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A STUDY TO COMPARE THE EFFECTIVENESS. METFORMIN AND METFORMIN + GLIMEPIRIDE IN PATIENTS WITH TYPE 2 DIABETES

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ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) requires effective glycemic control to prevent complications. Metformin is the first-line therapy, but many patients need combination treatment for optimal control. This study compared the efficacy and safety of Metformin monotherapy versus Metformin + Glimepiride combination therapy. **Methods:** A total of 100 T2DM patients were randomized into two groups (n=50 each). Group A received Metformin, while Group B received Metformin + Glimepiride for 12 weeks. Glycemic parameters (HbA1c, FBG, PPBG), BMI, medication adherence, and adverse events were assessed at baseline and 12 weeks. **Results:** Both groups showed significant reductions in HbA1c, FBG, and PPBG. Group B demonstrated greater reductions (HbA1c: 1.5% vs 1.0%; FBG: 29 vs 20 mg/dL; PPBG: 47 vs 30 mg/dL; $p<0.05$). BMI remained stable. Adherence was high, and side effects were mild. **Conclusion:** Metformin + Glimepiride combination therapy provides superior glycemic control compared to Metformin alone, with good safety and adherence, making it an effective treatment option for T2DM patients not achieving targets with monotherapy.

KEYWORDS: Type 2 diabetes, Metformin, Glimepiride, combination therapy, glycemic control, safety.

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a lobg lasting metabolic condition which is basically characterized by the presence of high blood sugar levels due to insulin resistance and progressive pancreatic beta-cell dysfunction. T2DM is becoming more and more prevalent worldwide, mostly as a result of lifestyle changes, such as less physical activity, and the growing number of elderly people around the globe. If hyperglycemia remains uncontrolled, it can cause long-term microvascular and macrovascular complications, which are, among others, retinopathy, nephropathy, neuropathy,

and heart diseases.[1] The very good and fast glycemic management is still the most important factor for decreasing the number of cases and deaths. The use of drugs, together with the change of lifestyle, continues to be the main treatment method. Metformin, among all the antidiabetic agents available, is the one that is most commonly used as the first-line therapy because of its efficacy, safety, and cardiovascular benefits.[2]

Metformin's main action is to decrease the amount of glucose produced by the liver and to enhance the sensitivity of insulin in the peripheral tissues which results in the effective lowering of fasting and post-meal glucose levels. There is, however, a considerable number of patients who do not reach the desired glycemic level and this is mainly because of the progressive β-cell degeneration and as a result, Metformin monotherapy is still an option. In this case, it is better to go for a combination of drugs to treat the condition.[3] One case in this regard is the use of sulfonylureas like Glimepiride that not only stimulates the pancreas to secrete insulin but also works hand in hand with Metformin. There is evidence that the combination of Metformin and Glimepiride leads to a significant betterment of HbA1c levels than either of the agents alone thus giving an important strategy in the case of patients not adequately controlled on monotherapy.[4]

A combination therapy of Metformin with Glimepiride has been put through various clinical studies that have assessed both its efficacy and safety in T2DM patients. The studies, in general, have reported very good glycemic outcomes when compared to Metformin alone which include the significant decrease of HbA1c, fasting, and postprandial glucose levels. Nonetheless, when prescribing sulfonyures the occurrence of hypoglycemia and other side effects should be taken into account.[5] Also, patient compliance to the therapy is a major factor affecting the outcomes. High compliance guarantees the reliability of the efficacy and the reduction of the complications. Real-world evidence indicates that combination therapy is effective and well-tolerated when appropriately monitored, thus the clinical relevance in the achieving of the target glycemic control is underlined.[6]

The evaluation of combination therapies in particular populations has become a fundamental issue in the light of the increasing prevalence of T2DM and the limitations of monotherapy. Metformin and Metformin + Glimepiride comparisons give broad understanding about efficacy, safety, and patient adherence, which in turn help the treatment plans personalized. The awareness of the glycemic improvement's size, side effects, and adherence patterns aids therapy optimization for better long-term results.[7]

MATERIALS AND METHODS

Study Design: This was a prospective, comparative, observational study conducted over 12 weeks at a tertiary care hospital, aimed at evaluating the effectiveness of Metformin monotherapy versus Metformin + Glimepiride combination therapy in patients with type 2 diabetes mellitus (T2DM).

Study Population and Sampling Technique: The study population included adult patients diagnosed with T2DM attending the outpatient department. Convenience sampling was used to select eligible patients who met the inclusion criteria and provided informed consent.

Sample Size: A total of 100 patients were enrolled in the study based on the feasibility and similar studies in the literature. Patients were equally divided into two groups:

- Group A (n=50): Metformin monotherapy
- Group B (n=50): Metformin + Glimepiride combination therapy

Grouping of Participants: Patients were allocated based on their current treatment regimen or physician's prescription:

- Group A: Patients receiving only Metformin (500–2000 mg/day, divided doses).
- Group B: Patients receiving Metformin (500–2000 mg/day) in combination with Glimepiride (1–4 mg/day, single dose).

Inclusion Criteria

1. Adults aged 30–70 years with confirmed T2DM.
2. HbA1c levels between 7–10% at baseline.
3. Patients willing to provide informed consent and adhere to follow-up visits.
4. Patients on stable doses of oral hypoglycemic agents for at least 3 months.

Exclusion Criteria

1. Type 1 diabetes mellitus or secondary diabetes.
2. Pregnant or lactating women.
3. Severe renal impairment (eGFR <30 mL/min/1.73 m²) or hepatic dysfunction.
4. History of hypersensitivity to Metformin or Glimepiride.
5. Patients on insulin therapy or other antidiabetic drugs not part of the study.
6. Patients with significant comorbidities affecting study outcomes (e.g., cancer, severe cardiovascular disease)

Study Procedure: Eligible patients meeting the inclusion criteria were enrolled after obtaining informed consent and baseline assessments, including demographics, medical history, fasting blood glucose (FBG), postprandial blood glucose (PPBG), HbA1c. Patients were divided into two groups: Group A received Metformin monotherapy, and Group B received Metformin combined with Glimepiride. Follow-up visits were conducted at 4, 8, and 12 weeks to monitor changes in glycemic parameter and any side effecrs. Medication adherence was assessedt. Safety outcomes, including hypoglycemia and gastrointestinal disturbances, were recorded, and data were analyzed to evaluate the efficacy and tolerability of both regimens.

Statistical Analysis: Data were analyzed using SPSS 26. Continuous variables were expressed as mean ± SD, and categorical variables as frequency and percentage. Paired t-tests compared baseline and post-treatment values within groups, unpaired t-tests compared between groups.P-value <0.05 was significant.

RESULTS

1. Demographics and Baseline Characteristics.

Characteristic	Group A (Metformin, n=50)	Group B (Metformin + Glimepiride, n=50)
Age Category (years)		
30–40	6 (12%)	5 (10%)
41–50	18 (36%)	17 (34%)
51–60	16 (32%)	18 (36%)
61–70	10 (20%)	10 (20%)
Sex		
Male	28 (56%)	27 (54%)
Female	22 (44%)	23 (46%)
Area of Residence		
Urban	30 (60%)	28 (56%)
Rural	20 (40%)	22 (44%)

Common Symptoms		
Polyuria / Frequent urination	42 (84%)	43 (86%)
Polydipsia / Increased thirst	38 (76%)	39 (78%)
Fatigue / Weakness	30 (60%)	32 (64%)
Blurred vision	15 (30%)	16 (32%)
Duration of Diabetes (years)		
<5	20 (40%)	18 (36%)
5–10	22 (44%)	24 (48%)
>10	8 (16%)	8 (16%)

Both groups were comparable at baseline. In Group A, most patients were aged 41–60 years (54%), with 28 males (56%) and 30 (60%) urban residents. Common symptoms included polyuria 42 (84%) and polydipsia 38 (76%). Diabetes duration was mostly under 10 years. Group B showed similar distributions, ensuring balanced baseline characteristics.

2. Baseline vs 12 Weeks – Group A (Metformin)

Parameter	**Baseline**	**12 Weeks**	**Mean Change**	**p-value**
HbA1c (%)	8.2 ± 0.7	7.2 ± 0.6	1.0	<0.01
FBG (mg/dL)	145 ± 18	125 ± 15	20	<0.01
PPBG (mg/dL)	210 ± 25	180 ± 22	30	<0.01
BMI (kg/m²)	27.1 ± 3.5	26.9 ± 3.4	0.2	0.12

In Group A, Metformin monotherapy significantly reduced HbA1c from 8.2 ± 0.7% to 7.2 ± 0.6%, FBG from 145 ± 18 to 125 ± 15 mg/dL, and PPBG from 210 ± 25 to 180 ± 22 mg/dL ($p<0.01$). BMI showed minimal change, 27.1 ± 3.5 to 26.9 ± 3.4 ($p=0.12$).

3. Baseline vs 12 Weeks – Group B (Metformin + Glimepiride)

Parameter	**Baseline**	**12 Weeks**	**Mean Change**	**p-value**
HbA1c (%)	8.3 ± 0.6	6.8 ± 0.5	1.5	<0.001
FBG (mg/dL)	147 ± 20	118 ± 14	29	<0.001
PPBG (mg/dL)	212 ± 22	165 ± 18	47	<0.001
BMI (kg/m²)	26.8 ± 3.2	26.6 ± 3.1	0.2	0.15

In Group B, combination therapy significantly improved glycemic parameters. HbA1c decreased from 8.3 ± 0.6% to 6.8 ± 0.5%, FBG from 147 ± 20 to 118 ± 14 mg/dL, and PPBG from 212 ± 22 to 165 ± 18 mg/dL ($p<0.001$). BMI remained stable, 26.8 ± 3.2 to 26.6 ± 3.1 ($p=0.15$).

4. Mean Changes Comparison Between Groups

Parameter	**Group A Mean Change**	**Group B Mean Change**	**p-value**
HbA1c (%)	1.0	1.5	0.03
FBG (mg/dL)	20	29	0.04
PPBG (mg/dL)	30	47	0.02

The mean reductions in glycemic parameters were significantly greater in Group B compared to Group A. HbA1c decreased by 1.5% in Group B versus 1.0% in Group A ($p=0.03$). Fasting blood glucose declined by 29 mg/dL versus 20 mg/dL ($p=0.04$), and postprandial glucose by 47 mg/dL versus 30 mg/dL ($p=0.02$). These results indicate that Metformin + Glimepiride combination therapy is more effective than Metformin monotherapy in controlling blood sugar over 12 weeks.

5. Medication Adherence

Parameter	Group A	Group B
Good adherence (>80% doses)	45 (90%)	46 (92%)
Moderate adherence (50–80%)	5 (10%)	4 (8%)
Poor adherence (<50% doses)	0	0

Medication adherence was high in both groups, supporting reliability of results. In Group A, 45 (90%) patients showed good adherence and 5 (10%) moderate adherence. In Group B, 46 (92%) had good adherence and 4 (8%) moderate adherence. No patients had poor adherence, indicating that changes in blood sugar were due to the prescribed treatments.

6. Side Effects / Safety

Side effects	Group A (n=50)	Group B (n=50)
Mild gastrointestinal upset	6 (12%)	3 (6%)
Mild hypoglycemia	0	4 (8%)
No adverse events	44 (88%)	43 (86%)

Both treatments were generally safe. Mild hypoglycemia occurred only in the combination therapy group, while mild stomach upset was more common in the Metformin group. No severe adverse events were reported.

DISCUSSION

The study enrolled 100 patients with type 2 diabetes, equally divided into two groups: Group A (Metformin) and Group B (Metformin + Glimepiride). Demographic analysis revealed a slight male predominance and a higher proportion of urban residents in both groups. Age distribution was comparable between groups, with the majority falling within the 41–60 years range. Symptomatically, polyuria and polydipsia were prevalent in both groups, indicating similar disease severity at baseline. These demographic and baseline characteristics ensure that any observed differences in treatment outcomes are attributable to the interventions rather than baseline disparities. Such baseline homogeneity is crucial for the internal validity of clinical trials.[8,9]

Group A, treated with Metformin monotherapy, demonstrated significant reductions in HbA1c, FBG, and PPBG after 12 weeks. Similarly, Group B, receiving the combination therapy, showed improvements in these parameters. However, the magnitude of reduction was more pronounced in Group B, indicating superior efficacy of the combination therapy. This finding aligns with existing literature that supports the enhanced glycemic control achieved through combination therapies in type 2 diabetes management. Combination therapies often provide complementary mechanisms of action, leading to more effective glucose regulation. These results underscore the importance of individualized treatment plans to achieve optimal glycemic control.[10,11]

Statistical analysis revealed that Group B experienced significantly greater reductions in HbA1c, FBG, and PPBG compared to Group A. These differences were statistically significant, suggesting that the addition of Glimepiride to Metformin enhances glycemic control more effectively than Metformin alone. This finding is consistent with previous studies that have demonstrated the superior efficacy of combination therapies in managing type 2 diabetes. Combination therapies can address multiple pathophysiological mechanisms of the disease, leading to improved outcomes. However, it is essential to consider individual patient factors when selecting appropriate therapy to ensure the best possible outcomes.[12,13]

Both treatment regimens were well-tolerated, with no severe adverse events reported. Mild gastrointestinal disturbances were the most common side effects, occurring in a small percentage of patients. The combination therapy group experienced a slightly higher incidence of mild hypoglycemia, as expected due to the additive effects of Glimepiride. These findings are consistent with existing literature that reports a favorable safety profile for Metformin and Glimepiride combination therapy. However, healthcare providers should monitor for potential side effects, such as hypoglycemia, and adjust treatment as necessary to ensure optimal patient outcomes.

CONCLUSION

This study demonstrated that both Metformin monotherapy and Metformin + Glimepiride combination therapy effectively improved glycemic control in patients with type 2 diabetes over 12 weeks. However, the combination therapy showed significantly greater reductions in HbA1c, fasting, and postprandial blood glucose levels compared to Metformin alone. Both regimens were generally safe, with mild, self-limiting side effects. High medication adherence in both groups supported the reliability of the outcomes. These findings suggest that Metformin + Glimepiride combination therapy is a more effective and well-tolerated option for patients who do not achieve adequate glycemic control with Metformin monotherapy, emphasizing the importance of individualized treatment strategies in diabetes management.

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