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Case Report

From chaos to control: A case study on the successful management of uncontrolled diabetes with insulin Glargine 300 U/mL

Dariya S S[1], Agarwal Deepak[2], Verma Snehlata[3]

[1.] *Senior Consultant Physician, S.M.S.Hospital Jaipur*
[2.] *S.R. Oncology, BMCRHC Jaipur*
[3.] *Associate Professor, LLRM Medical College Meerut UP*

ABSTRACT

Diabetes is a chronic disease that affects millions of people worldwide, with type 2 diabetes being the most common form. Despite advances in medical treatments, many patients with type 2 diabetes have still not achieved optimal glycemic control, which can lead to multiple complications. Insulin therapy is often necessary to achieve glycemic control in patients with diabetes, but often due to delay in treatment intensification or titration, which is also known as clinical/therapeutic inertia, leads to poor outcomes. This case report describes a 50-year-old female patient with uncontrolled type 2 diabetes and comorbid hypertension who was successfully treated with insulin Glargine 300 U/mL. Despite being on multiple antihyperglycemic medications, her HbA1c levels remained above 8% for the previous year. After initiating insulin therapy with glargine 300 U/mL and titrating the dose to achieve fasting blood glucose levels between 80-130 mg/dL, her self-measured plasma glucose levels improved significantly, and her HbA1c decreased to 7.5% at the 3-month follow-up. The patient reported no adverse events from insulin therapy, and her blood pressure, renal function, and urinary albumin to creatinine ratio remained within normal limits. The case highlights the potential benefits of insulin glargine 300 U/mL in achieving optimal glycemic control and improving comorbidities in patients with uncontrolled type 2 diabetes.

Keyword – Glycemic control; Hyperglycemia; Insulin glargine 300 U/mL; Type 2 diabetes; Uncontrolled diabetes mellitus

INTRODUCTION

Diabetes mellitus is a global health challenge with an estimated 451 million cases in 2017, projected to increase to 693 million by 2045. India has the highest number of individuals with diabetes in Southeast Asia, with an age-adjusted comparative prevalence of 9.8% and premature mortality of 50.7%. The epidemiological transition in India, along with aging, obesity, and hypertension, is driving the diabetes epidemic in both rural (5.2%) and urban (11.2%) areas. Indians have a distinct "thin-fat" phenotype, characterized by low lean body mass, high subcutaneous fat, and metabolic derangements that increase susceptibility to insulin resistance and type 2 diabetes. The early onset of type 2 diabetes in Indians increases the risk of developing microvascular and macrovascular complications. Unfortunately, diabetes is often diagnosed only after development of diabetic complications.[1]

Type 2 diabetes is a progressive disease that often requires exogenous insulin to maintain optimal glycemia. Insulin therapy is often necessary to maintain optimal glycemia in patients with type 2 diabetes, but delays in treatment intensification or titration, known as clinical/therapeutic inertia, are common. Retrospective cohort studies have shown that patients may experience delayed insulin intensification for at least 6 years, despite having high HbA1c levels. Lack of appropriate treatment intensification or improper titration is also evident in the US, where a significant proportion of people with diabetes who use insulin have high HbA1c levels. The main barriers to the initiation, intensification, and optimal titration of insulin therapy include fear of injections, burdensome regimens, fear of hypoglycemia, weight gain, and the perception that the need for insulin signals a failure of diabetes self-management. Addressing these barriers is crucial to promote prompt and persistent treatment intensification and prevent diabetes complications.[2]

In this case report, we have presented a patient with uncontrolled type 2 diabetes and comorbid hypertension who was successfully treated with insulin glargine 300 U/mL. Despite treatment with oral antihyperglycemic agents and lifestyle modifications, the patient's HbA1c levels remained above 8%, and their blood pressure was poorly controlled. After initiating insulin glargine 300 U/mL, the patient's HbA1c levels decreased to below 7% as well as her blood pressure was also better controlled. This case highlights the potential benefits of insulin glargine 300 U/mL in achieving optimal glycemic control and improving comorbidities in patients with uncontrolled type 2 diabetes.

*Corresponding author.
*E-mail id:*editor@accordedu.com

CASE PRESENTATION

A 50-year-old female with a 7-year history of type 2 diabetes, a teacher by profession employed as an educator, sought medical attention at a diabetes clinic due to suboptimal glycemic control despite receiving treatment with multiple antihyperglycemic medications. She reported engaging in daily physical activity and being a non-smoker. Her most recent laboratory results showed a current HbA1c of 8.8% (70 mmol/mol), with an HbA1c above 8% (64 mmol/mol) for the previous year; fasting blood glucose level of 202 mg/dL. Her blood pressure was 128/82 mmHg, and her estimated glomerular filtration rate (eGFR) was 92 ml/min/1.73 m^2. Her urine albumin to creatinine ratio (ACR) was normal.

In terms of her past medical history, she had previously tried a glucagon-like peptide 1 receptor agonist (GLP-1 RA) but stopped treatment due to gastrointestinal side effects. She had no established cardiovascular disease. Her mother had type 2 diabetes and died of myocardial infarction. Her current medication regimen included metformin (extended-release 1000 mg twice daily), a sodium-glucose co-transporter 2 (SGLT2) inhibitor (dapagliflozin 10 mg/day), sulfonylurea (glimepiride 4 mg/day), dipeptidyl peptidase 4 (DPP4) inhibitor (sitagliptin 100 mg once daily), two anti-hypertension medications (ramipril 10 mg once daily and amlodipine 10 mg once daily), and atorvastatin 40 mg once daily.

Currently, she had several concerns regarding starting insulin therapy despite her uncontrolled diabetes. She believed insulin injections would be inconvenient and difficult, especially since she works long hours and can't keep a regular schedule. Hypoglycemia was also a concern for her, as she had already experienced an event after initiating therapy with sulfonylurea. Additionally, she was worried about the potential self-care requirements and monitoring needed to ensure she can manage her diabetes while working as a teacher, which could impact her ability to effectively perform her job. Given her family history of cardiovascular disease, she was also concerned about the potential for weight gain associated with insulin therapy. All of these factors needed to be taken into consideration when deciding on the best treatment options for this patient.

Considering all above factors and to address her uncontrolled diabetes, insulin therapy was initiated, and the patient was started on second-generation basal insulin (BI) analog, insulin glargine 300 U/mL (Gla-300). She was instru cted to administer the insulin once daily, preferably at the same time every day, in the evening before bedtime. The insulin dosage was titrated every 3-4 days based on the fasting self-measured plasma glucose (SMPG) levels to achieve the target range of 80-130 mg/dL. After initiating insulin therapy with Gla-300 and titrating the dose to achieve fasting blood glucose levels between 80-130 mg/dL, her SMPG levels improved significantly. Over a period of 4 weeks, her pre-breakfast, post-breakfast, pre-lunch, post-lunch, pre-dinner, and 2 hours post-dinner SMPG levels decreased gradually, as shown in Table 1.

At her 3-month follow-up appointment, she reported no adverse effects from insulin therapy and her HbA1c had decreased to 7.5% (58 mmol/mol), indicating improved glycemic control. Her blood pressure, renal function, and urinary albumin to creatinine ratio remained within normal limits. She was advised to continue her current medication regimen, monitor her blood glucose levels regularly, and attend regular clinic appointments.

Hence we concluded that overall, insulin therapy with glargine 300 U/mL was effective in improving glycemic control and was well-tolerated with no reported adverse effects. Hence self-measured plasma glucose levels were helpful in monitoring the response to therapy as well as with guidance of dose titration.

QUESTIONS

1. What are the PK/PD profiles of second-generation basal insulin analogs compared to first-generation basal insulin analogs in terms of glycemic control and hypoglycemia risk?
2. How effective is Gla-300 in improving glycemic control and reducing hypoglycemia risk compared to other basal insulins (BI), especially in patients at high risk of hypoglycemia or requiring multiple daily doses of insulin?
3. What is the impact of Gla-300 on patient satisfaction, compliance, and persistence with insulin therapy compared to other basal insulins (BI)?
4. What are the barriers to initiating and titrating basal insulin (BI) therapy in type 2 diabetes, and how can second-generation basal insulin analogs, such as Gla-300, help to overcome these barriers and improve patient outcomes?

COMMENTARY

Type 2 diabetes is a chronic and progressive disease, characterized by impaired insulin secretion and action, leading to hyperglycemia. While lifestyle interventions and various oral antidiabetic medications can be effective in controlling blood glucose levels, many patients eventually require basal insulin therapy to maintain glycemic control. However, there are significant barriers to its prompt initiation and optimal titration, including patient fears of injections, hypoglycemia, weight gain, and burdensome regimens. Hypoglycemia is a major concern in diabetes management due to its associated morbidity and mortality. The fear of hypoglycemia can be a significant barrier

Table 1 : Blood glucose profile for 4 weeks

Week	Pre Breakfast (mg/dL)	2 hours Post Breakfast (mg/dL)	Pre Lunch (mg/dL)	2 Hours Post Lunch (mg/dL)	Pre-Dinner (mg/dL)	2 Hours Post Dinner (mg/dL)
1	163	204	148	198	176	215
2	153	189	141	182	170	204
3	140	175	131	166	160	193
4	131	163	122	155	152	182

to optimal glycemic control, and it can limit the willingness of patients to initiate and titrate insulin therapy. The development of second-generation BI analogs has been a significant advancement in the treatment of diabetes. These newer agents provide comparable glycemic control with lower risks of hypoglycemia compared to first-generation BI analogs, making them a viable option for patients who may be at higher risk of hypoglycemia.

Current guidelines recommend using BI analogs rather than neutral protamine Hagedorn insulin (NPH) due to the reduced risk of hypoglycemia. The ideal BI analogs should exhibit a pharmacokinetic and pharmacodynamic profile with minimal within-day variability and an extended duration of action, resulting in improved glycemic control with reduced potential for hypoglycemia between meals. Among BI analogs, second-generation BI analogs, including Gla-300 and insulin degludec (Ideg), demonstrate more stable and prolonged PK/PD profiles than Gla-100, which is associated with a lower risk of hypoglycemia. These BI analogs may be preferred for the management of diabetes to provide better glycemic control and minimize the risk of hypoglycemia, especially for patients with a high risk of hypoglycemia or who have previously experienced hypoglycemic events.[2]

In the EDITION 3 study, Gla-300 demonstrated comparable glycemic control with a lower risk of hypoglycemia than first-generation BI during the initial 8 weeks of therapy. The BRIGHT study showed similar HbA1c reductions and variability in 24-hour self-monitored plasma glucose between Gla-300 and insulin degludec (Ideg). However, during the insulin titration period, Gla-300 had lower rates of confirmed hypoglycemia than IDeg, which could increase people's confidence to properly self-titrate their insulin. Early glycemic control has been shown to provide improved long-term outcomes.[2]

The EDITION 4 trial compared the efficacy and safety of once-daily Gla-300 and Gla-100 in patients with T1DM while continuing mealtime insulin. Both groups had a similar reduction in HbA1c and FPG from baseline to 6 months. The rates of overall confirmed hypoglycemia were lower in the Gla-300 group than in the Gla-100 group, particularly during the night. The rate of severe hypoglycemia was low and similar between the two groups. There were no significant differences in insulin dose, weight change, or treatment satisfaction between the two groups. Participants in both groups reported similar levels of hypoglycemia fear and health-related quality of life. Overall, Gla-300 was well-tolerated and demonstrated similar efficacy and safety compared to Gla-100 in patients with T1DM.[3]

The case presented highlighted the challenges and considerations involved in managing type 2 diabetes in a patient with suboptimal glycemic control despite receiving multiple antihyperglycemic medications. The decision to initiate insulin therapy with Gla-300, a second-generation BI analog, was effective in improving the patient's glycemic control and was well-tolerated with no adverse effects reported.

In summary, Gla-300 offers several advantages over other basal insulins for individuals with type 1 or type 2 diabetes. It may be particularly beneficial for those at high risk of hypoglycemia, individuals who require multiple daily doses of insulin, and those who need flexibility in their insulin administration schedule. Gla-300 also requires a lower total dose volume than Gla-100, potentially causing less pain at the injection site. Additionally, Gla-300 is associated with lower weight gain, making it a valid option for managing diabetes when weight loss is a therapeutic objective. The advantages of Gla-300 over other basal insulins include its lower risk of hypoglycemia and potentially higher patient satisfaction, better compliance, and persistence with therapy.[3]

CONCLUSION

In conclusion, individuals with type 2 diabetes uncontrolled on oral hypoglycaemic agents require basal insulin to achieve and maintain adequate glycemic control. The second-generation BI analogs such as Gla-300, are viable options for those who need to intensify their antihyperglycemic regimens to meet personalized glycemic targets. These medications offer improved hypoglycemia profiles, dosing flexibility, and lower weight gain compared to older insulin formulations. Ultimately, the choice of basal insulin should be based on individual patient factors, including risk of hypoglycemia, comorbidities, and cost considerations.[2]

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