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Original Research Article

Retrospective real-life efficacy assessment of teneligliptin in Indian T2DM patients

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ABSTRACT

Background: Teneligliptin is been introduced recently in Indian market and data available are limited on Indian patients. Hence, the hospital based real life retrospective evaluation was planned out to evaluate, the efficacy of teneligliptin in type 2 diabetes mellitus in Indian population. Hence study was designed, a retrospective evaluation, of efficacy of teneligliptin in type 2 diabetes mellitus in Indian population.
Methods: Data of 775 patients, who were prescribed teneligliptin was collected from hospital records. Teneligliptin 20mg was prescribed to all patients who were uncontrolled on other OHAs and for a mean duration of 8 weeks. Parameter evaluated in this study were change in FBG, PPBG and HbA1c from the baseline at 8week. With profile of outcome i.e. response and failure rates were also assessed with respect to age, gender, BMI and duration of diabetes.
Results: Of 775 patients were enrolled, 427 were males and 348 females. The average age was 53.04 years among the study population. The mean duration of diabetes was 23 months. There was significant change in HbA1c, fasting and postprandial blood glucose levels at 8 week of teneligliptin therapy. Changes in HbA1c, FPG and PPG from baseline to end of study were-1.22±1.12% (p=0.001), -35.8±25.5mg/dl (p=0.001) and -60.7±28.6mg/dl (p=0.001) respectively. Out of 775 patients, 106 (13,7%) were non-responders where it was further sub analysed with different parameter such as age, gender, BMI and duration of diabetes in order to observe response of teneligliptin in diabetic patients.
Conclusions: This real life retrospective evaluation showed efficacy of teneligliptin in real world scenario. It can be an effective alternative to conventional gliptins available for prescription in India.

Keywords: BMI, Diabetes, FBG, HbA1c, PPBG, Teneligliptin

INTRODUCTION

Diabetes is one of the largest global health emergencies of the 21st century.[1] 415 million adults globally and approximately 72.9 million adults in India are currently

estimated to have diabetes.[1] The disease is amongst the top ten causes of disability and accounts for more than 4 million deaths a year and ~11% of total healthcare spending worldwide.[2]

Moreover, the prevalence of type 2 diabetes mellitus in Asia is expected to increase over the next 20 years due to a sedentary lifestyle combined with the increase in obesity and overweight resulting from economic development, and the changes in diet.[1]

Managing diabetes is the utmost importance for medical profession ensuring the minimal adverse effect and optimal efficacy. Presently there are multiple options available to treat diabetes mellitus. There are different classes of oral and injectable anti-diabetic drugs, like biguanides thiazolidinedione, glinides, sulphonyl urea, alpha glucosidase inhibitors, DPP-4 inhibitors, glucagon-like peptide-1 agonists (GLP-1), Insulin and latest SGLT 2 inhibitors are available on board for glycemic control.[2-4]

Dipeptidyl peptidase-4 (DPP-4) inhibitors have recently emerged as a new class of oral anti-diabetic agents that increase circulating concentrations of the glucagon-like peptide-1 (GLP-1) and have relatively limited adverse effects. The DPP-4 inhibitors block the rapid inactivation of GLP-1 and improve glycemic control. DPP4 inhibitors have shown good efficacy and tolerability. Currently they are considered one of the first line drugs as in the authoritative guideline of ADA and AACE for treating diabetes.[3,4]

Teneligliptin, a DPP 4 inhibitor was approved for the treatment of type 2 diabetes in June 2012 in Japan and May 2015 in India. Teneligliptin is a selective and long-lasting DPP 4 inhibitor with an elimination half-life of 24.2hours in plasma.[5] Teneligliptin is a novel DPP 4 inhibitor that has been shown to produce significant increase in plasma active GLP-1 concentration after breakfast, lunch and dinner. The PPG lowering effects of once-daily teneligliptin are sustained throughout the day.[6]

Since, teneligliptin is been introduced recently in Indian market and data available are limited on Indian patients. Hence, the hospital based real life retrospective evaluation was planned out to evaluate, the efficacy of teneligliptin in type 2 diabetes mellitus in Indian population.

Hence study was designed, a retrospective evaluation, of efficacy of teneligliptin in type 2 diabetes mellitus in Indian population.

METHODS

The population in the study was taken from regular diabetic special OPD follow up cases in a tertiary care hospital in Mumbai. 1200 such patients were taken in the study who were having regular follow up were considered.

Inclusion criterion

- Type 2 Diabetic patients on OHAs combination of Sulphonylurea plus metformin plus voglibose or pioglitazone.
- All these patients were having poor glycemic control despite the combinations of OHAs with full dose and good compliance.
- Those patients willing to complete the study and ready for compliance of drug and blood tests.

Exclusion criterion

- Patients with incomplete follow up or not willing to complete the study were excluded.
- Type 1DM, patients on Dialysis, Pregnancy, on steroids and on insulin were also excluded.
- Those requiring surgical interventions, cardiac abnormality and travelling away during study period were excluded.

After explaining to patients, teneliglptin 20mg was introduced in them. Teneligliptin was continued with regular follow up for 6months (with mean follow up duration of 8 weeks). All these patients were questioned for any complications, adverse drug reactions. Also advised to report any untoward reactions.

At every follow up all data of anthropometry, blood test and clinical examination findings were recorded. After excluding, out of 1200, total 775 patients were taken for statistical evaluation with complete follow up. The data of all patients, including regular follow up investigation and body parameters at every follow up was tabulated. This whole data was analysed for clinical correlation, with use of SSPS software by statistician.

Parameter evaluated in this study were change in FBG, PPBG and HbA1c from the baseline at 8week. Also, with profile of outcome i.e. response and failure rates were also assessed with respect to age, gender, BMI and duration of diabetes.

Statistical analysis

Patients' demographic characteristics (age, sex, disease profile, and existing medications) and glycaemic parameters (HbA1c, FPG and PPG values for baseline and 2 month) were documented. Numerical data of HbA1c, FPG and PPG from baseline to 2 months after initiating teneligliptin was analysed by two tailed paired-t test and qualitative data was analyzed by fisher exact test. SPSS statistical software was used for analysis. Statistical tests were considered significant if p-value was less than 0.05 at confidence interval of 95%.

RESULTS

Of 775 patients were enrolled, 427 were males and 348 females. The average age was 53.04 years among the

study population. The demographic data is presented in (Table 1). The mean duration of diabetes was 23months (Table 2).

Table 1: Demographic data.

Parameters	N (775)
Avg. Age (yrs)	53.04 ± 10.95
Age in yrs (%)	
< 55	427 (55.1%)
≥ 55	348 (44.9%)
Sex (%)	
Male	427 (55.1%)
Female	348 (44.9%)
BMI in kg/m^2 (%) (N = 686)	
< 23.5	138 (20.1%)
≥ 23.5	548 (79.9%)
Duration of DM years (%)	
<5	307 (39.6%)
≥ 5	468 (60.4%)

Table 2: Duration of diabetes.

Parameters	Mean duration (months) (N = 775)
Mean	23.38
SD	33.84
Range	000.00-144.00
Median	8.00

There was a significant change in mean HbA1c levels, mean fasting and post prandial blood glucose levels among study cases at the end of 2months of the teneligliptin therapy. The mean HbA1c baseline was 8.42±1.45 % which significantly reduced to 7.20±1.10 % at 8weeks with a significant differences from of 1.22±1.12 % (p= 0.001) from the baseline (Figure 1).

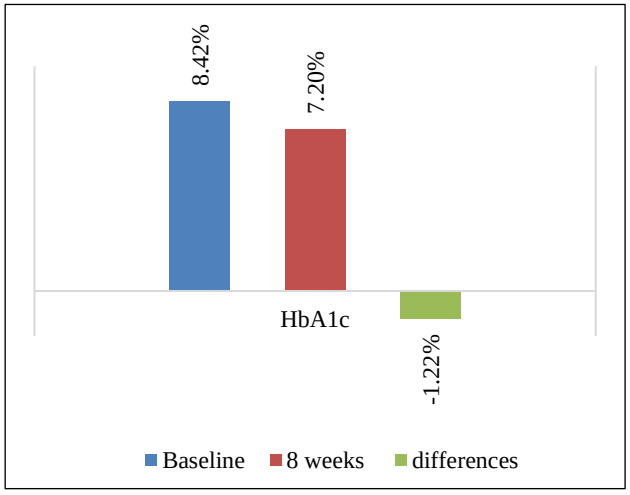

Figure 1: Changes in mean HbA1c among study cases.

At end of treatment, mean HbA1c showed a significant fall of 14.5% from baseline (mean difference of 1.22 %). The mean fasting blood glucose at baseline was 170.4±28.9mg/dl which significantly reduced to 134.6±26.6mg/dl at 8week with a differences of 35.8±25.5 mg/dl (p= 0.001) from the baseline (Figure 2). Whereas the mean post prandial blood glucose observed at baseline was 235.6±30.6mg/dl significantly reduced to 174.9±27.3mg/dl at 8week with a differences of 60.7±28.6 mg/dl (p=0.001) from the baseline (Figure 3). At end of treatment, mean fasting blood glucose showed a significant fall of 21.06% whereas mean post prandial blood glucose showed a significant fall of 25.8% from baseline.

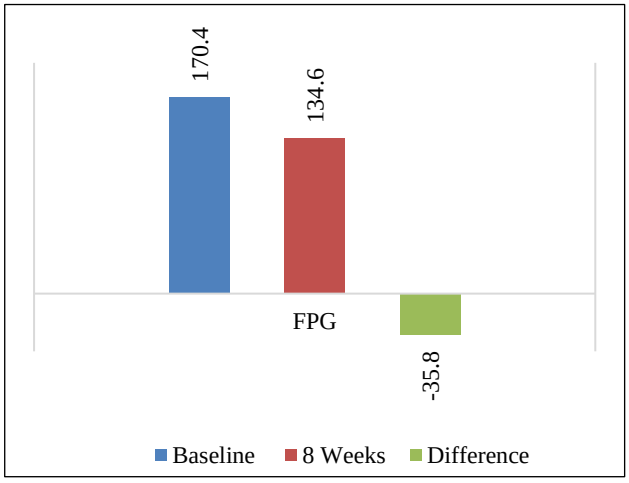

Figure 2: Changes in mean fasting blood glucose among study cases.

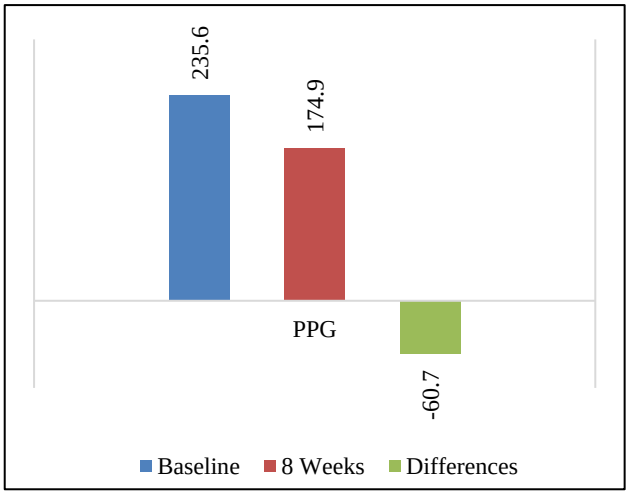

Figure 3: Changes in mean post prandial blood glucose among study cases.

The response (FPG <130mg/dl and PPG <160mg/dl after 8 week of starting teneligliptin) and failure rate among the patients at end of treatment was calculated. It was observed that 86.3% patients responded to the study treatment whereas 13.7% did not respond (Figure 4). Out of 775 patients, 106 were non-responders.

Different parameters such as age, gender, BMI and duration of diabetes were considered in order to observe

response of teneligliptin in diabetic patients. It was noted that 91.1% of the cases falling in age group <55 years responded to the treatment which was significantly more as compared to 80.5% of the cases who belonged to ≥55 years age group (Table 3). 89.2% of the male cases responded to the treatment which was significantly more as compared to 82.8% of the female cases (Table 3).

Around 94.2% of the cases with BMI <23.5kg/m^2 responded to the treatment which was significantly more as compared to 85.0% of the cases with BMI ≥23.5kg/m^2 (Table 3). 91.9% of the cases who had diabetes from <5 years responded to the treatment which was significantly more as compared to 82.7% of the cases who had diabetes from ≥5 years (Table 3).

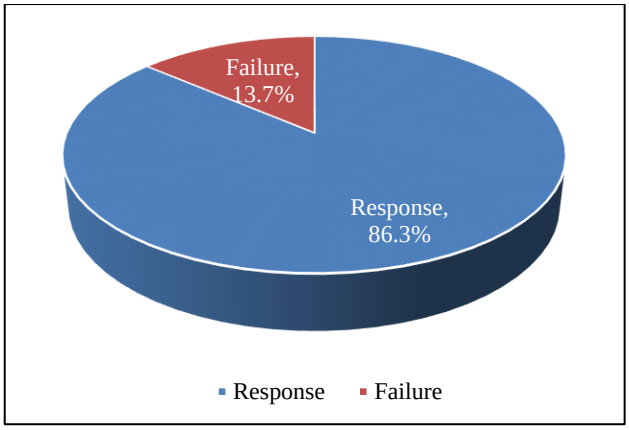

Figure 4: Profile of outcome.

Table 3: Association between various parameter and response among study cases.

Various parameter	No of cases (N = 775)	Outcome				P – value
		Response		Failure		
		N	%	N	%	
Age group						
< 55	427	*389	91.1	038	08.9	P = 0.001, *Significant
≥ 55	348	280	80.5	068	19.5	
Gender						
Male	427	^{0}381	89.2	046	10.8	P = 0.009, ^{0}Significant
Female	348	288	82.8	060	17.2	
BMI (kg/m^2)						
< 23.5	138	†130	94.2	008	05.8	P = 0.004, †Significant
≥ 23.5	548	466	85.0	082	15.0	
Duration of DM (Years)						
< 5	307	‡282	91.9	025	08.1	P = 0.001, ‡Significant
≥ 5	468	387	82.7	081	17.3	

DISCUSSION

DPP-4 inhibitors undoubtedly constitute an innovative class of oral agents for the treatment of T2DM which have enlarged the therapeutic possibilities and are used as fourth therapeutic agent in combination with metformin, sulphonylurea and pioglitazone. In the previous study earlier use of triple drug combination concluded that with proper patients selection, of metformin, glibenclamide and pioglitazone can be safely used in patients receiving insulin with good glycemic parameters.[7] But in the patient where even triple drug therapy fails to control the glycemic parameter leads to early use of insulin to achieve the target glycemic goal. So, instead of early initiation of insulin can we look for the fourth drugs where it can be giving to control the glycemic parameters and achieving the target goal.In different clinical trial conducted in Japan, Korea, it has been shown to be safe and effective in T2DM patients when used either as monotherapy or in combination with other conventional OAD's.[5]

In the Indian study conducted by Ghosh S et al, observed that HbA1c reduction was correlated strongly with the presence of the number of concomitant antidiabetic medications. HbA1c reduced by 0.98%, 1.11%, 1.51%, 1.62% and 1.65% in patients receiving one drug therapy (teneligliptin monotherapy), two drugs, three drugs, four drugs and five drugs therapies with teneligliptin respectively.[8]

The results of the present study showed that 8weeks of teneligliptin when added to metformin+ sulphonylurea + pioglitazone, as fourth agent, was shown to be effective in significantly reducing HbA1c, FPG and PPG levels in Indian patients with T2DM.

In a 24-week, randomized, parallel clinical trial, type 2 diabetes patients inadequately controlled (glycosylated

haemoglobin A1c [HbA1c] ≥7.5% to ≤10%), by dual combination of metformin and another traditional oral hypoglycemic agent (glimepiride, acarbose or pioglitazone), saxagliptin, sitagliptin and vildagliptin were added as third drug in randomized fashion. After 24weeks, HbA1c, FBG, and P2hBG of each group were significantly decreased (saxagliptin vs vildagliptin vs sitagliptin: HbA1c: -1.2% vs -1.3% vs -1.1%; FBG: -32.4 mg/dl vs -43.2 mg/dl vs -27 mg/dl; P2hBG: -61.2 mg/dl vs -66.6 mg/dl vs -57.6 mg/dl). This results were similar to results of our study.[9]

HbA1c reduction, similar to this study was seen when Sitagliptin was added to Metformin+SUs combination in 52 week trial conducted by Mamza J et al.[10] In another a 24-week trial, when T2DM patients (n=93), who were on optimum dosage of metformin and sulphonylurea, were additionally treated with 100mg sitagliptin daily, mean HbA1c was reduced by 0.41% (P<0.007) at the end of 6 months.[11]

Additionally, it was also noted in this study that a large number of males in the age group of less than 55 years and having BMI <23.5kg/m^2 responded to teneligliptin treatment.

As it is a retrospective study, it has certain limitations. Possibility of selection bias cannot be ruled out. It is not possible to comment on adverse events. Data was collected only for duration of 2months. Long term studies are warranted to address the shortcomings of the present study.

CONCLUSION

This real life retrospective evaluation showed efficacy of teneligliptin in real world scenario. It can be an effective alternative to conventional gliptins available for prescription in India.

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Conflict of interest: None declared
Ethical approval: Not required

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