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Original Research Article

Safety and Efficacy of DDP-4 Inhibitor Teneligliptin, as add on Therapy in Type-2 Diabetes Patients Inadequately Controlled with Dual Combination Oral Hypoglycemic Agents: Placebo Controlled Study

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Abstract

Aim: To evaluate the safety and efficacy of DDP-4 inhibitor Teneligliptin, as add on therapy in type-2 diabetes patients inadequately controlled with dual combination oral hypoglycemic agents

Materials and Methods: This is 24-week prospective interventional clinical study in 104 patients of T2DM who had inadequate Glycemic control with dual combination of metformin and other oral hypoglycemic agents. Patient attending the Outdoor Patient Department of medicine department of Patna Medical College and Hospital, Patna from July 2020 to March 2021 for treatment of type 2 diabetes mellitus.

Results: This study showed significant reductions in HbA1C from baseline to 24-week, mean HbA1C difference before and after addition of teneligliptin was 0.84%. significant reduction in fasting blood glucose level from baseline to 24 week, mean fasting blood glucose level difference before and after addition of teneligliptin was 26.61 mg/dl. A significant reduction in serum triglyceride level, with mean triglyceride level reduction of 45.58 mg/dl after addition of teneliptin to dual combination of traditional oral hypoglycemic agents.

Conclusion: The current study demonstrated that addition of teneligliptin to dual therapy such as metformin with glimepiride, acarbose etc, showed significant reduction in HbA1C level, fasting blood glucose level, and post-prandial blood glucose level.

Keywords: Teneligliptin, HbA1C, Metformin

Background

The global prevalence of diabetes was estimated to be 9.3% of the world's adult population in 2019 and projected to reach 10.2% by 2030 and 10.9% by 2045 [1]. Diabetes is a progressive disease, with progression associated with worsening glycemic control and increased risk for chronic hyperglycemia-induced complications, including microvascular and macrovascular diseases [2]. These co-morbidities exacerbate the burden of diabetes on individuals and healthcare systems. Consequently, optimal glucose

management is required to prevent or delay the onset of complications [3].

Dipeptidyl peptidase-4 (DPP-4) inhibitors increase the levels of active incretin hormones by inhibiting DPP-4 activity, improving hyperglycemia in a glucose-dependent manner through the stimulation of insulin secretion and inhibition of glucagon secretion. Consequently, DPP-4 inhibitors have been used as antidiabetic drugs that can decrease glucose fluctuations in diabetic patients, with good safety [4, 5]. DPP-4 inhibitors are currently the most popular add-on therapy to metformin and sulfonylureas (SU) and their use has gradually increased in recent years [6].

DPP-4 has multiple binding sites that determine the potency and selectivity of different DPP-4 inhibitors. In comparison to other DDP-4 inhibitors, teneligliptin has a unique structural feature that enables relatively stronger binding [7]. Previous studies have shown that teneligliptin can significantly reduce glycosylated hemoglobin (HbA1c) when administered as monotherapy or as adjuvant to metformin, glimepiride, or insulins [8–12]. Meta-analyses showed that compared with placebo, DPP-4 inhibitors lowered HbA1c by 0.65% [13] and teneligliptin lowered HbA1c by 0.82%, a significant reduction [14]. These somewhat larger changes may indicate that teneligliptin has a greater efficacy than other DPP-4 inhibitors, but only limited information on switching from other DPP-4 inhibitors to teneligliptin is currently available. This placebo-controlled study evaluated the safety and efficacy of DDP-4 inhibitor Teneligliptin, as add on therapy in type-2 diabetes patients inadequately controlled with dual combination oral hypoglycemic agents.

Materials and methods

This is 24-week prospective interventional clinical study in 104 patients of T2DM who had inadequate Glycemic control with dual combination of metformin and other oral hypoglycemic agents. Patient attending the Outdoor Patient Department of medicine department of Patna Medical College and Hospital, Patna from July 2020 to March 2021 for treatment of type 2 diabetes mellitus.

Inclusion Criteria

- Patients between 25-70 yr of age group
- Patients with type-2 DM who were inadequately controlled by dual combination of traditional oral hypoglycemic agents with HB1c of 7.5-10 %
- BMI of 23.5-30kg /m^2 and could afford the comparatively higher cost of treatment.

Exclusion Criteria

- History of type 1 diabetes mellitus or diabetes due to pancreatic injury or secondary forms of diabetes
- Acute metabolic diabetic complications such as ketoacidosis or hyperosmolar state (coma) within past 6 months
- Myocardial infarction, unstable angina or coronary artery bypass surgery within past 6 months
- Gestational diabetic mellitus or pregnancy
- Patients with congestive heart failure, liver disease such as cirrhosis or chronic active hepatitis or with any of the following laboratory abnormality at visit 1 were also excluded: alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 2 times the upper limit of normal, total bilirubin >2 times UNL, serum creatinine levels (men >1.5 mg/l ; women >1.4 gm/l), fasting triglyceride >500mg/dl.

Sample Size

104 patients diagnosed with type 2 diabetes mellitus on dual combination of traditional oral hypoglycemic agents with HbA1c of 7.5 to 10 and BMI of 22.5-30 kg/m2 were found eligible for

enrollment. Patients were required to have been treated with metformin and other oral hypoglycemic agent for at least 12 weeks and be on a stable recommended dose.

Patients were subjected to the following investigations:

1. HbA1c levels
2. Fasting lipid profiles
3. Blood sugar (fasting/ post prandial)
4. SGPT/SGOT
5. Serum creatinine

Statistical analysis

The recorded data will be compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 20 (SPSS Inc., Chicago, Illinois, USA).

Descriptive statistics included computation of percentages, means and standard deviations will be calculated. Statistical test applied for the analysis was paired t-test. The level of confidence interval and p-value will be set at 95% and 5%.

Results

Table 1: Age and gender distribution of the study population

Age (years)	Patients
<50	36
50-65	50
>65	18
Gender	.
Male	55
Female	49
BMI (kg/m2)	
Normal weight (18.5-24.9)	30
Over weight (25 – 29.5)	74

Table 2: Mean HbA1C, Fasting blood glucose, Post-prandial blood glucose level before and after adding Teneligliptin

Before and after adding Teneligliptin	At 0 week	At 24 weeks	P-value
Mean HbA1C (%)	9.05	8.21	<0.001
Mean Fasting blood glucose (mg/dl)	163.93	137.32	<0.001
Mean Post-prandial blood glucose level	195.32	170.84	<0.001

Table 3: Mean SGPT level, serum Creatinine Level, serum triglyceride level before and after adding Teneligliptin

Before and after adding Teneligliptin	At 0 week	At 24 week	P-value
Mean SGPT Level (IU/L)	34.57	34.44	0.302
Mean Serum Creatinine Level (mg/dl)	0.97	0.98	0.334
Mean serum Triglyceride Level (mg/dl)	271.02	225	<0.001

Discussion

The current study evaluated the efficacy and safety of adding teneligliptin as add-on therapy to dual combination of metformin and oral hypoglycemic agents (glimepiride, acarbose, pioglitazone) in patients with in adequate glycemic control. This study showed significant reductions in HbA1C from baseline to 24 week, mean

HbA1C difference before and after addition of teneligliptin was 0.84% .

This study showed significant reduction in fasting blood glucose level from baseline to 24 week, mean fasting blood glucose level difference before and after addition of teneligliptin was 26.61 mg/dl.

Similarly, there was significant reduction in post-prandial glucose level from baseline to 24-week, mean post prandial blood glucose level difference before and after addition of teneligliptin was 24.84 mg/dl.

This study also showed no significant change in SGPT level and creatinine level before and after addition of teneligliptin.

There was significant reduction in serum triglyceride level, with mean triglyceride level reduction of 45.58 mg/dl after addition of teneliptin to dual combination of traditional oral hypoglycemic agents.

The main adverse event with metformin was mild diarrhea, with acarbose was bloating and mild diarrhoea, and with pioglitazone was edema due to fluid retention and weight gain.

However, the symptoms were transient in the majority of the study participants and the casual relationship between the study drugs and symptoms is uncertain.

Conclusion

The current study demonstrated that addition of teneligliptin to dual therapy such as metformin with glimepiride, acarbose etc, showed significant reduction in HbA1C level, fasting blood glucose level, and post-prandial blood glucose level.

There was significant change in SGPT and serum creatinine level from baseline to end of 24 weeks, hence hepatic and renal safe.

There was also significant reduction in triglyceride level from baseline to end of 24 weeks, hence good control on serum triglyceride level.

Limitation in our study

Firstly, 24 week is too short study duration to evaluate long term Glycemic control, weight loss, and Beta cell preservation.

Secondly, patients were enrolled based on specific criteria and were followed according to the study schedule, which may not reflect the real clinical use.

Thirdly, as the patients were evaluated at outpatient, no specific compliance data were collected.

Moreover, our study is small and had an open-label design (both health provider and patients are aware of drug or treatment), which are both limiting factors for the generalization of the data, the limitation should be considered.

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