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Original Article

Retrospective, Observational Study to Understand the effectiveness of Alogliptin on Glycaemic variability through Continuous Glucose Monitoring (CGM) in T2DM Indian Patients: A Real-World Evidence

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A R T I C L E I N F O

Keywords:
Glycaemic variability (GV),
Continues glucose monitoring (CGM),
Alogliptin,
time in target range (TIR).

A B S T R A C T

Aim: This study aimed to assess effectiveness of Alogliptin 25 mg on Glycaemic variability (GV) through continues glucose monitoring (CGM) in patients with T2DM in retrospective observational real-world settings.
Materials and Methods: 15 patients who received Alogliptin over existing anti-diabetic treatment as routine clinical practice in management of T2DM were analysed retrospectively from single centre. Data collected from past medical records. FreeStyle Librepro 1.0.6 was used for CGM. CGM was done 15 days prior to adding Alogliptin and repeated approximately after 3 weeks that for next 15 days. Percentage time in target range (TIR) (70- 180mg/dl), Percentage time above target and Percentage time below target,and Mean BG level were assessed prior and after adding Alogliptin in existing treatment regimen.
Results:Significant improvement seen in Percentage time in target range (TIR) (70-180mg/dl) from 65% to 80% (+15% P value 0.00037) and significant reduction seen in Percentage time above target from 32% to 16% (- 16%, P value 0.0002). There was non-significant increase in Time below Therapeutic range from 3% to 5% (+2%, P=0.3116.).Significant reduction in Average blood glucose level seen after adding Alogliptin in existing treatment regimen from 157 mg/dl to 134 mg/dl (-23 mg/dl, P0.00034).
Conclusion: Alogliptin was found to be effective and well tolerated when added to the patients who were uncontrolled on other oral anti-diabetic medications. It effectively showed improvement in continues glucose monitoring (CGM) parameters like Time in therapeutic range (TIR) and significant improvement seen in glycaemic variability.
Limitations: Small sample size and retrospective, observational study.

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Introduction

The escalating incidence of Type 2 Diabetes Mellitus (T2DM) globally, with a pronounced prevalence in the South Asian demographic, particularly in India, represents a substantial public health challenge.

Current projections by the International Diabetes Federation anticipate a dramatic escalation in the diabetic population in India, estimating a staggering 80 million individuals affected by 2025. Traditional pharmacologic interventions for T2DM frequently exhibit a decrement in therapeutic efficacy over time, leading to suboptimal glycaemic regulation and accompanying adverse pharmacological reactions.[1]

The therapeutic landscape for T2DM encompasses a spectrum of pharmacotherapeutic classes, utilized either as monotherapy or in synergistic combinations.

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Incretin-based therapies, especially the DPP-4 (dipeptidyl peptidase-4) inhibitors, or gliptins, have emerged as a focal point in T2DM management due to their role in augmenting patient outcomes. DPP-4 is a proteolytic enzyme ubiquitously expressed, responsible for the rapid inactivation of incretin hormones such as glucose-dependent insulinotropic polypeptide (GIP) and Glucagon-likepeptide-1(GLP-1), secreted by enteroendocrine cells in response to nutrient ingestion.

Inhibition of DPP-4 enzymatic activity by gliptins prolongs the bioactivity of incretins, thereby enhancing insulin synthesis and secretion, and concurrently suppressing glucagon release. This modulates glucose homeostasis effectively.[2]

Alogliptin, a selective DPP-4 inhibitor, has been recognized for its efficacy in optimizing glycaemic control, particularly when used adjunctively with diet and exercise modifications. Endorsed by the USFDA in 2013 for both monotherapy and combination therapy with metformin, Alogliptin's approval was predicated on extensive clinical trials involving over 8,000 T2DM patients for monotherapy and additional trials with more than 2,500 patients for combination therapy. Despite its established safety and efficacy profile, there is a paucity of data regarding Alogliptin's impact on continuous glucose monitoring (CGM).[3,4]

The usage of newer diabetes technology (specifically for blood glucose monitoring) has advanced at an almost exponential rate over the past few years. Rational use of CGM can also be transformative for many of patients with type 2 diabetes. It can empower these individuals, help

support self-care, and reduce the burden of type 2 diabetes on the patient.

Use of professional or intermittent CGM should always be coupled with analysis and interpretation for people with diabetes, along with education as needed to adjust medication and change lifestyle behaviors. CGM provides a continuous measurement of the interstitial glucose over time and offers the opportunity to detect glucose variations, hypoglycaemic events, and time in range (TIR).[5]

Therefore, we aim to assess the effectiveness of Alogliptin at dosages of 25 mg through CGM in T2DM Indian patients, within the context of a retrospective observational study in a real-world setting. This approach would provide valuable insights into the effectiveness of Alogliptin in managing blood glucose levels in patients with T2DM, specifically how it affects time spent within, above, and below the target glucose range. It's a good example of how retrospective data can be used to assess treatment outcomes in a real-world clinical setting.

Material and Methods:

Fifteen patients who received Alogliptin over existing anti-diabetic treatment as routine clinical practice in management of T2DM were analysed retrospectively from single centre. Data collected from past medical records. Free Style Librepro 1.0.6 was used for CGM. CGM was done 15 days prior to adding Alogliptin and repeated 3 weeks after that for next 15 days.

Percentage time in target range (70-180mg/dl), Percentage time above target and Percentage time below target,Mean Blood glucose(BG) level were assessed prior and after adding Alogliptin in existing treatment regimen.Continuous Glucose Monitoring(CGM) was done 15 days prior to adding Alogliptin and repeated approximately after 3 weeks that for next 15 days.

Results:

The baseline characteristics of the Indian patients with type 2 diabetes included in this study are summarized in Table 1.

Table 1:Baseline Characteristic of the patients

Demographic Parameters	
No. of Patients	15
Male	11
Female	4
Average Weight	74 Kg
Average Duration of Diabetes	2 years
Mean HbA1c	8.86%
Other Oral Antidiabetic Agents	Glimepiride,Gliclazide and Metformin

End point analysis

Time in Range (TIR)(between 70 and 180 mg/dL, or 3.9 and 10 mmol/L)
The analysis revealed a significant improvement in the proportion of time that patients' blood glucose levels were within the target range of 70-180 mg/dl. Patients spent 65% of the time within this range, which increased to 80% following the addition of Alogliptin (Fig.1). This 15% increase is statistically significant (P-value of 0.0037).

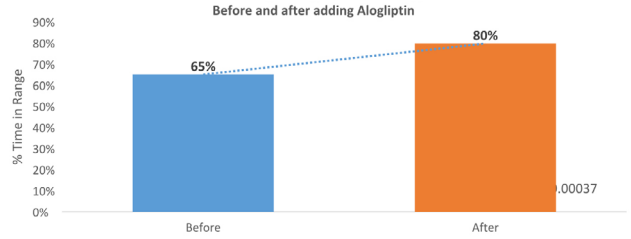


Fig.1 Average Percentage change in Time in Range prior to Alogliptin and after three weeks of addition of Alogliptin to the existing therapy

Time above Range (> 180 mg/dL or 10 mmol/L)

Concurrently, there was a notable decrease in the percentage of time above range, this metric decreased from 32% to 16%, a reduction of 16 percentage points (P-value= 0.0002) as shown in Fig.2.

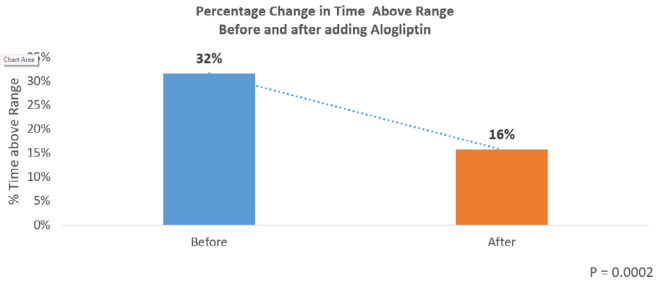


Fig.2 Average Percent change in Time above Range prior to Alogliptin and after three weeks of addition of Alogliptin to the existing therapy

Time below range (< 70 mg/dL or < 3.9 mmol/L)

The data shows an increase in the time below the therapeutic range from 3% to 5%. This is a relative increase, but it is described as "non-significant". The P-value associated with this reduction is 0.3116.

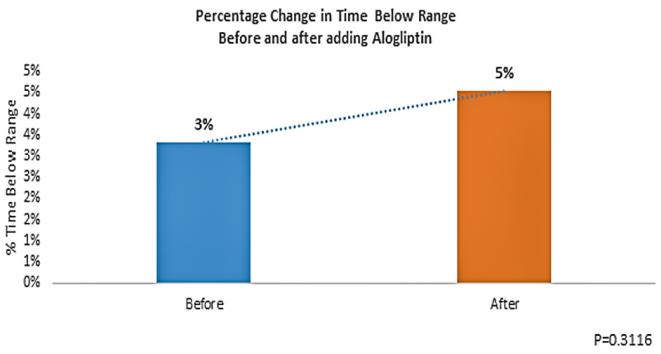


Fig.3 Average Percent change in Time below Range prior to Alogliptin and after three weeks of addition of Alogliptin to the existing therapy

Mean blood glucose level.

There was substantial decrease in the mean blood glucose level, from an initial value of 157 mg/dl to a post-treatment value of 134 mg/dl (P-value of 0.00034). This represents a clinically meaningful reduction of 23 mg/dl (Fig.4).

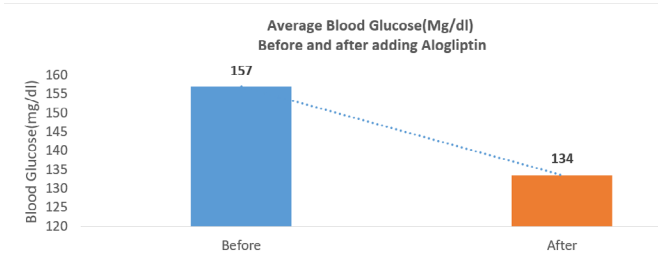


Fig.4Average blood glucose prior to Alogliptin and after three weeks of addition of Alogliptin to the existing therapy

Overall, the results from this analysis demonstrate that the addition of Alogliptin to existing treatment regimens can lead to significant improvements in Glycaemic variability. These improvements are statistically significant and clinically important, offering potential benefits in terms of reduced complications and improved quality of life for patients managing their blood glucose levels.

Discussion

There is enough evidence to suggest that glycaemic variability (GV) contribute independently to diabetes-related complications. The use of CGMs has been endorsed by the American Diabetes Association (ADA) in its Standards of Medical Care in Diabetes, the International Society for Pediatric and Adolescent Diabetes (ISPAD), the American Association of Clinical Endocrinologists (AACE), , and the Endocrine Society. The use of CGM is globally increasing in all age groups.[4]

CGM provides a continuous measurement of the interstitial glucose over time and offers the opportunity to detect glucose variations, hypoglycemic events, and time in range (TIR).[5]

Guidance on target for assessment of glycaemic control in patients with diabetes,(Fig. 5)

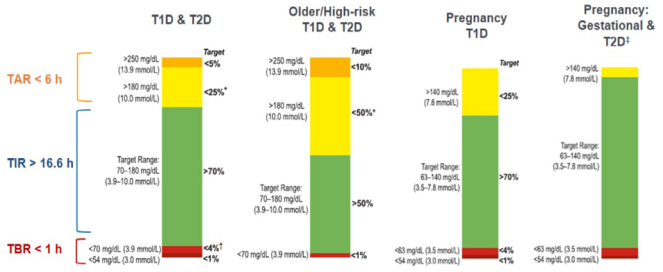


Fig.5Continuous glucose monitoring-based targets for different diabetes populations.

- A time in range (70–180 mg/dL, or 3.9–10 mmol/L) aim of greater than 70% is advised for most individuals with type 1 or type 2 diabetes; a 5% increase toward this target is considered clinically relevant.

- Reducing glycemic excursions is the main objective; elderly people or those who are more vulnerable should aim for less strict targets. A recommended target for a time below range (< 70 mg/dL or < 3.9 mmol/L) is less than 4%, and for a time above range (> 180 mg/dL or 10 mmol/L) is fewer than 25%. (On rare occasions, glucose readings in the range of 70 to 140 mg/dL may be utilized as a backup range, particularly in relation to comparability studies and regulatory concerns.)

These targets should be individualized: the personal use of CGM with the standardized data presentation provides all necessary means to accurately tailor diabetes management to the needs of each individual with diabetes.[5]

Recent South Asian expert census highlighted the TIR recommendations for South Asian population. It has been shown that a TIR of > 70% corresponds to an HbA1c level of < 7.5% for the Indian population.[6]

In this retrospective study evaluating the safety and effectiveness of alogliptin in Indian patients with Type 2 Diabetes Mellitus (T2DM) using continuous glucose monitoring (CGM), we observed that alogliptin significantly improved glycemic control as evidenced by reductions in mean glucose levels, glycemic variability, and the percentage of time spent in hyperglycemia. Additionally, alogliptin was well-tolerated, with no significant increase in the incidence of hypoglycemia or adverse events.

The increase in the percentage of time within the target glucose range (from 65% to 80%) is a significant finding. Studies have shown that maintaining blood glucose within this range can reduce the risk of microvascular and macrovascular complications.[7]Our results align with these studies, suggesting that Alogliptin can be a valuable addition to T2DM management.

The decrease in time above the target glucose range (from 32% to 16%) is particularly noteworthy. High blood glucose levels are a known risk factor for diabetic complications such as nephropathy and retinopathy.[8] These findings suggest that Alogliptin can help in mitigating this risk.

The slight increase in time below the target glucose range was non-significant. This could be interpreted as Alogliptin not increasing the risk of hypoglycaemic events, which is a crucial consideration in diabetes treatment. The absence of a significant increase in hypoglycaemia aligns with the findings of Rosenstock et al., who also reported a low incidence of hypoglycaemia with Alogliptin.[9]

The observed reduction in mean blood glucose levels (23 mg/dl) is consistent with previous studies investigating DPP-4 inhibitors like Alogliptin. For instance, DeFronzo et al. reported similar reductions in their study group, reinforcing the efficacy of Alogliptin in lowering blood glucose levels.[10]This reduction is clinically relevant as it brings patients closer to recommended HbA1c goals, potentially decreasing the risk of diabetes-related complications.

Implications for Clinical Practice in India

The findings of this study have significant implications for the management of T2DM in India. Given the high burden of diabetes and the need for effective, safe, and accessible treatments, alogliptin presents a viable option for glycemic control in Indian patients. The use of CGM in this study highlights the importance of monitoring not just HbA1c but also glycemic variability and time in range (TIR), which are emerging as critical parameters in diabetes management.

Conclusion:

Alogliptin was found to be effective when added to the patients who were uncontrolled on other oral anti-diabetic medications. It effectively showed improvement in continuoes glucose monitoring (CGM) parameters like Mean blood glucose, more number of patients were in Time in Target range i.e (70-180mg/dl) after adding Alogliptin to existing anti-diabetic medications & well tolerated.

Strengths, Limitations and Future Research:

A key strength of our study is the use of CGM, which provides a more comprehensive assessment of glycemic control compared to HbA1c alone. However, as a retrospective study, there are inherent limitations, including the potential for selection bias and the inability to establish causality. Additionally, our study was limited to a single center, which may affect the generalizability of our findings to the broader Indian T2DM population. The sample size is relatively small, and the study duration was limited, which may affect the generalizability of the results. Future research should focus on larger and more diverse populations over extended periods. Additionally, examining the long-term effects of Alogliptin on diabetic complications would be valuable.

Source of Funding:
None.

Conflict of Interest

Dr. Abhijit Anil Trailokya, Dr. Amar Shirsat associated with Indoco Remedies Ltd. Mumbai, Dr Shaijesh Wankhede helped in analysing the data and manuscript writing.

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