ORIGINAL RESEARCH

Assessment of efficacy and safety of glimepiride-metformin versus glibenclamide-metformin combination in type-2 diabetics uncontrolled with metformin alone

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ABSTRACT
Background: Metformin is a commonly prescribed oral medication for the management of type 2 diabetes mellitus. It is typically used as a first-line treatment because of its effectiveness, safety profile, and relatively low cost. The present study was conducted to assess efficacy and safety of glimepiride-metformin versus glibenclamide-metformin combination in type-2 diabetics uncontrolled with metformin alone. **Materials & Methods:**50 patients uncontrolled type 2 diabetic patients of both genders were measured. Patients were divided into 2 groups of 25 each.Group I patients received two pills of glimepiride (1 mg)/metformin (500 mg) and group II patients received glibenclamide (5 mg)/metformin (500 mg) po once a day. Dosage was increased to a maximum of four pills in order to reach the glycemic control goals (fasting glucose ≤7.2 mmol/l, postprandial glucose b10.0 mmol/l, A1C b7%, or an A1C ≥1% reduction). Serum fasting and postprandial glucose, hemoglobin A1c (A1C), high-density lipoprotein cholesterol, and triglycerideswas compared in both groups. **Results:** There were 14 males and 11 females in group I and 13 males and 12 females in group II. In group I and group II, mean fasting blood sugar (mg/dl) at baseline was 174.2 and 172.6, at 4 weeks was 160.4 and 152.0, at 8 weeks was 148.4 and 134.8 and at 12 weeks was 122.6 and 120.6 in group I and group II respectively. Postprandial blood sugar(mg/dl) at baseline was 248.4and 244.6, at 4 weeks was 200.6 and 204.6, at 8 weeks was 190.2 and 194.2 and at 12 weeks was 168.4 and 182.3 in group I and group II respectively. Lipid profile (mg/dl)TC was 176.4 and 184.2, LDL- C was 92.6 and 91.8, HDL- C was 40.2 and 41.3 and TGs was 164.8 and 167.5 in group I and group II respectively. The difference was significant (P< 0.05). Nausea was seen in 3 in group I and 5 in group II, abdominal pain seen in 5and 4, metallic taste in 2 and 5 and hypoglycaemia in 2 and 4 in group I and II respectively. The difference was significant (P< 0.05). **Conclusion:** Glimepiride and metformin combination therapy has superior effect on PPBS level reduction and significantly lesser incidence of hypoglycaemia as compared to glibenclamide and metformin combination group.
Key words: Metformin, Lipid profile, glibenclamide

INTRODUCTION

Metformin is a commonly prescribed oral medication for the management of type 2 diabetes mellitus. It is typically used as a first-line treatment because of its effectiveness, safety profile, and relatively low cost. In patients with uncontrolled type 2 diabetes mellitus, metformin can be a valuable therapeutic option. It works by reducing glucose production in the liver,

improving insulin sensitivity in peripheral tissues, and slowing down glucose absorption in the intestines.[1]These actions help lower blood glucose levels and improve glycemic control. When initiating metformin therapy in patients with uncontrolled diabetes, it is important to start at a low dose and gradually increase it over time to minimize gastrointestinal side effects such as nausea, vomiting, and diarrhea. Adherence to the prescribed dose and regular follow-up with a healthcare professional are crucial for monitoring the patient's response to treatment and adjusting the dosage if needed.[2]

It is worth noting that metformin is not suitable for all individuals. Some contraindications include severe kidney impairment, liver disease, heart failure, and certain other medical conditions. Additionally, some patients may not adequately respond to metformin alone, and additional or alternative medications may be necessary to achieve optimal blood glucose control. It is essential for individuals with uncontrolled type 2 diabetes to work closely with their healthcare team to develop an individualized treatment plan that includes lifestyle modifications, medication management, and regular monitoring of blood glucose levels.[3]

On one hand, glibenclamide/metformin is the oral antidiabetic combination most used in the clinical practice today; on the other hand, glimepiride—considered as a third-generation sulfonylurea agent—has several beneficial pharmacological effects over glibenclamide, a second-generation sulfonylurea.[4] Glimepiride combined with metformin in a single dose presentation has proved to be effective and safe for type 2 diabetes patients who fail with monotherapy on oral antidiabetic agents.[5]The present study was conducted to assess efficacy and safety of glimepiride-metformin versus glibenclamide-metformin combination in type-2 diabetics uncontrolled with metformin alone.

MATERIALS & METHODS

The present study consisted of 50 patientsuncontrolled type 2 diabetic patients of both genders. All gave their written consent to participate in the study.

Data such as name, age, gender etc. was recorded. Serum fasting and postprandial glucose, hemoglobin A1c (A1C), high-density lipoprotein cholesterol, and triglycerides were measured. Patients were divided into 2 groups of 25 each.Group I patients received two pills of glimepiride (1 mg)/metformin (500 mg) and group II patients received glibenclamide (5 mg)/metformin (500 mg) po once a day. Dosage was increased to a maximum of four pills in order to reach the glycemic control goals (fasting glucose ≤7.2 mmol/l, postprandial glucose b10.0 mmol/l, A1C b7%, or an A1C ≥1% reduction). Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Groups	Group I (25)	Group II (25)
Method	glimepiride (1 mg)/metformin (500 mg)	glibenclamide (5 mg)/metformin (500 mg)
M:F	14:11	13:12

Table I shows that there were 14 males and 11 females in group I and 13 males and 12 females in group II.

Table II Assessment of parameters

Parameters	Variables	Group I	Group II	P value
Fasting blood sugar (mg/dl)	Baseline	174.2	172.6	0.04
	4 weeks	160.4	152.0	
	8 weeks	148.4	134.8	
	12 weeks	122.6	120.6	
Postprandial blood sugar (mg/dl)	Baseline	248.4	244.6	0.05
	4 weeks	200.6	204.6	
	8 weeks	190.2	194.2	
	12 weeks	168.4	182.3	
Lipid profile (mg/dl)	TC	176.4	184.2	0.12
	LDL- C	92.6	91.8	
	HDL- C	40.2	41.3	
	TGs	164.8	167.5	

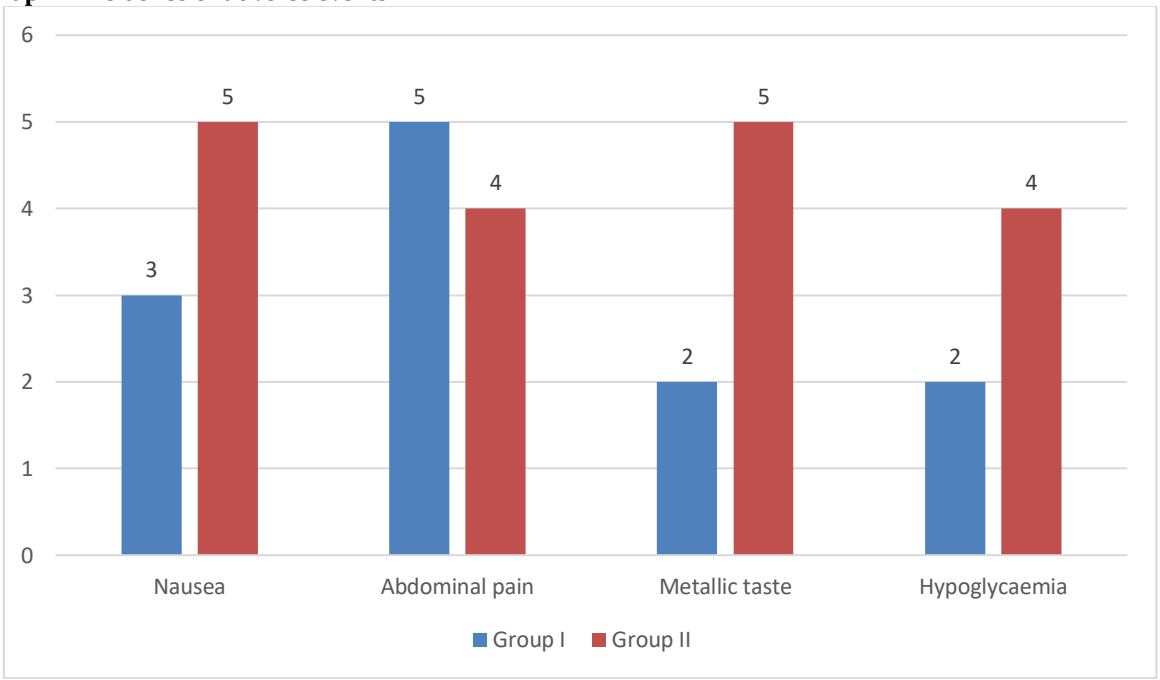
Table II shows that in group I and group II, mean fasting blood sugar (mg/dl) at baseline was 174.2 and 172.6, at 4 weeks was 160.4 and 152.0, at 8 weeks was 148.4 and 134.8 and at 12 weeks was 122.6 and 120.6 in group I and group II respectively. Postprandial blood sugar(mg/dl) at baseline was 248.4 and 244.6, at 4 weeks was 200.6 and 204.6, at 8 weeks was 190.2 and 194.2 and at 12 weeks was 168.4 and 182.3 in group I and group II respectively. Lipid profile (mg/dl)TC was 176.4 and 184.2, LDL- C was 92.6 and 91.8, HDL- C was 40.2 and 41.3 and TGs was 164.8 and 167.5 in group I and group II respectively. The difference was significant (P< 0.05).

Table III Incidence of adverse events

Adverse events	Group I	Group II	P value
Nausea	3	5	0.05
Abdominal pain	5	4	0.82
Metallic taste	2	5	0.01
Hypoglycaemia	2	4	0.03

Table III, graph I shows that nausea was seen in 3 in group I and 5 in group II, abdominal pain seen in 5 and 4, metallic taste in 2 and 5 and hypoglycaemia in 2 and 4 in group I and II respectively.

Graph I Incidence of adverse events



DISCUSSION

Insulin resistance occurs early in type 2 diabetes disease process and may lead to progressive beta cell failure and overt diabetes.[6] Monotherapy can slow down but does not prevent the progression of the disease.[7] Successful management requires combination therapy that addresses both insulin resistance and beta cell dysfunction.[8] Clinical trials support the use of combinations of antidiabetic agents with complementary mechanisms of action such as a sulfonylurea/metformin.[9]The present study was conducted to assess efficacy and safety of glimepiride-metformin versus glibenclamide-metformin combination in type-2 diabetics uncontrolled with metformin alone.

We found that there were 14 males and 11 females in group I and 13 males and 12 females in group II. Gonzalez et al[10]conducted a study on 152 uncontrolled type 2 diabetic patients. Serum fasting and postprandial glucose, hemoglobin A1c (A1C), high-density lipoprotein cholesterol, and triglycerides were measured. After random allocation, all patients received two pills of glimepiride (1 mg)/metformin (500 mg) or glibenclamide (5 mg)/metformin (500 mg) po once a day. Each study group included 76 patients. No significant differences in basal clinical and laboratory characteristics between groups were found. At the end of the study, A1C concentration was significantly lower in the glimepiride/metformin group (P=.025). A higher proportion of patients from the glimepiride group (44.6% vs. 26.8%) reached the goal of A1C b7% at 12 months of treatment. A higher proportion of hypoglycemic events were observed in the glibenclamide group (28.9% vs. 17.1%,).

We found that in group I and group II, mean fasting blood sugar (mg/dl) at baseline was 174.2 and 172.6, at 4 weeks was 160.4 and 152.0, at 8 weeks was 148.4 and 134.8 and at 12 weeks was 122.6 and 120.6 in group I and group II respectively. Postprandial blood sugar(mg/dl) at baseline was 248.4 and 244.6, at 4 weeks was 200.6 and 204.6, at 8 weeks was 190.2 and 194.2 and at 12 weeks was 168.4 and 182.3 in group I and group II respectively. Lipid profile (mg/dl)TC was 176.4 and 184.2, LDL- C was 92.6 and 91.8, HDL- C was 40.2 and 41.3 and TGs was 164.8 and 167.5 in group I and group II respectively. Gawali et al[11]compared the effects of combination therapy using metformin and glimepiride with metformin and glibenclamide combination on glycaemic control (HbA1c and plasma glucose) and lipid profiles {Total cholesterol (TC), Triglyceride (TG), low density lipoprotein cholesterol (LDL-C),High density lipoprotein cholesterol (HDL-C)} in type 2 diabetes mellitus patients who have inadequately control with

metformin and glibenclamidemonotherapy. Primary efficacy end points were changes in fasting blood sugar (FBS) and postprandial blood sugar (PPBS) from baseline to 4weeks, 8weeks and 12weeks and changes in HbA1C from baseline to final assessment i.e. at 12 weeks. At the end of 12 weeks difference in reduction in fasting blood sugar(FBS) and Glycosylated haemoglobin (HbA1c)between the treatment groups was not statistically significant.But reduction in postprandial blood sugar (PPBS) was statistically more significant in glimepiride and metformin groups.

We found that nausea was seen in 3 in group I and 5 in group II, abdominal pain seen in 5 and 4, metallic taste in 2 and 5 and hypoglycaemia in 2 and 4 in group I and II respectively.

The limitation the study is small sample size.

CONCLUSION

Authors found that Glimepiride and metformin combination therapy has superior effect on PPBS level reduction and significantly lesser incidence of hypoglycaemia as compared to glibenclamide and metformin combination group.

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