

Research Article

Efficacy of teneligliptin in type 2 diabetes mellitus

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ABSTRACT

Background: Teneligliptin is a novel, highly selective dipeptidyl peptidase-4 (DPP-4) inhibitor. The aim of the study was to assess the effectiveness of Metformin in combination with teneligliptin in Indian patients with type 2 diabetes mellitus who were inadequately controlled with metformin monotherapy.

Methods: Patients with glycated haemoglobin (HbA1c) of 7.0–10.0% and on metformin upto 1000 mg/day were selected for the study. 130 Known diabetic patients were selected, out of which only 56 patients were eligible as per the criteria. these patients were randomly divided into two groups, group A comprises 28 patients whose baseline FBS, PPBS, HbA1c was determined and the patients were put on teneligliptin 20 mg per day apart from metformin 1gm /day, Group B comprises of 28 patients whose baseline FBS, PPBS, HbA1c were determined and these patients were already on metformin 500mg-1gm per day but there glycemic control was poor, all these patients in group b received an escalation of Metformin dose upto 2.5gm/day, to achieve glycemic control and patients were monitored closely with proper diabetic diet counselling.

Results: The mean baseline HbA1c in teneligliptin group was 8.23% when compared to 8.07% in the Metformin group. The primary endpoint of the study was to monitor the changes in HbA1c levels from baseline to week 30. It was observed that the mean HbA1c for teneligliptin group after 30 weeks was 7.21% versus 7.63% in metformin group. HbA1c was significantly reduced in the Group A patients.

Conclusions: In conclusion, the addition of teneligliptin to metformin treatment was effective and well tolerated in patients with type 2 diabetes. Teneligliptin has long half-life of 26.9 hours along with it also has a unique pharmacokinetic advantage which allows convenient once daily administration irrespective of food, superadded it has a dual mode of elimination via renal and hepatic, and hence can be administered safely in renal impairment patients. In mild to moderate hepatic impairment no dosage adjustment is required. The appropriate approach towards managing diabetes should be not only glycemic control but also preservation of islet cell function early and to delay progression of a disease. Teneligliptin add-on to Metformin during the early course of treatment helps in delaying the exhaustion of pancreatic islet function.

Keywords: Teneligliptin, Glycemic levels, Type 2 diabetes mellitus, Metformin, Hyperglycemia, FBS, PPBS

INTRODUCTION

Teneligliptin belongs to third generation DPP-4 inhibitor and it is approved for type 2 diabetes mellitus patients.¹ It is currently available in Japan, India, Argentina and South Korea. It is under pre-registration in Indonesia and

under Phase I trials in US and Phase II trials in Denmark, Germany, Hungary, Lithuania, Poland, Romania and UK. The aim of the study was to assess the effectiveness of Metformin in combination with teneligliptin in Indian patients with type 2 diabetes mellitus who were inadequately controlled with metformin monotherapy.

Metformin is widely used as an oral agent for the treatment of type 2 diabetes mellitus. It is recommended as an initial monotherapy. Metformin helps in weight loss and has a record of efficacy and safety, with a lowest risk of hypoglycaemia.²

Teneligliptin consists of a rigid “J-shaped” structure formed by five rings, out of which four are connected directly to DPP-4 which provides strongest binding to DPP-4 enzymes as compared to other Gliptins. All DPP-4 inhibitors are similar in terms of mechanism of action and safety; however, they differ considerably in terms of pharmacokinetic and pharmacodynamic profiles.

DPP-4 enzyme has several binding sites namely S1, S2, S1', S2' and S2 extensive subunit. DPP-4 inhibitors are classified into 3 classes based on their interaction at DPP-4 subsites (Class 1, Class 2 and Class 3). Class 1 inhibitors (Vildagliptin and Saxagliptin) bind to S1 and S2 and are considered as fundamental/basic inhibitors. Class 2 (Alogliptin and Linagliptin) bind to additional site of S1, S2 and S1' and may produce more DPP-4 inhibition than Class 1, Linagliptin additionally binds to the S2' subsite. Class 3 inhibitors (Sitagliptin and Teneligliptin) binds to S1, S2 and additional site of S2 extensive and produce more extensive DPP-4 inhibition.³

METHODS

This study was conducted at Esani Diabetes and multi-speciality centre to assess similarity of efficacy of anew agent to a standard treatment. In the present study 130 known diabetic patients were selected from Esani diabetes and multispeciality centre, out of which only 56 patients were eligible as per the criteria.

these patients were randomly divided into two groups, group A comprises 28 patients whose baseline FBS, PPBS, Hba1c was determined and the patients were put on teneligliptin 20 mg per day apart from metformin 1gm /day, Group B comprises of 28 patients whose baseline FBS, PPBS, Hba1c were determined and these patients were already on metformin 500 – 1gm per day but there glycemic control was poor, all these patients in group b received an escalation of Metformin dose upto 2.5gm/day, to achieve glycemic control and patients were

monitored closely with proper diabetic diet counselling for ensuring the compliance to Diet, Drug and Exercise.

Inclusion criteria

- Men and women with type2 diabetes(18–65years of age)
- HbA1c7.0–10.0%.
- Known diabetic patient on metformin only.

Exclusion criteria

- Type 1 diabetes mellitus,
- Pre-existing cardiac disease,
- Pre-existing renal impairment (Serum Creatinine≥1.4 mg/dl for males or ≥1.2mg/dl in females),
- Elevated levels of Hepatic enzymes.
- Creatine phosphokinase (greater than 2 time supper limit of normal)
- Patients on other OHA like Sulphonylurea, Insulin, SGLT 2 Inhibitors, and Alpha Glucosidase Inhibitors.

Statistical analysis

The results of FBS, PPBS, HbA1c obtained before and after the teneligliptin and metformin therapy was analyzed using SPSS v 20 software using paired t test and chi square analysis.

RESULTS

In this present study we had enrolled 56 known diabetic patients were selected, and these patients were randomly divided into two groups, Group A comprises 28 patients whose baseline FBS, PLBS, HbA1c was determined and the patients were put on teneligliptin 20 mg per day apart from metformin and Group B comprises 28 patients whose baseline FBS, PLBS, HbA1c was determined and this group of patients were on metformin dose of 500 – 1.5 gram per day. This group had received an escalated dose of Metformin upto 2.5gm/day, to achieve Glycemic control. Patients were monitored closely with proper diabetic diet counselling, HbA1c levels and Glycemic levels.

Table 1: Pre- study statically analysis of FBS, PPBS, HbA1c in both the groups.

	Teneligliptin (Group A)		Metformin (Group B)		T value	P value
	Mean	SD	Mean	SD		
FBS_PRE	154.36	21.99	162.07	20.68	1.35	0.182
PPBS_PRE	243.21	37.52	234.00	36.40	0.933	0.355
HBA1C_PRE	8.23	.86	8.07	0.68	0.795	0.43

Statistical analysis of pre study is as follows: group A the Mean FBS: 154.36 (SD±21.99), PPBS: 243.21 (SD±37.52), HBA1C: 8.23 (SD±0.86) versus Group B the mean FBS: 162.07 (SD±20.68), PPBS: 234 (SD±36.40), HBA1C: 8.07 (SD±0.68). There was no statistical significance observed between both groups prior to study (Table 1 and Figure 1).

Post 30 weeks of the treatment the mean FBS, PPBS, HBA1C was significantly lower in group A than group B

After 30 weeks of the treatment for both the group these are the following results. In group A the Mean FBS was 106.46 (±13.14) which was significantly lower than the mean FBS 116.43 (±17.50) in group B (p 0.019), Mean PPBS 171.36 (±30.71) in group A was significantly lower than mean PPBS 194.64 (±31.74) in group B (p 0.007), Mean HBA1C 7.21 (±0.35) in group A was significantly lower than Group B mea HBA1C: 7.63 (±0.50). (p 0.001). It is clearly evident that teneligliptin (Group A)

patients had greater reduction of Hba1c, FBS, and PPBS than compared to Metformin (Group B). In some patients of Group B when the dose of Metformin was escalated had developed Nausea, Diarrhea.

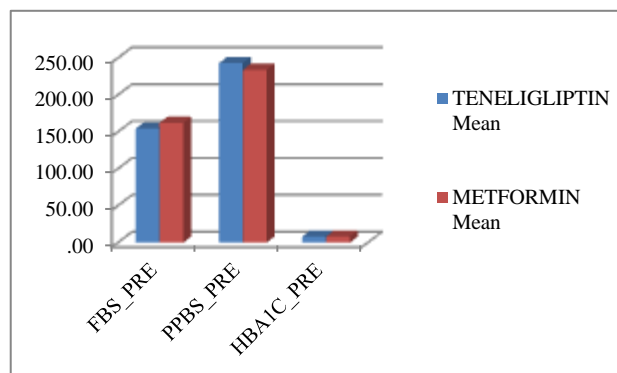


Figure 1: Pre- study statically analysis of FBS, PPBS, HBA1C in both the groups.

Table 2: Post study statically analysis of teneligliptin and metformin groups.

	Teneligliptin (Group A)		Metformin (Group B)		T value	P value
	Mean	SD	Mean	SD		
FBS_post	106.46	13.14	116.43	17.50	2.41	0.019
PPBS_post	171.36	30.71	194.64	31.74	2.79	0.007
HBA1C_post	7.21	0.35	7.63	0.50	3.54	0.001

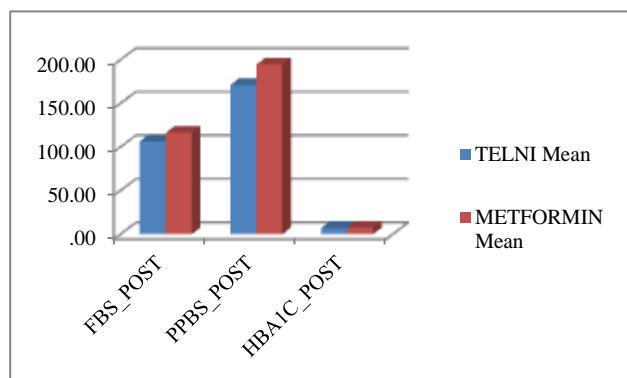


Figure 2: Bar diagram showing the mean data of FBS, PPBS, HBA1C, in Group A versus Group B.

The mean baseline HbA1c in teneligliptin group was 8.23% when compared to 8.07% in the Metformin group. The primary endpoint of the study was to monitor the changes in HbA1c levels from baseline to week 30. It was observed that the mean HbA1c for teneligliptin group after 30 weeks was 7.21% versus 7.63% in metformin group.

HbA1c was significantly reduced in the Group A patients. The incidence of Gastro-intestinal adverse

events was more in metformin group than teneligliptin groups. In patients treated on metformin an additional dosage of teneligliptin once daily was effective and it was well tolerated in Indian patients with type 2 diabetes mellitus. There was neither any significant change observed with respect to lipid profile and body weight.

DISCUSSION

International Diabetes Federation (IDF) and the American Association of Clinical Endocrinologists (AACEs), suggest that an HbA1c ≤6.5% is the appropriate target for patients with type 2 diabetes and reduces the risk for microvascular events.⁴

The mean baseline HbA1c in teneligliptin group was 8.23% when compared to 8.07% in the Metformin group. The primary endpoint of the study was to monitor the changes in HbA1c levels from baseline to week 30. It was observed that the mean HbA1c for teneligliptin group after 30 weeks was 7.21% versus 7.63% in metformin group.

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groups. In patients treated on metformin an additional dosage of teneligliptin once daily was effective and it was well tolerated in Indian patients with type 2 diabetes mellitus. There was neither any significant change observed with respect to lipid profile and body weight.

Kutoha E et al, had selected newly detected type 2 diabetes patient to whom Teneligliptin was started as a monotherapy the duration of treatment was for about 3 months.

There was Significant reduction in HbA1c (from 10.34 to 8.38; $p < 0.00001$) and fasting blood glucose (from 211.3 to 167.3 mg/dL; $p < 0.0002$).⁵

Bloom garden et al, has shown that different oral anti hyperglycaemic agents have similar efficacy when the data are corrected for differences in baseline HbA1c values. The impact of the reduction in FPG levels was moderately greater for metformin group compared to the sitagliptin group of patients.⁶

Kim et al 2015 studied in combination of teneligliptin with metformin in known type 2 diabetic Korean patients whose glycaemic status were not under controlled with metformin monotherapy. In teneligliptin group Mean baseline of HbA1c was 7.9% and 7.8% in placebo group.⁷

Wakaba T et al study was to evaluate the effects of teneligliptin on 24 hour blood glucose control and gastrointestinal hormone responses to a meal tolerance test, and to investigate the glucose-lowering mechanisms of teneligliptin.⁸ Teneligliptin was given once a day for 3 days significantly lowered fasting and postprandial glucose levels. Significant elevations of fasting and postprandial active GLP-1 and postprandial active GIP levels were observed.

CONCLUSION

The addition of teneligliptin to metformin treatment was effective and well tolerated in patients with type 2 diabetes. Teneligliptin has long half-life of 26.9 hours along with it also has a unique pharmacokinetic advantage which allows convenient once daily administration irrespective of food, superadded it has a dual mode of elimination via renal and hepatic, and hence can be administered safely in renal impairment patients.

In mild to moderate hepatic impairment no dosage adjustment is required. The appropriate approach towards managing diabetes should be not only glycemic control

but also preservation of islet cell function early and to delay progression of a disease. Teneligliptin add-on to Metformin during the early course of treatment helps in delaying the exhaustion of pancreatic islet function.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

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