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Expert opinion on the use of teneligliptin in the management of type 2 diabetes mellitus

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Abstract
Objective: To gain a comprehensive understanding of the prescription practices of teneligliptin in Indian healthcare settings.
Methodology: This cross-sectional study involved analyzing the perspectives of experts from various regions in India regarding the use of teneligliptin as mono therapy or as an add-on therapy with other oral anti-diabetic drugs for the management of type 2 diabetes mellitus (T2DM) patients.
Results: The survey assessed the preferences of experts for several dipeptidyl-peptidase 4 (DPP-4) inhibitors namely sitagliptin, vildagliptin, linagliptin, teneligliptin, and saxagliptin. Approximately 40% of the 961 respondents reported that 11-20% of their diabetic patients received teneligliptin as mono therapy. Out of the 962 responses received, 43% reported a mean HbA1c reduction within the range of 0.75-1% when using teneligliptin. When teneligliptin was used in combination with metformin, around 50% of patients reported reaching the HbA1c target range of 26-50%. The most commonly reported benefits were improved renal safety (29.50%), reduced risk of hypoglycemia (34.71%), and avoidance of weight gain (33.08%). These findings provide significant evidence supporting the effectiveness and acceptability of teneligliptin as a DPP-4 inhibitor for the management of patients with T2DM.
Conclusion: The study concluded that teneligliptin can be used as an effective treatment option either as mono therapy or in combination with other anti-diabetic medications to achieve glycemic control. By understanding the nuances of teneligliptin prescription practices, healthcare practitioners can tailor their approach to diagnosis, management, and treatment, ensuring that patients receive personalized care based on their specific clinical presentations and individual needs.

Keywords: Type 2 diabetes mellitus, teneligliptin, mono therapy, metformin, dipeptidyl-peptidase 4 inhibitors

Introduction

Diabetes is a prevalent non-communicable disease that has reached epidemic proportions in several countries. It is ranked as the tenth leading cause of death globally, affecting approximately 415 million people. This number is projected to surge to 642 million by the year 2040. Recent findings indicate that diabetes was responsible for 5 million deaths. Notably, the People's Republic of China, India, the United States, and the Russian Federation have recorded the highest rates of diabetes-related fatalities [1]. Being a chronic illness, diabetes calls for continual medical care to mitigate associated risks and other types of treatment beyond glycemic management [2]. Prioritizing the prevention of short-term and long-term diabetes-related complications must be the primary focus of treatment.

Incretin-related therapies such as dipeptidyl peptidase-4 (DPP-4) inhibitors have revolutionized the treatment of type 2 diabetes mellitus (T2DM). These therapies work by mimicking or enhancing the action of incretin hormones, which play a crucial role in regulating glucose metabolism. Among these DPP-4 inhibitors, teneligliptin has gained popularity and has been approved in multiple countries, including Argentina, India, and Japan [3, 4]. It was introduced in India in May 2015 and has quickly gained attention as a preferred choice among DPP-4 inhibitors due to its cost-effectiveness. It costs roughly a quarter to a fifth less than other DPP-4 inhibitors namely sitagliptin, linagliptin, vildagliptin, and saxagliptin [5]. This affordability factor has contributed to its widespread prescription in India. However, it is worth noting that currently, the data is only available from a modest phase III clinical trial for teneligliptin usage in India, underscoring the need for further research and exploration of its long-term effectiveness and safety profile in the Indian population [6].

Teneligliptin has shown efficacy in helping in maintaining optimal glycemic control and reducing insulin resistance [7, 8]. By increasing the levels of incretin hormones, it promotes insulin production and inhibits glucagon release, thereby regulating blood sugar levels [9]. Numerous clinical trials and real-world research have been conducted to determine the effectiveness and safety of teneligliptin [10, 11, 12]. Both as mono therapy and in conjunction with other anti-diabetic drugs, it has been demonstrated to significantly lower HbA1c levels and enhance glycemic control in individuals with T2DM [13, 14]. Teneligliptin is generally well-tolerated with a low frequency of adverse effects. Typical side effects include nasopharyngitis, headaches, and digestive problems. However, individual responses to medications can vary, and some patients may experience uncommon side effects. Therefore, healthcare providers need to monitor patients closely and address any potential concerns or adverse reactions that may arise [15].

The prescription decisions for teneligliptin should be based on a comprehensive assessment of the patient's clinical profile, considering factors such as overall health, renal function, drug history, and specific treatment goals. Hence, the current study was intended to better understand the prescription practices of teneligliptin in Indian settings, which would contribute to informed decision-making and guide healthcare providers in determining the suitability and effectiveness of teneligliptin as part of a comprehensive treatment plan for T2DM.

Methodology: A cross sectional, multiple-response questionnaire based survey among physicians specialized in treating T2DM patients in the major Indian cities from June 2022 to December 2022.

Questionnaire: The questionnaire booklet titled PRIDE (Expert opinion on Teneligliptin and its combinations) study was sent to the doctors who were interested to participate. The PRIDE study questionnaire included 20 questions about the opinions of experts on prescribing teneligliptin for T2DM patients in their clinical practice. It also involved inquiries concerning newly diagnosed T2DM patients, the utilization of teneligliptin across different age groups, and the assessment of side effects in these patients. The study was performed after obtaining approval from Bangalore Ethics, an Independent Ethics Committee which was recognized by the Indian Regulatory Authority, Drug Controller General of India.

Participants: An invitation was sent to professionals across India based on their expertise and experience in treating diabetes in the month of March 2022 for participation in this Indian survey. About 976 clinicians from major cities of all Indian states representing the geographical distribution shared their willingness to participate and provide necessary data. Physicians were instructed to complete the questionnaire independently, without seeking advice from their peers. Before the execution of the PRIDE Study, each clinician provided written informed consent.

Statistical Methods

Descriptive statistics was performed, and the frequency of occurrence and its associated percentage were used to depict the distribution of each variable. Pie charts and bar charts were generated using Excel version 2013 (16.0.13901.20400).

Results

The study included a total of 976 participants, with the majority from Kerala (16.80%) followed by 11.98% from Karnataka. Other states such as Tamil Nadu, Odisha, and West Bengal had participation rates >5%. The survey evaluated the preferred treatment choices of the respondents among different DPP4 inhibitors namely sitagliptin, vildagliptin, linagliptin, teneligliptin, and saxagliptin. The breakdown of the data is as follows: Sitagliptin: Among the 746 respondents, 27.07% ranked sitagliptin as their top choice, while 7.10% ranked it as their fifth choice. Vildagliptin: Out of the 846 respondents, 31.08% ranked vildagliptin as their second choice, while 3.43% ranked it as their fifth choice. Linagliptin: Among the 800 respondents, 16.5% ranked linagliptin as their first choice, while 6.37% ranked it as their fifth choice. Teneligliptin: Out of the 867 respondents, 34.02% ranked teneligliptin as their top choice, while 2.88% ranked it as their fifth choice. Saxagliptin: Among the 649 respondents, the majority (74.11%) ranked saxagliptin as their fifth choice, while only a small percentage ranked it as their first or second (5.54% each) choice.

Out of the 961 respondents, about 40% of the respondents indicated that 11-20% of their diabetic patients were on teneligliptin s therapy, while 22% indicated that <10% of their patients were on the same treatment. Approximately 29% of the respondents indicated that 21-40% of their patients were on teneligliptin, while only 8.94% of them indicated that >40% of their patients were on the same treatment (Figure 1).

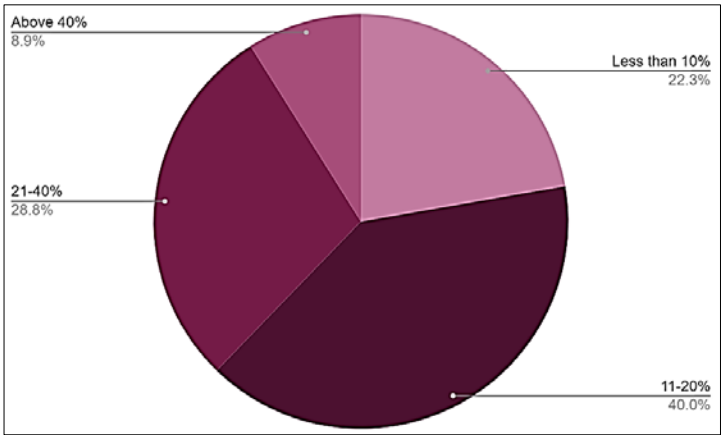

Fig 1: Diabetic patients undergoing teneligliptin mono therapy after metformin failure

Out of the 962 respondents, approximately 43% indicated a mean HbA1c reduction in the range of 0.75-1%, while 31% indicated it in the range of 0.5-0.75%. Around 23% of the respondents indicated the change to be >1%. The benefits of using teneligliptin for achieving glycemic targets were reported by 29% of respondents. Around 26% reported that teneligliptin had no effect on weight. Renal benefits were reported by 21% of respondents, and 22% noted that teneligliptin was cost-effective. Other reported benefits, although in fewer patients, included compliance, glucose-dependent action, reduced risk of hypoglycemia, lower pill burden, no improvement in liver function, no hypoglycemia, and once-daily dosing of teneligliptin.

Out of the 956 respondents, approximately 50% reported that 26-50% of patients have achieved the HbA1c target when using teneligliptin + metformin. About 31%, 11%, and 8% of the respondents reported that 51-75%, >75%, and <25% of patients, respectively, had achieved the HbA1c target using teneligliptin + metformin (Figure 2).

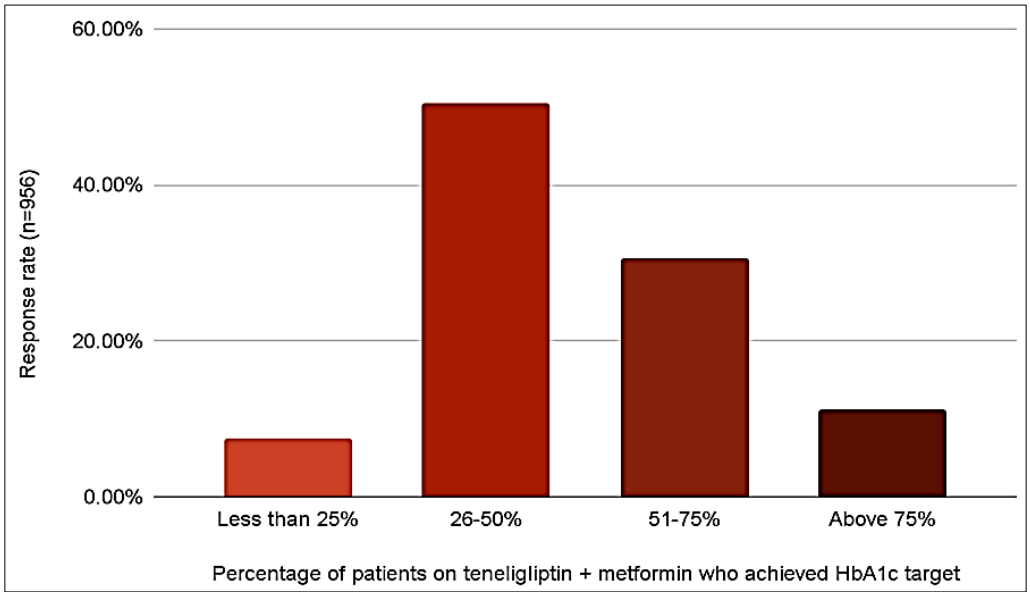

Fig 2: Proportion of patients on teneligliptin + metformin who achieved HbA1c target

The most commonly reported benefits include a reduced risk of hypoglycemia (34.71%) and weight gain (33.08%), and improved renal safety (29.50%). Approximately 27% of the respondents also reported other benefits that were not specified in the response options, including affordability, cost-effectiveness, glycemic control, once-daily dosing or reduced pill burden, reasonable cost, and good tolerability (Table 1).

Out of 960 respondents, 40% reported that the likelihood of using the combination of teneligliptin 20mg + pioglitazone 15mg in T2DM patients was <10%, and another 40% reported it to be in the range of 10-25%. Approximately 17% of the respondents reported that 25-50% of T2DM patients had the likelihood of using the same combination. However, a lower percentage of 0.62% of respondents reported that this combination is not applicable to diabetic patients.

Table 1: Benefits of using teneligliptin + metformin in clinical practice

Benefits of teneligliptin + metformin therapy	Response rate (n=2264)
Low risk of hypoglycemia	786 (34.71%)
Low risk of weight gain	749 (33.08%)
Better renal safety	668 (29.50%)
Other benefits	61 (26.99%)
Affordability	1 (1.63%)
Cost-effectiveness	7 (11.47%)
Glycemic control	1 (1.63%)
Mono therapy	1 (1.63%)
No dose adjustment	2 (3.27%)
Once daily dose/ reduced pill burden	1 (1.63%)
Well tolerated	1 (1.63%)
All the above	47 (77.04%)

Discussion

The findings of the current PRIDE study provide compelling evidence that teneligliptin is not only effective but also well-tolerated as a DPP-4 inhibitor for managing T2DM. The study highlights the potential benefits of teneligliptin as a viable treatment option, both as a mono therapy and in combination with other anti-diabetic agents, for achieving optimal glycemic control. However, it is crucial to emphasize that the use of teneligliptin, like any medication, should be personalized based on individual patient factors, including medical history and specific needs.

Of the 961 respondents, 39.96% and 28.82% indicated that 11-20% and 21-40% of their diabetic patients, respectively, were on teneligliptin mono therapy. The results of

teneligliptin treatment have consistently shown positive outcomes in terms of achieving glycemic targets, providing renal benefits, and not causing weight gain. Additional benefits reported by respondents include a reduced risk of hypoglycemia, improved compliance, glucose-dependent action, reduced pill burden, and no negative impact on hepatic function.

A study conducted by Xiaoxuan Li supports these findings, as it reported improved blood glucose levels and enhanced β-cell activity without an increased risk of hypoglycemia in T2DM patients who received teneligliptin [16]. Furthermore, other clinical studies have demonstrated that teneligliptin significantly improves glycemic control when used as mono therapy or in combination with other treatments. It is well tolerated by patients and is associated with a low incidence of hypoglycaemia [17, 18, 19]. Another notable aspect of teneligliptin is its pleiotropic effects, which extend beyond glucose management. Studies have suggested that teneligliptin may enhance endothelial function and reduce oxidative stress in blood vessels [20]. These distinct properties make teneligliptin an attractive therapeutic option for a wide spectrum of T2DM patients, including the elderly and patients with renal impairment.

The PRIDE study also evaluated the efficacy and safety of teneligliptin as an add-on therapy to metformin in patients with T2DM who had inadequate glycemic control on metformin mono therapy. Furthermore, the findings of the TREAT-INDIA study demonstrated that teneligliptin significantly improved glycemic control. The study evaluated the effectiveness of teneligliptin as a standalone treatment or in combination with other commonly prescribed antidiabetic medications [21].

The TREAT-INDIA study also noted that the dual therapy of metformin and teneligliptin is the second most popular teneligliptin combination therapy, with a usage rate of 28.06% [21]. In the present study, 50.41% of 956 respondents reported that 26-50% of patients had achieved the HbA1c target when using the teneligliptin + metformin combination. A review by Sharma *et al*. noted that in the teneligliptin + metformin group, a significantly larger percentage of patients attained the HbA1c <7% than in the placebo + metformin group (64.71% vs 13.24%; $p<0.001$) [22]. Moreover, other studies have also demonstrated substantial and clinically meaningful reductions in blood glucose levels with a 12-week decrease in HbA1c of 0.8% to 0.9%, which was sustained for up to 52 weeks of teneligliptin medication [23, 24]. of the 960 respondents, approximately 40% and 38% reported that the likelihood of using the combination of teneligliptin 20mg + pioglitazone 15mg in T2DM patients was <10% and between 10-25%, respectively. However, a smaller percentage of respondents (0.62%) indicated that this combination was not applicable. In a previous study, T2DM patients who were treated with 15-30 mg per day of pioglitazone and also received teneligliptin 20 mg for 12 weeks experienced changes in HbA1c levels, fasting blood glucose levels, and 2-hour postprandial blood glucose levels compared to their baseline values [3, 25]. Though teneligliptin + pioglitazone might have a favourable safety profile, the addition of teneligliptin to metformin was well-tolerated and resulted in a significant reduction in HbA1c levels and fasting plasma glucose levels [26, 27].

The present study has certain limitations that need to be acknowledged. Firstly, the study had a small sample size, potentially affecting the generalizability of the findings. Secondly, as the study relied on expert opinions, there is a possibility of bias influencing the results. Future studies with larger sample sizes and randomized controlled designs are needed to confirm the findings of the present study.

Conclusion

The present study provides valuable evidence supporting the efficacy and tolerability of teneligliptin as a DPP-4 inhibitor for the treatment of patients with T2DM. It demonstrates that teneligliptin can be used as a mono therapy or in combination with other antidiabetic agents to achieve glycemic control effectively. By understanding the nuances of teneligliptin prescription practice, healthcare professionals can tailor their approach to diagnosis, management, and treatment, ensuring that patients receive personalized care based on their specific clinical presentations and individual needs.

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