# Comparative Study Between Glimepiride and Glibenclamide in the Treatment of Type 2 Diabetic Patients in Al-Yarmouk Hospital

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## ABSTRACT:

**BACKGROUND:**

Second-generation sulfonylureas (SU) are efficacious, generally well-tolerated, cost-effective options for the medical management of diabetes. Glimepiride which is sometimes classified as a third-generation has benefits over other in that it has a considerably lower binding affinity for the B-cell receptor, result in a modulation of insulin release, and a decreased potential for inducing hypoglycemia.

**OBJECTIVE:**

This study was designed to evaluate the outcome of using glimepiride and glibenclamide in type 2 diabetic patients.

**PATIENTS AND METHODS:**

A single blinded randomized clinical trial was adopted, in which 64 already diagnosed diabetic patients (regardless disease duration) were recruited from Al-Yarmouk hospital, and randomized into two groups; 1st group (32 patients) treated with 5 mg glibenclamide, and 2nd group (32 patients) treated with 3 mg glimepride for 4 months. Fasting blood sugar (FBS), glycosylated hemoglobin (HbA1c) level, triglyceride, cholesterol, serum electrolyte (Na, K, Ca) level and pulse rate were measured at zero time (first visit)and at the end of the study (after 4 months).

**RESULTS:**

The result showed that both Fasting blood sugar, glycosylated hemoglobin, serum total cholesterol, triglyceride levels were decreased significantly in both treatment group but with greater reduction in group 2, serum electrolytes were not significantly affected, except calcium level which was increased significantly in glimepiride group only. Moreover, no significant effect observed regarding pulse rate compared to pretreatment period.

**CONCLUSION:**

Glimepride provide more potent glycemic control and better lipid profile compared to glibenclamide in type 2 diabetic patients.


***KEY WORDS:*** comparative study, glimepiride, glibenclamide, diabetic patients.

## INTRODUCTION:

Sulfonylureas have been used for type 2 diabetes for over 50 years [(1)]. They act by stimulating insulin release from the beta cells of the pancreas. They bind to sulfonylurea receptors found on the surface of pancreatic β-cells and this interaction leads to closure of $K^+$-ATP channels, the cell membrane is depolarized and insulin is released [(2)]. Glimepiride, a new third-generation sulfonylurea, is reported to have some extrapancreatic effects, such as improving peripheral glucose uptake in muscle [(3)]and reducing endogenous glucose production in liver [(4)] .

These effects are supposed to be achieved by facilitating insulin action; through these effects, glimepiride is considered to have therapeutical benefit in the treatment of type 2 diabetic patients compared with other older generation sulfonylureas (e.g. glibenclamide). [(5)] Benefits of glimepiride include rapid and complete absorption [(6,7)] and once-daily dosing. [(8)]It carries a relatively low risk of hypoglycemia. [(9)]

Compared with glibenclamide, glimepiride has a considerably lower binding affinity for the B-cell receptor, results in less fixed-receptor blockade

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than is observed with the other sulfonylureas, a modulation of insulin release, improve peripheral insulin sensitivity and a decreased potential for inducing hypoglycemia.[10]

Also glimepiride is believed to selectively target potassium channels in the pancreas over those in extrapancreatic tissues, such as cardiac, skeletal, and smooth muscle tissue, [11] so it is not like other sulfonylureas which have potential to inhibit the opening of cardiac ATPdependent potassium channels and may be harmful to ischemic myocardium by blunting the channel-dependent component of the ischemic preconditioning response. [12,13] This may explain why, in both animal and human studies, glimepiride has been associated with fewer cardiac events than have other sulfonylureas and may be safer to use in patients with cardiovascular disease. [14,15] Glimepiride may also decrease levels of fibrinogen, which is known to play a key role in vascular complications in patients with diabetes. [16] The present study was designed to evaluate the therapeutic effect of glimepiride on blood glucose, serum total cholesterol, triglyceride, serum electrolytes and pulse rate in comparison with glibenclamide in patients with type 2 diabetes mellitus.

## PATIENTS AND METHOD:

Sixty four patients already diagnosed with type 2 DM regardless of duration were recruited from Al-Yarmouk hospital, Their ages are 40 +/- 15 years, 65% of them were females and 35% were males, with body mass index range 20.5-26 kg/m$^2$. In a single blinded randomized clinical study, patients were randomized into two groups:

1$^{st}$ group (32 patients) were given 5 mg/day of glibenclamide before breakfast.

2$^{nd}$ group (32 patients) were given 3 mg/day of glimepiride with breakfast.

Patients were selected for the study by glycated hemoglobin level in the range between 7.8 & 9.2%. Patients with hypertension, heart failure or any other chronic disease, pregnancy and severe diabetic complications such as retinopathy, nephropathy, neuropathy or ischemic cardiovascular disease were excluded.

All patients signed written informed consent before initiation of any trial-related activities. Fasting blood was withdrawn for analyses of HbA1C, serum total cholesterol, triglyceride and serum electrolytes levels by standard laboratory techniques.

Blood samples were collected at the beginning of the study (baseline samples) and after 4 months of starting treatment to measure the possible change in the studied parameters.

Data were statistically evaluated using paired t-test to compare between pre- and post-treatment results. Unpaired t-test was utilized to compare between the results of studied parameters among patients groups. Values with $P<0.05$ were considered significantly different.

## RESULTS :

A description of clinical and laboratory parameters are given in the figures below:

In (Figure 1), Fasting blood sugar, glycosylated hemoglobin (HbA1c) were significantly decreased, as compared to baseline, but the reduction was greater in the glimepiride group. Beside that, serum total cholesterol & triglyceride showed improvement with glimepiride treatment, but not with glibenclamide treatment (Figure 2).

After glimepiride treatment, total serum cholesterol & triglyceride were obviously decreased. In addition it has been noticed that there was no significant effect in sodium & potassium for both groups compared to pretreatment value as shown in (Figure 3). On the other hand, there was a significant increase in calcium level with glimepiride group only. Moreover, significant reduction was observed regarding pulse rate in both treatment groups compared to pretreatment period (Figure 4).

## DISCUSSION:

Glimepiride, is different from the traditional SU drugs, it not only promotes second-phase insulin secretion but also stimulates first-phase insulin secretion [17], so Glimepiride reduces both fasting plasma glucose and postprandial plasma glucose levels, it can also lower HbA1c values comparing to other second-generation SUs, consistent with several studies which evaluated the effect of glimepiride versus glibenclamide [18].

Along with rapid blood glucose control and lipid metabolism improvement, glucose toxicity and lipotoxicity products in the plasma were relieved rapidly, thus the function of pancreatic B cells could be enhanced significantly [19,20]. The available data concerning the effect of sulfonylureas on postprandial lipid metabolism are inconsistent. However, most of the studies suggest that sulfonylureas improve postprandial lipemia ameliorating the postprandial increase in

chylomicrons (CM) and very low density lipoprotein (VLDL) triglycerides.[21] This effect is possibly due to the increased activity of leptin plasma level and hepatic lipase and to the reduction of glycemia and free fatty acids (FFAs) postprandially. [22]The reduction of intestinally-derived lipoproteins by sulfonylureas is of clinical importance because small CM remnants are highly atherogenic. [23] Moreover, decreased plasma glucose concentration following successful SU trearment improve fasting & postprandial hypertriglyceridemia. [24]

Serum Na, K and Ca were measured in this study because dehydration may occur due to hyperosmolar state which occur in a person with very high (usually considered to be above 300 mg/dl ) blood glucose levels, this may lead to loss of water and an increase in blood osmolarity. If fluid is not replaced (by mouth or intravenously), the osmotic effect of high glucose levels, combined with the loss of water, will eventually lead to dehydration. The body's cells become progressively dehydrated as water is taken from them and excreted so electrolyte imbalances are common and are always dangerous thus urgent treatment may be required [25]. Changes in pulse rate have no clinical importance since it occurs within the normal values.

Interestingly, there was an increase in Ca level in Glimepiride group. This unexpected result could be explained by the fact that Sulfonylureas stimulate insulin secretion from pancreatic β-cells and are widely used to treat type 2 diabetes. Their principal target is the ATP-sensitive potassium (KATP) channel, which plays a major role in controlling the β-cell membrane potential. Inhibition of KATP channels by glucose or sulfonylureas causes depolarization of the β-cell membrane; in turn, this triggers the opening of voltage-gated Ca2+ channels, eliciting Ca2+ influx and a rise in intracellular $Ca^{2+}$ which stimulates the exocytosis of insulin-containing secretory granules [26,27].

It can be assumed that the increase in Ca level could have a useful role in improving muscle weakness associated with the diabetic myotrophy. However, further studies are required to explore the possible influence of increased Ca level associated with glimepiride treatment.

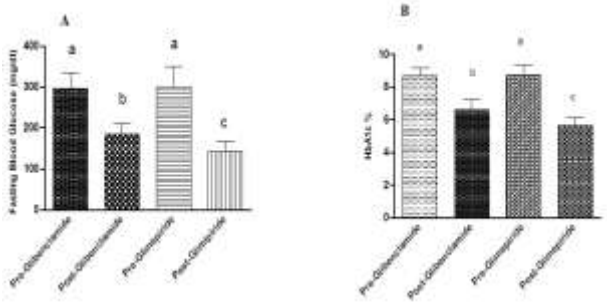

**Figure 1: Comparison between the effect glmepiride and glibenclamide on fasting blood GLUCOSE & glycosylated hemoglobin (HbA1c).**

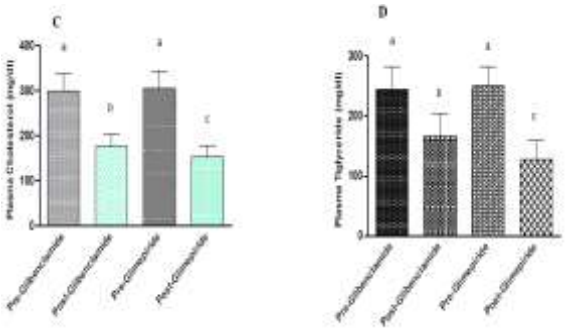


**Figure 2: Comparison between the effect glmepiride and glibenclamide on serum cholesterol and Triglyceride.**

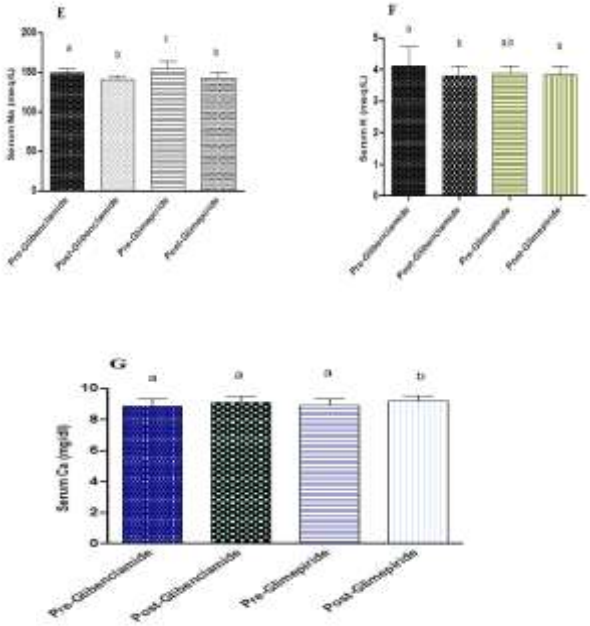


**Figure 3: Comparison between the effect glmepiride and glibenclamide on serum electrolyte (Sodium, potassium & calicium).**

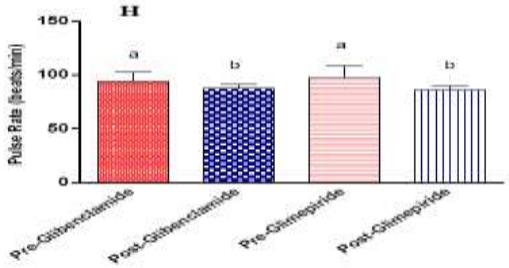


**Figure 4: Comparison between the effect glmepiride and glibenclamide on pulse rate.**

## CONCLUSION:

Glimepiride was found more potent in ameliorating hyperglycemia and impaired lipid profile compared to glibenclamide with an almost equivalent dosage.

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