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Comparative study of efficacy of GLIMEPIRIDE+METFORMIN versus TENELIGLIPTIN+METFORMIN in T2DM patients with high lipid profile.

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Abstract:
Diabetes mellitus is a metabolic disorder which is characterized by chronic hyperglycaemia caused by disturbances of metabolism due to impaired β cell function of pancreas or insulin resistance or both. Biguanides and Sulphonylureas are the most commonly prescribed drugs due to their efficacy and safety, but nowadays a new class of drugs, named as DPP4 inhibitors are used frequently alone or with combination with Biguanides with the better efficacy and safety profile. A total of 60 patients were chosen in the present study who met the inclusion criteria. They were divided into two equal groups—Group 'A' and Group 'B' based on their treatment plan. Patients of Group A were treated with GLIMEPIRIDE 1mg METFORMIN 500mg while patients of group B were treated with TENELIGLIPTIN 20mg plus METFORMIN 500mg. In the present study, we observed that the patients on Teneligliptin-Metformin exhibited better control over glycemic profile as well as lipid profile as compared to patients who are on Glimepiride-Metformin combination.

Key words: *Teneligliptin, Glimepiride, Metformin, HbA1C*

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I. Introduction

DM is classified into four types: T1DM, T2DM, Other types and Gestational diabetes according to ADA and WHO. It is the most common non-communicable disease and has been epidemic in various part of the world including India. T2DM, usually late onset, is caused due to increase in diet and decrease in physical activity with strong familial co- relation. Diagnostic criteria for Diabetes mellitus include classical triad of '3P' as polyuria, polydipsia and polyphagia plus random blood sugar ≥ 200mg/dL, OR fasting plasma glucose ≥ 126mg/dL OR 2h post prandial plasma glucose ≥ 200mg/dL OR HbA1C level ≥ 6.5% . Treatment of T2DM includes dietary changes, increased physical activities and lifestyle modification along with anti-diabetic medications. Oral medications more frequently used are Biguanides, sulphonylureas, and DPP IV inhibitors. In the present study, Glimepride-Metformin for group A and Teneligliptin- Metformin for group B were chosen.

II. Methods And Materials

The present study was carried out in outpatients department of Medicine department of JNKTMCH, Madhepura, Bihar. Total 60 patients were taken and were equally divided into two groups each containing 30. Combination of Glimepiride 1mg and Metformin 500mg, once a day before meal were given to one group and the combination of Teneligliptin 20mg and Metformin 500mg, once a day after meal were given to another group. Total time taken in the study was 6 months; each person was observed weekly upto 12 weeks. The primary aim is to measure FBG, PPBG and HbA1C before the study and after the study duration completed. The secondary aim is to determine the value of their lipid profile values before and after the treatment.

Inclusion Criteria

Patients with Type 2 Diabetes mellitus of either sex, aged 30-65 years, having fasting plasma glucose ≥126 mg/dL and post prandial plasma glucose ≥ 200 and HbA1c levels ≥6.5 were included in the present study.

Exclusion Criteria

- Patients with Type 1 diabetes mellitus.
- Patients with history of diabetic ketoacidosis in the past.

- Patients with history of surgery in the past six weeks.
- Patients allergic to any given medication.
- Patients with history of bleeding disorders.
- Pregnant and lactating females.
- Patients with history of drug abuse and steroid treatment.
- Patients with renal and hepatic disorders.
- Patients greater than 65yrs of age.
- Immunocompromised patients.
- Patients taking any other treatment which can alter glycaemic controland lipid profile.

This study involved twelve week study of 60 patients, of either sex, with Type 2 DM, attending the Medicine OPD at JNKTMCH, Madhepura,Bihar. The patients were randomly distributed into two groups—Group A and Group B; each containing 30 patients.
Written Informed Consent were taken from the patients taking the medicines in the present study and all the the benefits and risk involved were explained to every patient in their own language. Patients were advised to take diet control and regular exercise as per the protocol designed by W.H.O.

Groups
Group A: Patients were given combination of Glimepiride 1mg and Metformin 500 once a day before meal for 12 weeks.
Group B: Patients were given combination of Teneligliptin 20mg and Metformin 500mg once a day after meals for 12 weeks.
The patients were advised to report immediately in case they developed any adverse reaction e.g. nausea, vomiting, diarrhoea, flatulence, abdominal pain or any other side effect.

Parameters of study
Before the study started, history was taken, clinical examination was done on each patient. The routine investigation such as fasting blood glucose (FBG), postprandial blood glucose (PPBG), HbA1c and lipid profile were obtained.
The patients were investigated for FBG and PPBG every week up to twelve weeks and HbA1c and lipid profile were done at the start of the study and at the end of the study.

Statistical analysis
The results obtained were analyzed statistically for the significance using Student's 't' test (paired and unpaired).

III. Results:-

Table:1. Distribution of patients according to Age.

Age category (in years)	Group A (N=30)	Group B (N=30)
<40	4 (13.3%)	2 (6.7%)
40-49	6 (20%)	7(23.3%)
50-59	7 (23.3%)	12 (40%)
>60	13 (43.4%)	9 (30%)
Mean (in years)	52.7	53.7

N= number of patients (=30) in each group.

Table:2. Distribution of patients according to Gender.

Gender	Group A	Group B
Male	16 (53.3%)	17 (56.7%)
Female	14 (46.7%)	13 (43.3%)
Total	30	30

Table 1 shows age distribution of patients. In Group A, the mean average age was 52.7 whereas Group B had mean distribution of 53.7. In Group A, 16 patients were males and 14 patients were females, while in Group B, 17 patients were males and 13 patients were females as shown in Table 2.

Table:3. Distribution of patients as per presence or absence of co-morbidities.

Co-morbidities	Group A	Group B
Present	14 (46.7%)	16 (53.3%)
Absent	16 (53.3%)	14 (46.7%)

Table:4. Distributions as per types of co-morbidities.

CO-MORBIDITIES	Group A	Group B
Hypertension	7	8
Cardiovascular disease	3	4
Hypothyroidism	3	2
COPD/Asthma	1	2

Table 3 shows presence or absence of co-morbid conditions. In Group A, 14 patients had other co-morbidities while 16 patients did not have any other disease. In Group B, 16 patients had other co-morbid conditions while 14 patients had no any co-morbidity.
Table 4 shows the distribution of patients based on the type of co-morbid conditions. Most of the patients had hypertension in both the groups.

Table 5: Fasting blood glucose levels (Mean ± SD in mg/dl) over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
0 (at start)	140.13 ± 19.14	170.26 ± 31.60	4.466	0.000HS
1st	130.20 ± 18.38	161.81 ± 32.48	4.638	0.000HS
2nd	128.50 ± 24.67	157.36 ± 35.01	3.691	0.000HS
3rd	125.33 ± 18.63	150.87 ± 28.31	4.126	0.000HS
4th	123.43 ± 18.57	144.56 ± 29.07	3.355	0.001S
5th	120.76 ± 17.31	146.16 ± 27.56	4.274	0.000HS
6th	118.30 ± 16.49	152.63 ± 30.19	5.466	0.000HS
7th	116.83 ± 14.94	152.50 ± 33.21	5.364	0.000HS
8th	117.50 ± 11.12	147.16 ± 35.10	4.413	0.000HS
9th	114.83 ± 12.62	141.00 ± 33.87	3.965	0.000HS
10th	113.30 ± 9.94	133.67 ± 31.26	3.4	0.000HS
11th	109.50 ± 11.77	128.33 ± 31.26	3.252	0.002S
12th	105.33 ± 14.50	122.67 ± 29.56	2.884	0.006S

S=Significant ($p<0.05$; $p< 0.01$); HS=Highly significant ($p<0.001$).

On comparison between both the groups, there was highly significant difference in the FBG levels till third week of the study period ($p<0.001$). Thereafter there was a significant difference in the FBG levels between both the groups at 4th week of study period ($p<0.05$), then it was highly significant by the 10th week of study period ($p<0.001$) and significant in the 11th and 12th week of the study period ($p<0.05$); as shown in Table 5.

Table 6: Change in fasting blood glucose (Mean±SD in mg/dl) over a period of 12weeks in the study groups.

Durations(in weeks)	Group A	Group B	t' value	'p' value
0-1	9.93 ± 11.30	8.45 ± 12.56	0.48	0.633^{NS}
0-2	11.63 ± 15.16	12.90 ± 25.77	0.232	0.817^{NS}
0-3	14.80 ± 15.29	19.40 ± 20.62	0.981	0.330^{NS}
0-4	16.70 ± 15.21	25.70 ± 20.68	1.92	0.060^{NS}
0-5	19.37 ± 16.71	24.10 ± 19.97	0.996	0.324^{NS}
0-6	21.83 ± 16.70	17.63 ± 14.67	1.035	0.305^{NS}
0-7	23.30 ± 16.26	17.77 ± 13.48	1.435	0.157^{NS}
0-8	22.63 ± 16.19	23.10 ± 16.14	0.112	0.911^{NS}
0-9	25.30 ± 16.82	29.27 ± 13.67	1.003	0.320^{NS}
0-10	26.83 ± 14.08	36.60 ± 13.46	2.746	0.008^{S}
0-11	30.63 ± 11.13	41.93 ± 11.79	3.818	0.000^{HS}
0-12	34.80 ± 7.04	47.60 ± 7.73	6.708	0.000^{HS}

NS= Not significant (p>0.05); S=Significant (p<0.05; p< 0.01); HS=Highly significant (p<0.001).

As evident from Table 5, decrease in FBG was not significant between Group A and Group B up to 9 weeks (p>0.05) and then there was significant decrease in FBG in Group B than that of Group A in 10th week (p< 0.05) and thereafter there is highly significant decrease in FBG in Group B than Group A in 11th and 12th week of study period (p<0.001).

Table 7: Post prandial blood glucose levels (Mean ± SD in mg/dL) over a period of 12 weeks in study groups.

Week (Duration)	Group A	Group B	't' value	'p' value
0 (at start)	243.86 + 32.24	263.73 + 43.05	2.023	0.048^{S}
1st	277.60 + 39.95	243.27 + 45.92	1.41	0.164^{NS}
2nd	224.10 + 40.80	238.00 + 47.63	1.214	0.230^{NS}
3rd	220.80 + 38.82	229.13 + 45.76	0.761	0.450^{NS}
4th	213.40 + 36.70	226.63 + 44.99	1.248	0.217^{NS}
5th	205.87 + 33.28	229.73 + 41.35	2.463	0.017^{S}
6th	204.00 + 29.60	229.67 + 40.19	2.816	0.007^{S}
7th	200.73 + 26.85	226.33 + 41.25	2.849	0.006^{S}
8th	197.00 + 28.30	223.17 + 40.69	2.891	0.005^{S}
9th	196.00 + 29.90	215.83 + 41.14	2.136	0.037^{S}
10th	190.33 + 32.40	207.50 + 40.14	1.823	0.074^{NS}
11th	188.17 + 26.76	198.17 + 40.86	1.121	0.267^{NS}
12th	186.17 + 30.92	188.33 + 38.11	0.242	0.810^{NS}

NS= Not significant (p>0.05); S=Significant (p<0.05; p< 0.01)

There was significant difference in post prandial blood glucose level on comparison of the groups at the start of study period (p<0.05). Thereafter, it was not significant up to 4th week of study period (p>0.05), then again significant up to 9th week (p<0.05) and then again not significant up to 12th week of study period (p>0.05) (as shown in Table 7).

Table 8: change in post prandial blood glucose levels (Mean ± SD in mg/dL) overa period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
0-1	16.27 ± 22.19	20.47 ± 14.66	0.865	0.391^{NS}
0-2	19.77 ± 20.40	25.73 ± 16.28	1.252	0.215^{NS}
0-3	23.07 ± 17.53	34.60 ± 18.63	2.47	0.016^{S}
0-4	30.47 ± 17.24	37.10 ± 22.17	1.294	0.201^{NS}
0-5	38.00 ± 19.48	34.00 ± 22.42	0.738	0.464^{NS}
0-6	39.87 ± 20.65	34.07 ± 21.74	1.059	0.294^{NS}
0-7	43.13 ± 20.76	37.40 ± 22.80	1.018	0.313^{NS}
0-8	46.87 ± 22.72	40.57 ± 19.26	1.159	0.251^{NS}
0-9	47.87 ± 22.10	47.90 ± 19.53	0.006	0.995^{NS}
0-10	53.53 ± 20.72	56.23 ± 14.19	0.589	0.558^{NS}
0-11	55.70 ± 13.11	65.57 ± 11.40	3.111	0.003^{S}
0-12	57.70 ± 6.99	75.40 ± 10.47	7.701	0.000^{HS}

NS= Not significant ($p>0.05$); S=Significant ($p<0.05$; $p< 0.01$); HS=Highly significant ($p<0.001$).

There was no significant decrease in post prandial blood glucose levels in Group B than Group A upto 2 weeks ($p>0.05$), then significant decrease in Group B than Group A in 3rd week ($p<0.05$); and no significant decrease in Group B than Group A from 4th week to 10th week ($p>0.05$); and then again a significant decrease in Group B than Group A in 11th week ($p<0.05$) and then lastly a highly significant decrease in post prandial blood glucose levels were seen in Group B than Group A in 12th week of study period ($p<0.001$). (shown in Table 8).

Table 9: Serum HbA1c levels (Mean± SD) (in mg/dL) over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
Day 0	10.27 ± 1.61	11.78 ± 1.61	3.635	0.001^{S}
12th weeks	9.31 ± 1.58	10.49 ± 1.52	2.961	0.004^{S}

S=Significant ($p<0.05$, $p<0.01$).

On comparison between Group A and Group B, there were significant difference in the level of HbA1c at the baseline ($p<0.05$) as well as at the end of study duration ($p<0.05$); shown in Table 9.

Table 10: Change in serum HbA1c levels (Mean± SD) in mg/dL over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
0-12	0.96 + 0.181	1.29 + 0.15	7.746	0.000^{HS}

HS=Highly significant ($p<0.001$).

There was highly significant decrease in mean HbA1c in Group B than Group A at the end of study period ($p< 0.001$); as shown in Table 10.

Table 11: Serum total cholesterol levels (Mean ± SD in mg/dL) over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
Day 0	178.54 ± 64.43	171.90 ± 43.75	0.467	0.642^{NS}
12th week	162.67 ± 64.43	151.07 ± 41.50	0.832	0.409^{NS}

NS=Not significant ($p>0.05$).

On comparison between Group A and Group B, no significant difference were seen in the cholesterol levels at the baseline (p>0.05) as well as at the end of study (p>0.05), shown in Table 11.

Table 12: Change in serum total cholesterol levels (Mean± SD in mg/dL) over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	't' value	p' value
0-12	15.87 ± 4.42	20.83 ± 4.66	4.229	0.000HS

HS=Highly significant (p<0.001).

There was a highly significant decrease in serum cholesterol levels in Group B than Group A at the end of the study (p<0.001) (Table 12).

Table 13: Serum triglyceride levels (Mean ± SD) over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
Day 0	252.31 ± 83.72	228.16 ± 74.47	1.18	0.243NS
12th weeks	235.17 ± 83.63	205.47 ± 72.90	1.466	0.148NS

NS=Not significant (p>0.05)

On comparison between Group A and Group B, no significant difference were seen in triglyceride level at the baseline (p>0.05) as well as at the end of study period (p>0.05); shown in Table 13.

Table 14: Change in serum triglyceride levels (Mean ± SD in mg/dL) over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
0-12	17.15 + 4.70	22.70 + 3.65	5.114	0.000HS

HS= Highly significant (p<0.001).

There was a highly significant decrease in serum triglyceride levels in Group B than Group A at the end of the study period (p<0.001) (Table 14).

Table 15: Serum HDL levels (Mean ± SD) over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
Day 0	43.30 ± 12.47	44.93 ± 9.38	0.571	0.570NS
12th week	54.63 ± 12.88	58.87 ± 11.51	1.342	0.185NS

NS=Not significant (p>0.05).

On comparison between Group A and Group A, no significant difference were seen in the HDL levels at the baseline (p>0.05) as well as at the end of study period (p>0.05); shown in Table 15.

Table 16: Change in serum HDL Levels (Mean± SD in mg/dL) over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
0-12	11.33 ± 2.45	13.93 ± 8.71	1.578	0.120NS

NS=Not significant (p>0.05)

There was no significant increase in serum HDL levels on comparison of both groups at the end of study period (p>0.05) (Table 16).

Table 17: Serum LDL levels (Mean ± SD in mg/dL) over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	'p' value
Day 0	94.73 + 12.01	102.73 + 21.62	1.772	0.082^{NS}
12th week	84.00 + 10.62	87.20 + 18.34	0.827	0.412^{NS}

NS=Not significant (p>0.05).

On comparison between Group A and Group B, no significant difference were seen in the levels of LDL at the baseline (p>0.05) as well as at theend of study period (p>0.05) (Table 17).

Table 18: Change in serum LDL levels (Mean) in mg/dL over a period of 12 weeks in study groups.

Duration (weeks)	Group A	Group B	t' value	p' value
0-12	10.73 + 3.30	15.53 + 4.80	4.519	0.000^{HS}

HS=Highly significant (p<0.001)

There was a highly significant decrease in serum LDL levels in Group B than Group A at the end of the study period (p<0.001) as shown in Table 18.

IV. Discussion And Conclusion:

The present study was conducted in Jan Nayak Karpoori Thakur Medical college and Hospital for a period of six months from October 2020 to March 2021. In this study we compared the anti-hyperglycemic effect of Glimepiride and Metformin versus Teneligliptin and Metformin in the treatment of Type 2 DM patients uncontrolled with monotherapy. Total 60 patients of Type 2DM were included in the study and were divided in two groups of 30 each. The patients in each group received the treatment for a period of 12 weeks duration.
Group A patients were given Glimepiride 1 mg plus Metformin 500 mg once a day before meal.
Group B patients were given Teneligliptin 20 mg plus Metformin 500 mg once a day after meal.

The present study consisted of 33 males and 27 females. Majority of the patients were in the age group of 40-65 years.

In the study it was observed that there were highly significant reductions inthe mean FBG in Group A and Group B patients. However, the reductions in Group B were greater than in Group A at the end of 12 weeks of study period.

Similarly there were highly significant (p<0.001) reductions in PPBG in both the groups, but reductions in PPBG were also greater in Group B than that of Group A at the end of 12 weeks of study period.

In present study there were highly significant reductions in HbA1c levels in both the groups. However, the mean reduction in HbA1c was greater in Group B as compared to Group A.

In the study there was significant reduction in total serum cholesterol levels in both the groups (p<0.01). However, the reductions in Group B were greater than in Group A.
Similarly there were greater reductions in serum Triglycerides and serum LDL levels in Group B as compared to Group A at the end of 12th week of study. Whereas no any significant change in serum HDL levels was observed in both the groups.
Hence, Teneligliptin-Metformin combination has better control over glycemic profile as well as lipid profile as compared to patients who are on Glimepiride-Metformin combination.

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