Research Article

The Effect of Treatment with Glucophage or Glibenclamide, Alone or in Combination on the Serum Visfatin Level in Type 2 Diabetic Patients

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ABSTRACT

DM is the most common metabolic disorder worldwide and is a major risk factor for cardiovascular disease (CVD). Many risk factors for CVD, including hyperglycemia, abnormal lipid profiles, and alterations in inflammatory mediators, are carried by type two diabetes mellitus (T2DM) patients, a new adipocytokine, visfatin is associated with a wide range of biologic effects, including glucose and lipid metabolism, and has been implicated in the pathogenesis of diabetes and obesity. Visfatin is an adipocytokine that was identified in 2005. Visfatin has insulin mimetic effects; it binds to the insulin receptor at a different binding site than insulin and activates it. The aim of this study was to investigate the effects of metformin or Glibenclamide alone or in combination on serum visfatin levels, glycemic control, and lipid profile in TD2M patients. This study was carried out on type 2 diabetic patients with poor glycemic control at the Specialized Center for Diabetes and Endocrinology, Al-Kindi Teaching Hospital, Baghdad. Results of this study showed a significant reduction in serum visfatin concentration in different treated groups in comparison with newly diagnosed diabetic group in addition to changes in glycemic and lipid profile among groups. The treatment with metformin a hypoglycemic drug in T2DM is more effective in reducing serum visfatin level compared with other treatment regimen.

Keywords: TDM 2, visfatin, Glibenclamide, metformin, lipid profile.

INTRODUCTION

Diabetes mellitus is the most common metabolic disorder and is a major risk factor for cardiovascular disease (CVD) [1]. Many risk factors for CVD, including hyperglycemia, abnormal lipid profiles, and alterations in inflammatory mediators, are generate by type two diabetes mellitus (T2DM) patients [2, 3]. The most important risks for the development of insulin resistance and T2DM are increase body weight and excess adiposity [4]. A new adipocytokine, visfatin is associated with a wide range of biologic effects, including glucose and lipid metabolism, and has been implicated in the pathogenesis of diabetes mellitus and obesity. Visfatin is an adipocytokine that was identified in 2005[5]. This cytokine was named based on it being initially produced by visceral fat, Visfatin has a molecular weight of 52 kDa and is composed of 491 amino acid residues[6]. The auto crine effects of visfatin may play an important role in regulating insulin sensitivity in the liver[7]. It was previously described as a pre-beta cell colony- enhancing factor, which is abundantly expressed in visceral adipose tissue[8]. Visfatin has insulin mimetic effects; it binds to the insulin receptor at a different binding site than insulin and activate it. Moreover, visfatin is produced by macrophages and exerts proinflammatory properties contributing to atherosclerosis development[9]. Several clinical studies have reported that higher plasma visfatin levels are associated with a higher body mass index (BMI) and increase body fat[10], T2DM[11], obesity[5], and dyslipidemia[12]. Recently, the relationships between visfatin and metabolic disorders, such as insulin resistance and dyslipidemia, have been studied in humans, but many aspects of these relations are still unknown. One study showed increased levels of circulating visfatin [5], while another study confirmed reduced plasma visfatin levels in obesity[13]. Paradoxically, in humans, both weight reduction[5] and over-nutrition down regulated the circulating visfatin levels[14]. In various models of obesity, controversial findings related to visfatin levels, including increased[15], unchanged[16], or decreased in visfatin concentrations[17], have been reported.

The aim of this study was to investigate the effects of metformin or Glibenclamide alone or in combination on visfatin levels, glycemic control, and lipid profile in TD2M patients.

PATIENTS AND METHODS

This study was carried out on type 2 diabetics patients with poor glycemic control at the Specialized Center for Diabetes and Endocrinology, Al-Kindi Teaching Hospital, Baghdad. Total number of diabetic patients selected was (50) with age range of (40-64 years) who are:

Group 1: 10 healthy individual kept as positive control.

Group 2: 10 patients with type 2 DM newly diagnosed, and are without treatment kept as negative control.

Group 3: 10 patients with type 2 DM treated with Glucophage (metformin) for at least 6months ago.

Group 4: 10 patients with type 2 DM treated with Glibenclamide for at least 6 months.

Group 5: 10 patients with type 2 DM treated with combination of Glucophage and Glibenclamide for at least 6months ago. Venous blood specimens (10ml) were

withdrawn from each patient after an overnight fasting (12hr.). Eight ml of blood samples were transferred into plane tube to be centrifuged for (5-10) minutes to obtain serum. Fresh serum was used for the measurement of FSG, TC, TG, HDL-C, LDL-C and serum visfatin, the remainder of blood (2ml) was placed into an EDTA tubes for measuring %HbA1C within 1-2 hours. Serum glucose level were evaluated according to the method of Barhan and Trindoer, 1972, and glycated hemoglobin (HbA1C) level was determined according to the method of Abraham et al., 1978. ELISA method was employed to determine visfatin levels. Serum lipid profile was evaluated through the measurement of total cholesterol according to the method of Richmond et al., 1973, and triglycerides levels according to the method of Fossati and Principe, 1982, while Burstein et al. (1970) method was utilized for the measurement of high density lipoprotein–cholesterol (HDL–c) levels from which the serum concentrations of the low density lipoprotein–cholesterol (LDL–c) levels were calculated indirectly using Friedwald formula (Friedwald et al., 1972).

Statistical Analysis

SPSS software, version 23 was used to test the study data. And the results were expressed as mean ±standard deviation; P–values less than 0.05 were considered to be significant.

RESULTS

The study was conducted on 40 patients, comparison parameters between control group and new diagnosis diabetics group (Table 1). Table 2 showed significant reduction in fasting serum glucose level in patients who took a metformin, Glibenclamide, combination of these drugs, in comparison with group of newly diagnosed diabetics, the HbA1c significantly reduced in all study groups compared with newly diagnosed diabetic group, except in glibenclamide treated group reduced slightly but not statistically significant, while a reduction in total cholesterol concentration observed significant in metformin and combination treated groups while in Glibenclamide treated group reduction observed but not statistically significant**,** while a reduction in serum concentration level of TG, HDL, VLDL, LDL not statistically significant compared with newly diagnosed diabetics group that not taken any treatments, study also showed a significant reduction in LDL levels in metformin treated group. Meanwhile this study noticed a significant reduction in serum visfatin concentration in different treated groups in comparison with newly diagnosed diabetic group and when compared glibneclamide and combination treated groups with metformin treated group.

Table 1: comparison of measured parameters between control and newly diagnosed diabetic group.

Parameters	Control (Healthy) group	Newly diagnosed Diabetics group
FSG (mg/dl)	92.82 ± 7.86	282.11 ± 44.44*
HbA1c %	5.62 ± 0.399	10.17 ± 0.421*
TC (mg/dl)	176.38 ± 19.91	243.04 ± 33.10*
TG (mg/dl)	104.51 ± 46.55	232.23 ± 107.41*
HDL(mg/dl)	46.96 ± 16.13	34.40 ± 4.23*
LDL (mg/dl)	110.30 ± 23.20	162.18 ± 44.72*
VLDL (mg/dl)	20.91 ± 9.30	45.92 ± 21.79*
Visfatin (ng/dl)	93 ± 11.97	157.2 ± 20.43*

FSG, fasting serum glucose; HbA1c, Glycated Hemoglobin ,TC, total cholesterol; TG, triglycerides; LDL, HDL, low and high density lipoprotein; VLDL very low density lipoprotein - Results represent mean ± standard Deviation,*P<0.05 represent significant with control group.

Table 2: A comparison of measured parameters between newly diagnosed diabetics with groups treated with Metformin, Glibenclamide or Combination of both.

Parameters	Newly diagnosed Diabetics group	Metformin treated group (500mg 3times daily)	Glibenclamide treated group (5 mg twice daily)	Combination treated group (5\500 mg twice daily)
FBG (mg/dl)	282.11±44.44	219.06 ± 75.13*	229.63 ± 36.11*	220.2± 64.40*
HbA1c %	10.17 ± 0.421	8.24 ± 1.61*	9.7 ± 1.30	8.1 ± 1.45*
TC (mg/dl)	243.04 ± 33.10	192.09 ± 27*	225.04 ± 22.223	213.29 ±33.30*
TG (mg/dl)	232.23 ± 107.41	172.26 ± 52.79	180.66 ± 47.91	184.71± 31.10
HDL (mg/dl)	34.40 ± 4.23	37.38 ± 8.32	39.09 ± 4.06	37.88 ± 7.86
LDL (mg/dl)	162.18 ± 44.72	120.25 ± 23.13*	146.23 ± 31.78	138.45± 35.9
VLDL (mg/dl)	45.92 ± 21.79	34.43 ± 10.58	36.16 ± 9.49	36.49 ± 6.22
Visfatin (ng/dl)	157.2 ± 20.43	99.1 ± 19.63*	141.3 ± 19.68[a]	151.3 ± 16.08[a]

FSG, fasting serum glucose; HbA1c, Glycated Hemoglobin ,TC, total cholesterol; TG, triglycerides; LDL, HDL, low and high density lipoprotein; VLDL very low density lipoprotein - Results represent mean ± standard Deviation,*P<0.05 represent significant with newly diagnosed D.M group; (a): represent significantly different (P<0.05) with metformin treated group.

DISCUSSION

The present study was evaluated the effect of the oral antidiabetic drugs metformin, glibenclamide, and a combination of both on fasting blood glucose, HbA1c, lipid profile, serum visfatin concentration levels in type 2 diabetics patients. This study was carried out on type 2 diabetic patients with poor glycemic control. According to the results of this study, the table1 showed a significant elevation of serum visfatin, total cholesterol, TG, LDL-C, VLDL-C, HbA1c, fasting serum glucose in newly diagnosed diabetics compared with control group and reduced in HDL –C level. Serum visfatin levels were found to be significantly elevated in diabetic patients. In this study is in agreement with other studies which reported an increased blood visfatin levels in patients with T2DM [(10)]. Consistent with most findings, we found significantly higher visfatin levels in diabetic patients' newly diagnosed compared with the controls. There are limited data deals with the effect of anti-diabetic drugs on adipokines, especially on visfatin. It found that visfatin levels in the serum reduced after treated with metformin. The mean serum levels of visfatin in all treated groups receiving hypoglycemic drugs reduced when compared to untreated diabetic patients, but only metformin reduced the serum visfatin levels and reach to the normal level approximately. It was reported that visfatin secretion is regulated by insulin and glucose by pathway of phosphatidylinositol 3 kinase and protein kinase B [18]. The serum visfatin in glibenclamide and combination treated groups were reduced but not to the reduction level in Metformin treated group, this attributed to that glibenclamide causes hypoglycemia and weight gain, therefore the patient increase food consumption causing weight gain therefore level of visfatin remain high level.

CONCLUSIONS

The treatment with metformin a hypoglycemic drug in T2DM is more effective in reducing serum visfatin level compared with other treatment regimen.

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