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Effect of glimepiride versus teneligliptin in combination with metformin in type 2 diabetes mellitus patients

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Abstract:

BACKGROUND: Long-term metabolic disease type 2 diabetes mellitus (T2DM) is distinguished by elevated blood glucose, insulin resistance, and drought of insulin with dyslipidemia. Oral hypoglycemic agents lower blood glucose levels as well as prevent both short-term and long-term complications such as micro/macrovascular atherosclerosis, chronic kidney diseases, and chronic heart disease. This study aims to compare the effect of glimepiride versus teneligliptin in combination with metformin in T2DM patients attending a tertiary care hospital.

MATERIALS AND METHODS: This prospective, randomized, open-label study was initiated in a tertiary care hospital after obtaining IEC approval. Written informed consent was obtained. The sample size was calculated using "Statistics and sample size software." Ninety-seven patients satisfying the inclusion criteria were assigned to two groups using simple randomization with allocation 1:1. Group A received metformin + glimepiride while Group B received metformin + teneligliptin for 12 weeks. Fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycated hemoglobin (HbA1c), and lipid profile were recorded at the baseline and at the end of 12 weeks. This study was conducted for 1 year. Data were analyzed using SPSS version 23.0 software.

RESULTS: Out of 97 participants (Group A: 48 and Group B: 49), Group A showed a higher reduction in FBS (48.18 ± 9.64) whereas Group B showed 72.53 ± 5.01, 1.74 ± 0.42 of change in PPBS and HbA1c after 12 weeks.

CONCLUSION: The study found that combining metformin with teneligliptin was better tolerated and improved glycemic control and lipid profile compared to metformin plus glimepiride.

Keywords:

Glimepiride, glycated hemoglobin, metformin, teneligliptin, type 2 diabetes mellitus

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Introduction

Type 2 diabetes mellitus (T2DM) is a long-term metabolic disorder distinguished by elevated blood glucose, insulin resistance, and draught of insulin.[1] Rates of T2DM have increased markedly since 1960 in parallel with obesity.[2] As of 2014, there were approximately 422 million people diagnosed with T2DM compared to around 108 million in 1980.[3] As per the International Diabetes Federation, 537 million adults (20–79 years) worldwide have diabetes and this number is predicted to increase, to 643 million by 2030 and 783 million by 2045.[4] Oral hypoglycemic agents (OHAs) are used to reduce blood glucose levels, thereby preventing short and long-term complications such as micro and macrovascular atherosclerosis, chronic kidney diseases, and chronic heart disease.[5]

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Commonly used OHAs are biguanides, sulfonylureas, thiazolidinediones, alpha-glucosidase inhibitors, and the new drugs include amylin analogs, sodium-glucose co-transport 2 inhibitors, and dipeptidyl peptidase-4 (DPP-4) inhibitors.[6]

Currently, biguanides (metformin) together with lifestyle modifications (healthy eating, body weight control, and increased physical activity) are considered pivotal drugs.[7] The sulfonylureas reduce hyperglycemia by enhancing insulin secretion and decreasing triglyceride levels.[8] A novel class of OHAs known as DPP-4 inhibitors have just surfaced; these agents exhibit favorable effects in enhancing glycemic control, particularly postprandial hyperglycemic management, with minimal risk of hypoglycemia, weight gain, and improved lipid profile.[9]

In inadequately controlled T2DM patients, when teneligliptin and metformin were combined, a lower incidence of hypoglycemia, improved glycemic index, and decreased triglycerides were noted.[10]

In the present study, we sought to determine and compare the effects of 2 antidiabetic drugs, glimepiride (sulfonylurea), an insulin secretagogue, and teneligliptin (DDP-4 inhibitor) with metformin, in patients with poor glycemic control. This study aims to compare the effect of glimepiride versus teneligliptin as an add-on therapy with metformin in T2DM patients in a tertiary care hospital.

Materials and Methods

This prospective, randomized, open-label research was initiated after obtaining IEC approval (SVMCH/IEC/2017-Oct/21). Participant's written informed consent was acquired. Study participants were assigned to 2 groups using simple randomization with allocation 1:1. Group A: Patients received metformin 500 mg BD + glimepiride 1 mg/day orally in the morning after food for 12 weeks. Group B: Patients received metformin 500 mg BD + teneligliptin 20 mg once daily orally in the morning after food for 12 weeks. Venous blood sample was used to analyze the fasting blood sugar (FBS), postprandial blood sugar (PPBS), glycated hemoglobin (HbA1c), and lipid profile levels using the glucose oxidase method on an auto analyzer. Diet advice was given and adverse effects were monitored for safety assessment.

Selection criteria

1. Inclusion criteria
   - Male or female with T2DM
   - Patients inadequately controlled on metformin 1 g/day alone for a minimum of 12-week duration
   - Patients in the age group >30–60 years
   - Patients with HbA1c ≥7, FBS ≥110 mg/dL, and PPBS ≥180 mg/dL.
2. Exclusion criteria
   - Type 1 diabetes mellitus patients on Insulin therapy
   - T2DM patients on Insulin therapy
   - Patients on treatment with any anti-diabetic drug other than metformin
   - Patients with gestational diabetes mellitus, lactating mothers, and oral contraceptives
   - Patients allergic to metformin, glimepiride, and teneligliptin
   - Patients with comorbid conditions such as coronary artery disease, chronic kidney disease, thyroid disorders, and hypertension.

The sample size was calculated using "Statistics and sample size software" considering α Error – 5% β Error – 20% Confidence level – 95% based on previous study precision.[11] SPSS (Statistical Package for the Social Sciences - IBM Corporation, Chicago (Ill., USA) version 23.0 software was used for data analysis. Paired Student's *t*-test was used to analyze the significance within the group. An unpaired *t*-test was used to analyze the significance between the two groups. $P < 0.05$ was considered statistically significant. T2DM patients attending the diabetology outpatient department of a tertiary care hospital were screened and enrolled. The duration of the study was 1 year.

Results

One hundred sixty-three patients were screened, and 100 eligible patients were randomized into two groups [Figure 1].

Table 1 represents the basic demographic profile and clinical characteristics. Out of 97 participants, in Group A, 35.41% were male and 64.58% were female while 38.77% were male and 61.22% were female in Group B. The mean age of the patients was 52.12 ± 10.78 years, and 53.02 ± 8.48 years in Group A and Group B with, disease duration of 4.89 ± 3.42 years and 5.5 ± 3.86 years, respectively. The BP recorded in Group A and Group B were 136.46 ± 20.47/83.75 ± 9.59 and 130.61 ± 20.25/80.00 ± 10.00, respectively.

Table 1: Demographic profile and clinical characteristics

Group	A (*n*=48)	B (*n*=49)
Number of males, *n* (%)	17 (35.41)	19 (38.77)
Number of females, *n* (%)	31 (64.58)	30 (61.22)
Age	52.12±10.78	53.02±8.48
Weight	61.10±7.83	66.02±14.73
Disease duration	4.89±3.42	5.5±3.86
Systolic blood pressure (mmHg)	136.46±20.47	130.61±20.25
Diastolic blood pressure (mmHg)	83.75±9.59	80.00±10.00

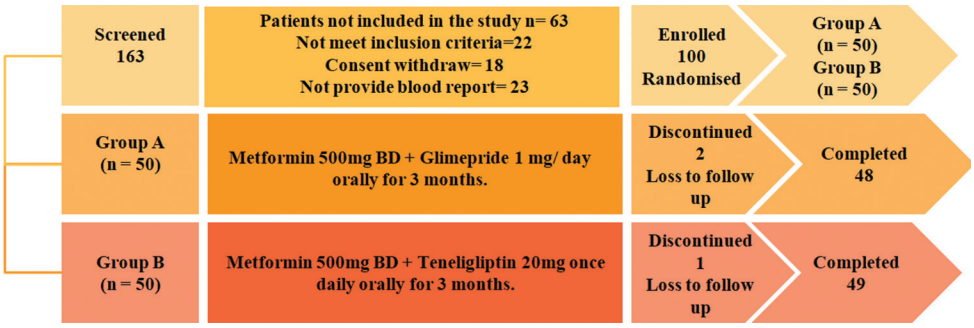

Figure 1: Patient disposition chart

Glycemic parameters

The mean decrease in HbA1c from baseline to the 12th week was 1.32 ± 0.32 in Group A and 1.74 ± 0.42 in Group B, as shown in Table 2, with a $P = 0.03$*. FBS levels decreased from 187.81 ± 74.26 to 139.63 ± 64.62, showing a mean decrease of 48.18 ± 9.64 in Group A and 38.2 ± 9.98 in Group B ($P = 0.04$*). There was a significant reduction (0.02*) in levels of PPBS as 58.42 ± 26.36 in Group A and 72.53 ± 5.01 in Group B.

Lipid profile

Total cholesterol significantly decreased in Group B (21.15 ± 3.8; $P = 0.001$**) compared to Group A (10.12 ± 1.3), as shown in Table 2. Triglycerides were found to be 110.80 ± 48.00 at baseline and 106.73 ± 34.32 after 12 weeks in Group A, with a mean reduction of 4.07 ± 13.68 ($P = 0.04$*), and for Group B, 110.91 ± 61.38 and 103.19 ± 51.43, respectively, with a mean reduction of 7.72 ± 9.95 ($P = 0.02$*). When compared to Group B, low-density lipoprotein (LDL) values for Group A were 118.47 ± 43.28 and 108.24 ± 41.22 at baseline and after 12 weeks. In Group A, the mean changes in high-density lipoprotein (HDL) and very LDL (VLDL) levels were 4 ± 1.36 and 2.22 ± 0.03, while in Group B, they were 5.03 ± 1.18 and 3.9 ± 0.04, respectively. At the end of 12 weeks, Group B had a significantly lower mean change in HDL and VLDL than Group A ($P = 0.03$* between groups).

Table 2: Mean change in glycated hemoglobin, fasting blood sugar, postprandial blood sugar, and blood lipid levels

Parameters	Group A (*n*=48)	Group B (*n*=49)
FBS		
Baseline	187.81±74.26	157.21±53.15
After 12 weeks	139.63±64.62*	119.01±63.13*
Change in FBS	48.18±9.64	38.2±9.98
PPBS		
Baseline	273.85±74.29	285.74±56.89
After 12 weeks	215.43±47.93*	213.21±51.88*
Change in PPBS	58.42±26.36	72.53±5.01
HbA1c		
Baseline	9.74±2.36	9.70±1.87
After 12 weeks	8.42±2.68*	7.96±1.45*
Change in HbA1c	1.32±0.32	1.74±0.42
TC		
Baseline	186.15±51.98	180.53±53.99
After 12 weeks	176.03±50.68*	159.38±57.79*
Change in TC	10.12±1.3	21.15±3.8
TG		
Baseline	110.80±48.00	110.91±61.38
After 12 weeks	106.73±34.32*	103.19±51.43*
Change in TG	4.07±13.68	7.72±9.95
LDL		
Baseline	117.75±45.93	118.47±43.28
After 12 weeks	111.57±43.95*	108.24±41.22*
Change in LDL	6.18±1.98	10.23±2.06
HDL		
Baseline	44.55±5.84	45.60±6.43
After 12 weeks	40.55±4.48*	40.57±5.25*
Change in HDL	4±1.36	5.03±1.18
VLDL		
Baseline	24.93±9.44	20.14±7.66
After 12 weeks	22.71±9.41*	16.24±7.62*
Change in VLDL	2.22±0.03	3.9±0.04

*P<0.05 from baseline to end of 12 weeks using paired *t*-test (within group comparison). TC=Total cholesterol, TG=Triglycerides, HbA1c=Glycated hemoglobin, PPBS=Postprandial blood sugar, FBS=Fasting blood sugar, LDL=Low-density lipoprotein, HDL=High-density lipoprotein, VLDL=Very LDL

Discussion

This study focused on comparing, the effects of glimepiride versus teneligliptin as an, add-on therapy with metformin in T2DM patients. HbA1c <6.5%–7% interprets good control of DM.[12] According to the American Diabetic Association (ADA) 2021, for diabetic individuals, metformin is the ideal treatment and if glycemic control is not achieved, sulfonylureas or DPP-4 inhibitors can be added.[13]

Since sulfonylureas such as glimepiride have strong efficacy and safety profiles, they are the most recommended initial addition to metformin. It has a dual mode of action – lowers insulin resistance and enhances glucose utilization through glucose transporter-4 generating glycemic reduction with minimal risk of hypoglycemia or weight gain.[14] The variations in HbA1c noted in this present study for Group A (1.32 ± 0.32) were almost similar (1.47) to those achieved by Bommineni *et al*.[15]

DPP-4 inhibitors function by raising levels of glucagon-like peptide, which stimulates the release of insulin and increases the sensitivity of beta cells to glucose.[16,17] According to Kim *et al*. meta-analysis, DPP-4 inhibitors may have a greater ability to lower HbA1c levels.[18] This research showed a change of 1.74 ± 0.42 in HbA1c (Group B).

Glimepiride has also improved first- and second-phase insulin secretions, as it is completely absorbed after oral administration.[19] Furthermore, the results of change in FBS (48.18 ± 9.64) in Group A resemble the result of research conducted by Parmar and Goswami (41.08 ± 35.02).[20]

Patil reported that once-daily teneligliptin lowered PPBS and it was sustained throughout the day.[21] A change of 72.53 ± 5.01 in PPBS was noted in Group B which was on par with Raghavan *et al*. where a change of -49.8 was noted.[22]

Increased expression of DPP-4 in the liver promotes nonalcoholic fatty liver disease, and inhibition of this cycle by a DPP-4 inhibitor decreases the lipid level.[23] Both groups had significant reductions in VLDL and triglycerides; but, as demonstrated by Nishanth *et al*.; Group B experienced a greater reduction in LDL (10.23 ± 2.06) than Group A (10.02 ± 1.03).[24]

It is noteworthy that DPP-4 inhibitors have not been linked to an increased risk of hypoglycemia, gastrointestinal side effects, or other side effects, according to systematic reviews and meta-analyses.[25-28] Yet, in this study, treatment-emergent adverse effect incidence was similar with glimepiride and teneligliptin where four patients in each group reported, two episodes of hypoglycemia.

The current study included only 97 patients without comorbidities, more data from a larger patient group and longer follow-ups are needed to assess the safety and effectiveness for comorbidities such as hypertension, kidney disease, and cardiovascular diseases.

Conclusion

The study found that combining metformin with teneligliptin was better tolerated and improved glycemic control and lipid profile compared to metformin plus glimepiride. As a result, teneligliptin may be a preferable option for T2DM due to its various advantages.

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Conflicts of interest
There are no conflicts of interest.

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