# Judicious Use of Modern Technology with Antihyperglycemic Agents: The Changing Landscape of Type 2 Diabetes Management

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## Abstract

**Background:** Continuous subcutaneous insulin infusion (CSII) pump has shown good outcomes in patients with both type 1 and type 2 diabetes mellitus. Here, we present an individual with type 2 diabetes and obesity who was on a high dosage of insulin and oral hypoglycemic agents (OHA) were able to get diabetes under good control with weight reduction after using a hybrid artificial closed-loop insulin pump system along with glucagon-like peptide 1 receptor agonist (GLP-1RA) and sodium-glucose co-transporter-2 (SGLT-2) inhibitor. **Case Presentation:** A 60-year-old lady with type 2 diabetes presented with uncontrolled blood sugars despite high doses of insulin and a combination of OHAs. She was also depressed and frustrated due to uncontrolled blood sugars despite repeated changes made in her treatment plan using an insulin pump along with GLP-1RA (dulaglutide) and SGLT-2 inhibitor (empagliflozin). **Results:** After changing the treatment plan, her HbA1c levels decreased from 10.1% to 7.3% after 3 months. The microalbuminuria reverted to normoalbuminuria (59.9–12.2 µg/mg of creatinine). Improvement has been observed in the fasting C-peptide levels from 0.50 to 0.86 pmol/L and stimulated C–C-peptide levels from 1.2 to 2.05 pmol/L. As she lost nearly 7 kg of weight, she felt satisfied with a better quality of life. Even her depression settled down. **Conclusion:** Use of CSII pump along with dulaglutide and empagliflozin helped in controlling blood sugars, bringing down weight with an overall improvement in mental health and renal function; in this, difficult to treat the patient.

**Keywords:** CSII pump, GLP-1RA, SGLT-2I, T2DM

## Introduction

India has the second-largest diabetic patient population. Current trends are alarming. As per the recent data from the Indian Council of Medical Research–India Diabetes study, there are 101 million people with diabetes along with 136 million people with prediabetes in India.[1] The number of people with obesity is also very high (254 million).[1] The twin epidemic of diabetes and obesity (Diabesity) makes it difficult for clinicians to manage hyperglycemia. With the increasing duration of diabetes, the beta cells tend to fail. This along with increased insulin resistance makes the treatment difficult. Antidiabetic agents like sulfonylurea, glinides, glitazones, and insulin tend to increase body weight. Glucagon-like peptide 1 receptor agonist (GLP-1RA) and sodium-glucose co-transporter-2 (SGLT-2) inhibitors have shown good weight loss, apart from good glycemic control.[2] CSII pumps have shown good outcomes in both type 1 and type 2 diabetic subjects.[3] Here, we present a case of an obese patient with uncontrolled diabetes, who was managed with the Medtronic MiniMed™ 780G CSII pump along with injectable GLP-1RA (dulaglutide) and SGLT-2 inhibitor (empagliflozin) (Medtronic, CA, USA).

**Received:** 05-Dec-2023, **Revised:** 08-Jan-2024, **Accepted:** 12-Jan-2024, **Published:** 18-Mar-2024

Access this article online

Quick Response Code:

Website: https://journals.lww.com/JODB

DOI: 10.4103/jod.jod_127_23

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**How to cite this article:** Srivastava BK, Anjana RM, Amutha A, Ramuu M, Sriraam M, Mohan V. Judicious use of modern technology with antihyperglycemic agents: The changing landscape of type 2 diabetes management. J Diabetol 2024;15:119-22.

## Case Presentation

The participant's consent was sought regarding her data use. A 60-year-old lady with type 2 diabetes with a duration of 14 years and obesity, presented with tiredness and uncontrolled blood sugars. Her height was 153 cm, weight was 87.4 kg, and her body mass index was 37.3 kg/m$^2$. She had a positive history of diabetes. Physical examination revealed a heart rate of 76 beats/min and blood pressure of 126/78 mm Hg. Examination of the cardiovascular, respiratory, and other systems were normal. She was being treated with a higher dosage of multiple daily dosages of insulin (basal-bolus regimen) injections (>100 units/day) along with sulfonylurea (gliclazide—160 mg), metformin (1 g), and dipeptidyl peptidase 4 inhibitors. She was on antihypertensive and lipid-lowering drugs also. Despite repeated adjustments in her insulin dosage, her blood sugar levels were persistently high as shown by her grossly elevated blood glucose and glycosylated hemoglobin (HbA1c) levels. She was also on treatment for depression.

Her fasting plasma glucose level was 164 mg/dL (9.11 mmol/L), and postprandial blood sugar was 225 mg/dl (12.5 mmol/L). Her HbA1c was 10.1%. The fasting C-peptide value was 0.5 pmol/L, and the stimulated value was 1.2 pmol/L showing that her beta cell function was poor. The hemogram was normal. The lipid profile showed elevated serum triglycerides. Liver function tests, blood urea, serum creatinine, and serum electrolytes were all within normal limits. Microalbuminuria level was positive (59.9 µg/mg of creatinine). Pancreatic enzymes were within normal range.

Considering her higher HbA1c levels and poor response to basal-bolus regimen along with oral hypoglycemic agents, a change in treatment plan was mandated. The recordings of her continuous glucose monitoring before the change of treatment are shown in Figure 1.

As can be seen, most of the glucose levels were above the target range. Because of poor C-peptide, higher HbA1c with a higher need for insulin dosage, the advantages of Medtronic MiniMed™ 780G CSII pump were explained to the patient and she accepted the same. In addition, GLP-1RA dulaglutide was given weekly once along with SGLT-2 inhibitors (empagliflozin) and metformin was continued.

## Results

The changed treatment plan resulted in favorable outcomes. Her blood glucose levels decreased. The daily insulin dose was reduced from 113 to 59 units. On continuous glucose monitoring, time in range (70–180 mg/dL improved significantly from 47% to 91%, and time above range (>180 mg/dL) reduced from 43% to 9%. The continuous glucose monitoring (CGM) after the change in the treatment is shown in Figure 2.

Her fasting plasma glucose decreased from 164 to 95 mg/dL and HbA1c levels from 10.1% to 7.3% after 3 months. The

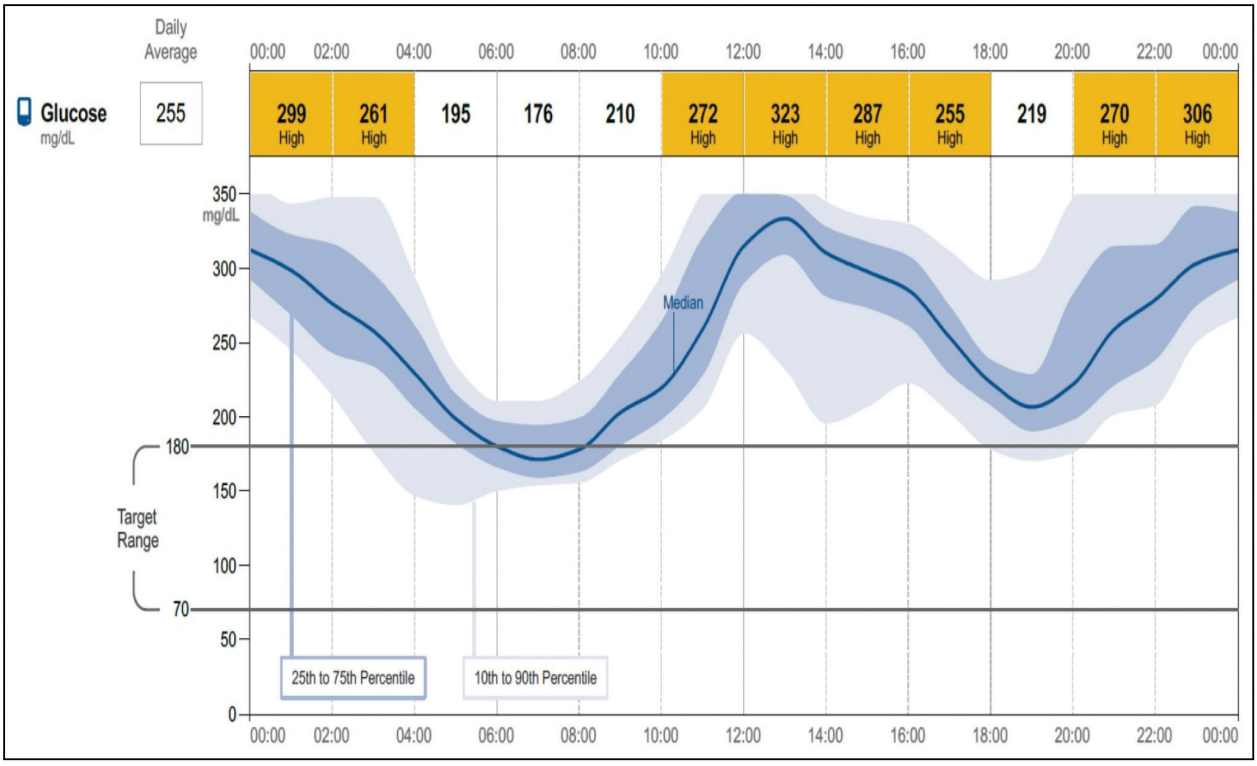


**Figure 1:** Recordings of continuous glucose monitoring

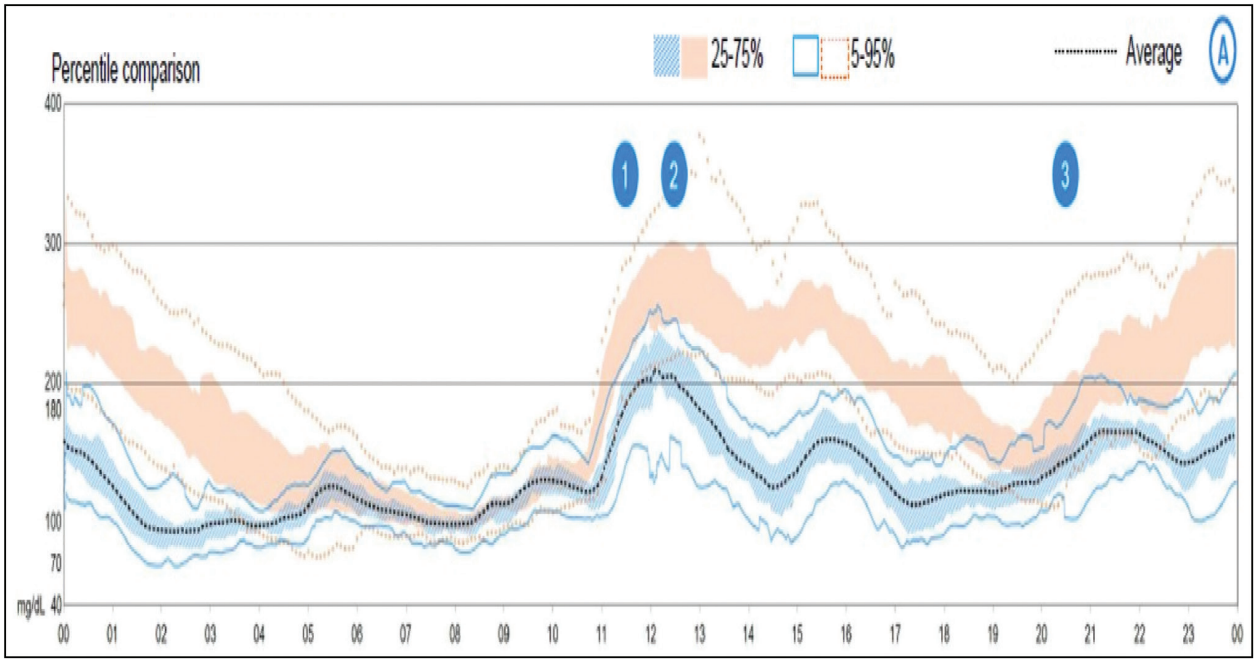


**Figure 2:** Improvement in continuous glucose monitoring with changed treatment plan

microalbuminuria reverted to normoalbuminuria (59.9–12.2 µg/mg of creatinine). There were also improvements in the fasting C-peptide levels from 0.5 to 0.86 pmol/L and stimulated C-peptide levels from 1.2 to 2.05 pmol/L. Within a year of follow-up, the daily need for insulin was further reduced to 33 units per day (nearly 70% reduction in dosage from the baseline). She also had a 7 kg weight loss (87.4–80.4 kg). Her depression also settled down.

The patient felt very much satisfied with her result and the current treatment. Most of the time, her sugars were in the acceptable range neither unacceptably high nor low as per her recent follow-up data. She felt the treatment was flexible and convenient, and it had helped her to understand her diabetes better.

## Discussion

Type 2 diabetes (T2DM) management in obese subjects gets complicated due to twin issues of impaired insulin secretion and insulin resistance. With the increasing duration of diabetes, the beta cell function gradually keeps on declining.[4,5] Diabetes being a chronic disorder, could also lead to reduced quality of life and as in this case to depression.

Weekly once, GLP-1RA dulaglutide has shown good glycemic control with weight loss in the Assessment of Weekly AdministRation of LY2189265 (dulaglutide) in Diabetes trials.[6] Researching Cardiovascular Events with a Weekly Incretin in Diabetes trial has shown that dulaglutide can be used for glycemic control in T2DM subjects with either previous cardiovascular disease or cardiovascular risk factors.[7]

The SGLT-2 inhibitor empagliflozin has shown a reduction in HbA1c and cardiovascular events in T2DM subjects.[8] Empagliflozin has also been shown to increase insulin sensitivity in insulin-resistant T2DM subjects.[9] We have also published on the beneficial effect of drugs like GLP-1RA and SGLT-2 inhibitors in combination on glycemic control with weight loss in Asian Indian T2DM subjects.[2]

CSII pumps are a beneficial tool in the management of glycemic control in type 1 and type 2 diabetic subjects. MiniMed™ 780G insulin pump is an Advanced hybrid closed-loop insulin pump system, which is an algorithm-based insulin delivery device with features of auto-correction of hyperglycemia and suspension if low blood sugars occur. It has shown better and smoother glycemic control with significant improvement of the time in range in various trials.[10] After initiation of MiniMed™ 780G insulin pump along with weekly once injection dulaglutide and SGLT-2 inhibitors, there was marked improvement in glycemic profile, C-peptide, body weight, and a better time in range. This improvement has resulted in a better quality of life for her and the depression also improved. The probable reasons for the improvement in the C-peptide levels could be due to a reduction in insulin resistance and alleviation of glucotoxicity.

## Conclusion

This study teaches us that while using insulin and oral hypoglycemic drugs for T2DM management, we must take into consideration the pathophysiology and try to correct insulin resistance as well as improve beta cell function. In this case, using an advanced insulin pump

along with drugs like GLP-1RA and SGLT-2 inhibitor helped to break the insulin resistance, reduce weight, and achieve good control of diabetes. Needless to say, all these are expensive tools but this patient was able to afford the treatment. Reducing the costs of these modern diabetes tools can help to improve diabetes control in a much larger number of people with uncontrolled diabetes both in India as well as in other countries.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

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