34	22	95
%	100	100	100	100

The majority of the patients in the present study having MS were females. Different studies report quite varied effects of gender on the MS in different populations. In USA, MS is more prevalent in white males than in females. In American blacks, Mexican American, Korea, Iran, India, Oman, women had higher prevalence of MS than men. The reason may be related to sedentary lifestyle of women at these regions of the world.[14]

Distribution of the patients according to age in the present study revealed that prevalence of MS tends to increase with increasing age. Isezuo and Ezunu[25] and Thomas et al[26] also showed that prevalence of MS tend to increase with increasing age.

It is well known that individual components of MS are high risk factors for cardiovascular morbidity and mortality. Further, in adults who have type 2 diabetes, the presence of MS is associated with a five fold increase in cardiovascular risk independent of age, sex, smoking status and glycated hemoglobin.[27] Thus the diagnosis of MS in patients might hold promise for enhanced prevention of diabetes and cardiovascular diseases.

CONCLUSION

Prevalence of MS is high in patients with type 2 diabetes mellitus. It is more common in female than males and increased with increasing age. Metformin was found to have favorable effects on the frequency of MS and its markers as compared with glibenclamide. Identification of MS in non diabetic patients is important as this group represent the highly susceptible group for the development of type 2 diabetes (prediabetic group).

Conflicts of Interest Notification Page: No potential conflicts exist. We had full excess to all the data in the study and take complete responsibility for the integrity of the data and the accuracy of the data analysis.

Table-VII: Distribution of patients with MS.

Age (year)	*Group*			*Percentage*		
	Glib.	*Met.*	*Control*	*Glib.*	*Met.*	*Control*
≤ 40	4	6	7	10.3	17.6	31.82
40.1-50	7	7	12	17.9	20.6	54.55
50.1-60	20	18	3	51.3	53	13.63
>60	8	3	-	20.5	8.8	------
Total	39	34	22	100	100	100

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