CASE REPORT
ENDOCRINE

Diseases & Research

Progressive Improvement in Glycemic Variability with Add-on Alogliptin: A Continuous Glucose Monitoring Based Case Study in Type 2 Diabetes Mellitus

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Abstract: In this case study, a middle-aged woman with uncontrolled type 2 diabetes mellitus (T2DM), despite being on a combination of oral antidiabetic drugs (OADs), achieved good glycemic control with the add-on therapy of alogliptin after 4 weeks. Add-on alogliptin not only improved her overall glycemic control but also reduced glycemic variability as assessed by continuous glucose monitoring (CGM) data. She spent an increasingly longer proportion of time within the target range of (80–140) mg/dL after initiation of alogliptin without any symptomatic hypoglycaemic events.

Keywords: Alogliptin; Continuous glucose monitoring; Dipeptidyl Peptidase-4 Inhibitor; Glycemic variability.

Introduction

Type-2 diabetes mellitus (T2DM) is a chronic metabolic disorder with characteristic higher blood glucose levels. Inadequate insulin secretion and increased insulin resistance are considered as the primary defects in the pathogenesis of T2DM[1]. HbA1c is the gold-standard for monitoring glycemic control in diabetes mellitus (DM). However, glycemic variability (GV), is now being considered as a more meaningful measure of glycemic control than HbA1c in the clinical practice[2]. Short-term GV can be calculated from self-monitoring of blood glucose (SMBG) measurements for a long time, but this method is being gradually replaced by continuous glucose monitoring (CGM). CGM, with interstitial glucose measurements, is now considered to provide a more comprehensive record during the day and night periods as compared to SMBG[3].

Emerging evidence suggests that GV might play a significant role in the development of diabetic complications even in individuals with well-controlled glucose profiles[2]. Several studies have shown that there is an association between large glycemic fluctuations and microvascular and macrovascular complication in DM[3]. Hyperglycemia as well as hypoglycemia has been implicated in the increased cardiovascular (CV) risk in DM[2]. One meta-analysis of 20 studies which included 95,783 individuals found a progressive relationship between the GV and CV risk[4]. Therefore, it is evident that, along with good HbA1c control, there is a need of reduction in GV for better prevention of diabetes related complications.

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Alogliptin in T2DM

Dipeptidyl peptidase (DPP-4) inhibitors are incretin-based therapies, which are widely used for the management of T2DM. They have lower risk of hypoglycemia and had weight-neutral effect[5]. Alogliptin is an oral dipeptidyl peptidase-4 (DPP-4) inhibitor which has been found to improve glycemic control in a glucose-dependent manner[6]. As a selective DPP-4 inhibitor, it is used primarily in the management of T2DM[6]. Clinical trials have shown that alogliptin effectively lowers HbA1c and fasting blood glucose levels[6]. The cardiovascular safety of alogliptin was assessed in the EXAMINE trial. The trial showed that alogliptin did not increase the risk of major adverse cardiovascular events (MACE) compared to placebo, affirming its cardiovascular safety[7].

The objective of this case study is to understand efficacy of add-on alogliptin on glycemic variability in T2DM patient monitored through continuous glucose monitoring (CGM).

Case presentation

Patient demographics

A 58-year-old woman with a history of T2DM for over 15 years. She has been under treatment for T2DM but struggled with achieving optimal glycemic control.

Medical history

She was diagnosed with T2DM > 15 years ago. Over the years, her treatment regimen included sulfonyl urea combined with metformin and voglibose. At the time of follow-up visit, she was prescribed with glimepiride 2 mg + Metformin (500 mg) before breakfast and was prescribed with glimepiride 1 mg + Metformin

500 mg + Voglibose 0.2 mg before dinner. Despite this, she had inadequate glycemic control, her estimated HbA1c was 9.1%.

Intervention

She was prescribed with add-on therapy of 12.5 mg of alogliptin twice in a day (total daily dose of 25 mg). CGM was introduced to her for better understanding of her glycemic patterns. She agreed for the CGM thus, Free Style Libre Pro 1.0.6 was used. She was educated on the use of the CGM device, including sensor placement, calibration, and interpreting the data. She was provided with a smartphone application to monitor her glucose levels in real-time and receive alerts for hypo- and hyperglycemia. First CGM was done between 16 April 2024–30 April 2024 and second CGM was repeated between 18 May 2024–31 May 2024 (Refer Fig. 1 and Fig. 2). The CGM Time in range (TIR) was purposefully kept between (80–140 mg/dL), basically to understand effect of alogliptin on tight glycemic control, (Refer Fig. 1−6).

Outcomes: Glycemic variability and trends

Average blood glucose level, percentage time in target range (TIR), percentage time above target range (TAR) and percentage time below target range (TBR) were determined after addition of alogliptin to the existing antidiabetic treatment regimen. On the day of initiation of alogliptin, her average glucose was 215 mg/dL, TIR was 10% and TBR was 0% and TAR was 90%, (Refer Table 1).

The patient was scheduled for follow-up visits every two weeks for the first three months to monitor her response to alogliptin. After 4 weeks of add-on treatment with alogliptin and CGM was done, this time TIR (Time in therapeutic range) was purposefully kept between 80–140 mg/dL. Along with Alogliptin strict diet control with advice on exercise was given. Her estimated HbA1c % was decreased to 6.8% from 9.1%. Her average blood glucose became 148 mg/dL, Time in target range (TIR) (80−140 mg/dL) improved to 47% from 10% and Time above target range reduced from 90% to 50%. There were no symptoms of hypoglycemia experience by patient after addition of

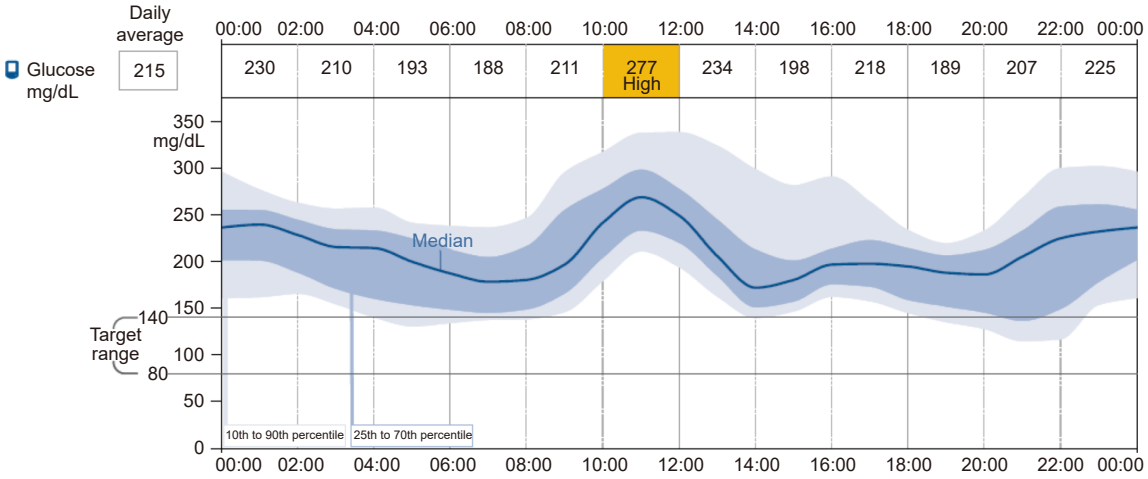

Fig. 1. CGM daily patterns (with ambulatory glucose profile) for 15 days (immediately after add-on treatment with alogliptin) [16 April 2024–30 April 2024].

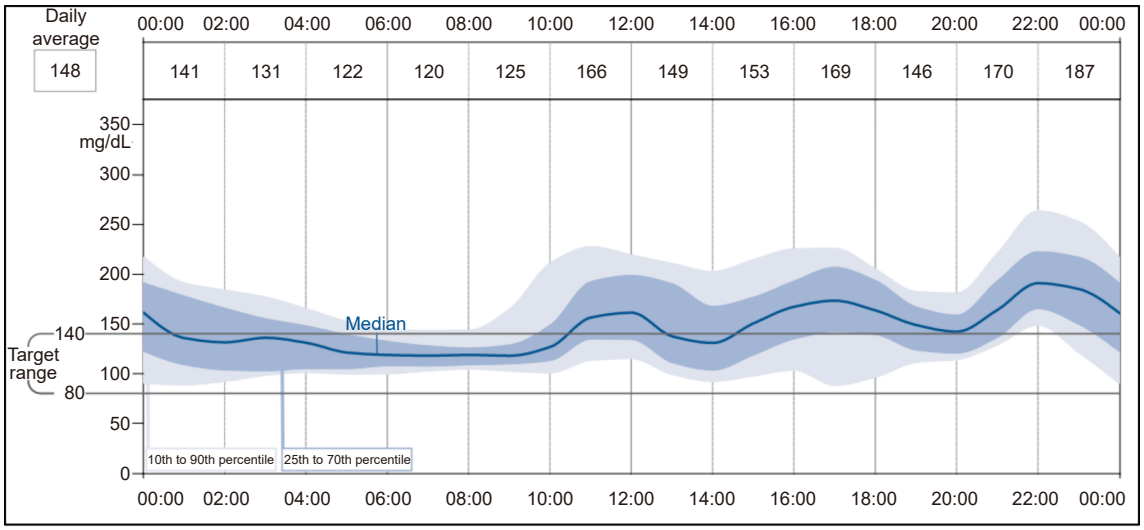

Fig. 2. CGM daily patterns (with ambulatory glucose profile) after 4 weeks of add-on treatment with alogliptin [18 May 2024–31 May 2024].

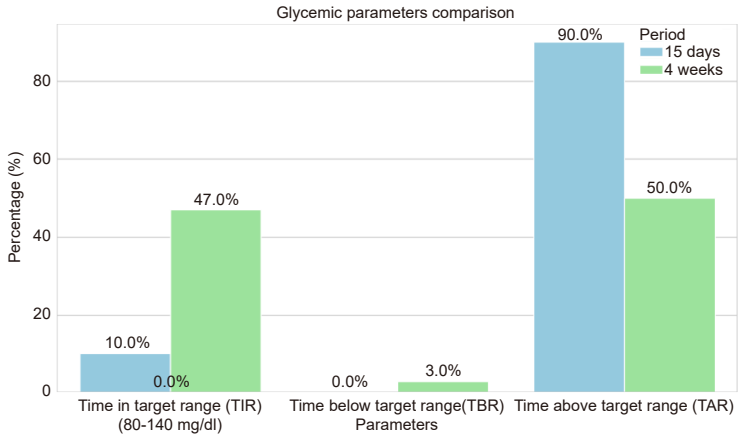

Fig. 3. Comparison of Average glycemic parameters (TIR, TBR, TAR).

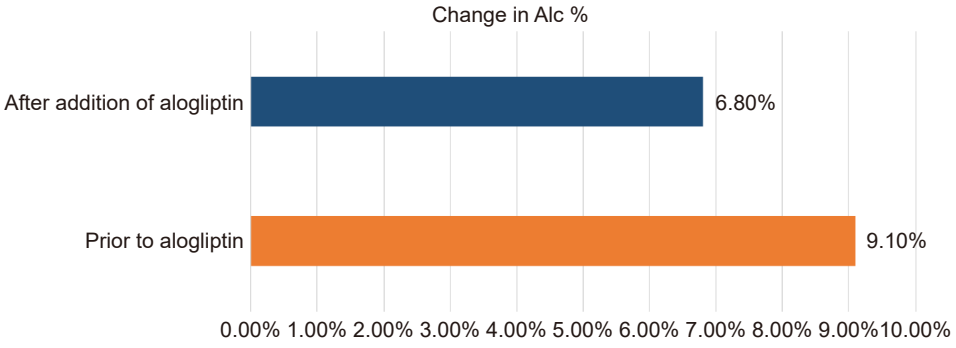

Fig. 4. Change in estimated HbA1c %.

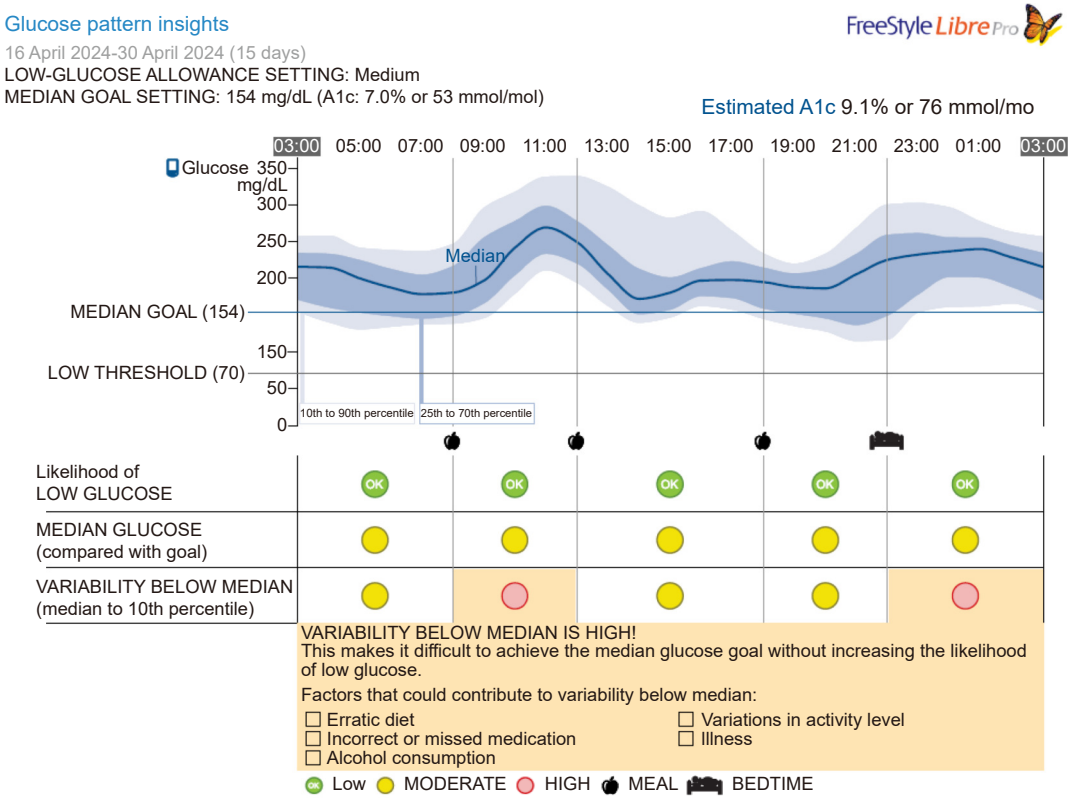

Fig. 5. Glucose Pattern Insights for 15 days (immediately after add-on treatment with alogliptin) [16 April 2024–30 April 2024].

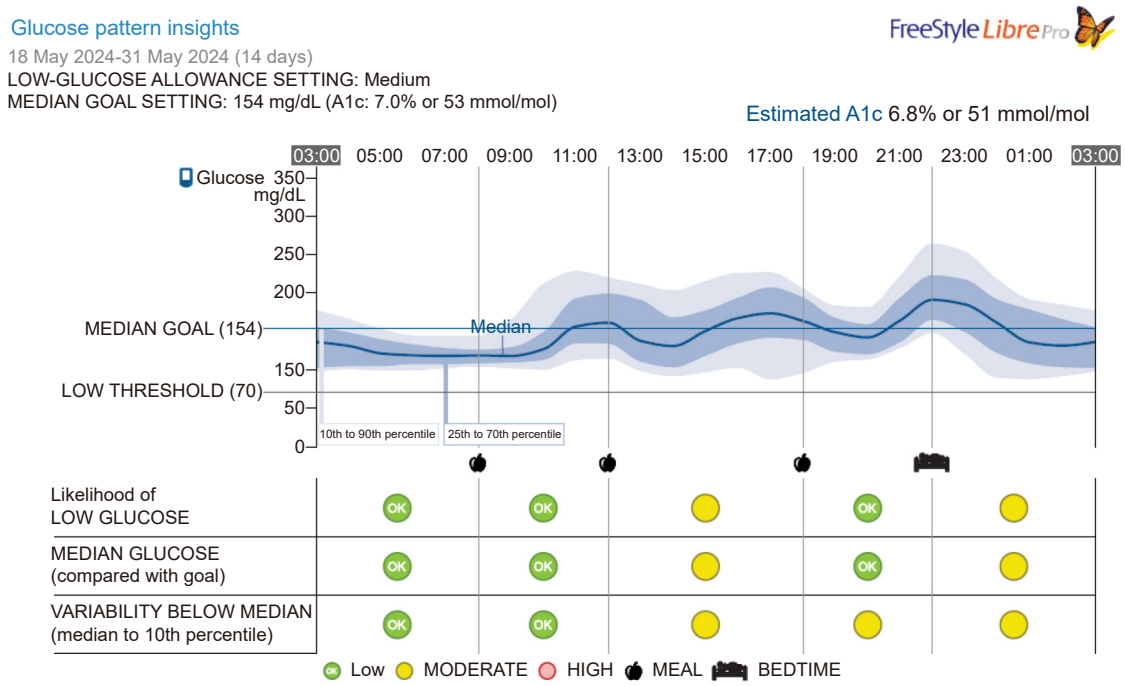

Fig. 6. Glucose Pattern Insights for 15 after 4 weeks of add-on treatment with alogliptin [18 May 2024–31 May 2024].

alogliptin though Time below target range (TBR) was increased by 3%. (refer Table 2, Fig. 3).

Table 1. Average glycemic parameters for 15 days immediately after addition of alogliptin (16 April 2024–30 April 2024)].

Parameter	For 15 days (Immediately After Addition of Alogliptin)
Average Glucose (mg/dL)	215
Time in target range (TIR) (80–140 mg/dL)	10%
Time below target range (TBR)	0%
Time above target range (TAR)	90%

Table 2. Average glycemic parameters for 15 days, after 4 weeks of add on alogliptin (18 May 2024–31 May 2024).

Parameter	For 15 days (After 4 Weeks Treatment with Add-on Alogliptin)
Average Glucose (mg/dL)	148
Time in target range (TIR) (80–140 mg/dL)	47%
Time below target range (TBR)	3%
Time above target range (TAR)	50%

Discussion

In the present case study, the middle-aged woman with uncontrolled T2DM despite treatment with combination of sulfonyl urea, metformin and voglibose gained good glycemic control with add-on treatment with alogliptin. There was progressive reduction in the glycemic variability. As evident from the CGM data, her blood glucose levels were in the target range of 80–140 mg/dL for the increasingly longer proportion of time after addition of alogliptin. The rationale for selecting alogliptin was based on its efficacy in reducing HbA1c, low risk of hypoglycemia, and suitability for the middle-aged individuals.

HbA1c is considered as a gold standard for monitoring glycemic control in DM; however, it has limited role in assessing short-term outcomes and day-to-day glucose fluctuations[2]. CGM devices can assess short term glycemic variability and may provide a broad spectrum of additional glucose management metrics, like TIR, TBR, TAR and glucose variability[2].

Growing clinical evidence indicates that significant glycemic variability, particularly when accompanied by hypoglycemia, can have a harmful effect on the onset and progression of diabetes complications[3]. Postprandial spikes in blood glucose, as well as hypoglycemic events are considered to be associated for increased CV events in DM. Therapeutic strategies can be directed towards minimizing glycemic variability for potential prevention of onset and progression future complications of diabetes[3].

DPP-4 inhibitors have the potential to improve glycemic control and to reduce glucose fluctuations, by increasing the active serum GLP-1 and GIP concentrations via glucose-dependent insulin secretion[5]. The glucose dependent glycemic control exerted by DPP-4 inhibitors also have potential to reduce risk of severe hypoglycemia in individuals with T2DM[5]. Alogliptin is frequently used in combination with metformin or other antidiabetic medications, including sulfonylureas and thiazolidinediones, to enhance glycemic control[6].

Studies demonstrate that alogliptin, administered alone or in combination with other agents, can significantly reduce HbA1c[6]. Alogliptin is generally well tolerated, with a low incidence of hypoglycemia and minimal impact on body weight[6].

Conclusion

The present case study demonstrates that, administration of add-on alogliptin to existing anti-diabetic drugs in T2DM individual decreased average blood glucose levels and also reduced wide glycemic fluctuations as observed from CGM data. There was improvement in proportion of time spent in target range (80–140 mg/dL) by 37% from initial 10% to 47% but still tight glycemic control was required and there was 40% reduction in percentage time spent above range. There was no documented symptomatic hypoglycaemia during the study period of six weeks. This data demonstrates that, alogliptin may be an important treatment modality to decrease daily glycemic fluctuations and HbA1c % in people with T2DM.

Limitations

This case study is based on retrospective, observational data that may not be generalizable to larger populations. CGM data, though comprehensive, lack contextual information on lifestyle factors (diet and exercise) that impact glucose levels. CGM was started immediately after addition of Alogliptin (no CGM data available before additional of Alogliptin). Short-term monitoring may also limit the ability to capture long-term trends. Further studies with larger sample sizes are warranted to assess the effects of alogliptin on GV in broader patient populations.

Abbreviations

CGM, Continuous Glucose Monitoring; CV, Cardiovascular; DM, Diabetes Mellitus; DPP-4, Dipeptidyl Peptidase-4; GV, Glycemic Variability; HbA1c, Glycated Hemoglobin; MACE, Major Adverse Cardiovascular Events; OADs, Oral Antidiabetic Drugs; SMBG, Self-Monitoring of Blood Glucose; T2DM, Type-2 Diabetes Mellitus; TAR, Time Above Range; TBR, Time Below Range; TIR, Time in Range.

Ethical approval and consent to participate

Written informed consent has been obtained from the patient(s) to publish this paper.

Conflict of Interest Statement

Dr. Abhijit Anil Trailokya and Mr. Avinash Talware are associated with pharmaceutical Industry.

Acknowledgments

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Authors' contributions

SE supervised and monitored the patient, conceptualized the case study, and also conducted data analysis. AAT and AT contributed to data analysis, prepared graphical representations, and drafted the manuscript. All authors were involved in manuscript writing, critical review, and final approval of the submitted version.

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