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AACE Clinical Case Reports

Case Report

Commercialized Hybrid Closed-Loop System (Minimed Medtronic 670G) Results During Pregnancy

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ABSTRACT

Objective: Hybrid closed-loop (HCL) devices can achieve tight glycemic control but are rarely used in pregnancy, which remains an off-label indication. We present a case of a pregnant patient with type 1 diabetes mellitus (T1DM) who used the Medtronic MiniMed 670G HCL system.
Methods: MiniMed 670G includes an advanced automode option (HCL therapy), which our patient used from the first trimester to the end of the pregnancy.
Results: An unplanned pregnancy was detected in the T1DM patient, with a glycated hemoglobin level of 8.7 mmol/L (7.1%). The patient started sensor-augmented pump therapy at week 13. Subsequently, she entered automode (HCL) at week 16. The time in range (3.7-7.8 mmol/mol, 63-140 mg/dL) increased from 46.8% to 51.3% after HCL initiation. The glycated hemoglobin level remained close to 48 mmol/mol (6.5%) until the end of the pregnancy. Furthermore, the time under range (<3.7 mmol/mol, <63 mg/dL) remained below the optimal 4% level during the gestation. Finally, a healthy male baby was born at week 37. No safety events were recorded.
Conclusion: This case represents the successful off-label use of HCL during pregnancy in a patient with T1DM.

Introduction

Recent advances in insulin delivery and real-time continuous glucose monitoring (RT-CGM) have made a particularly meaningful impact on the care of patients with type 1 diabetes mellitus (T1DM).[1] Closed-loop artificial pancreas systems have been under development for several years, and their use has consistently improved glucose control in outpatient settings.[2] The presence of preexisting T1DM in pregnancy increases the risk of adverse maternal and neonatal outcomes and often requires advanced technological treatment in order to achieve tight glycemic control.[3] The use of closed-loop automated insulin delivery systems has suggested an improvement of glycemic control in pregnant woman with T1DM in investigational trials. Despite study design limitations, such as small number of patients and crossover designs, some benefits over time in the range and reduction of hypoglycemia have been described.[4,5] Automated insulin delivery system development

includes diverse smart algorithms to calculate the necessary amount of insulin according to the RT-CGM values. Medtronic MiniMed 670G (MM670G) was the first commercialized hybrid closed-loop (HCL) system. It is considered an HCL system because it only automates basal insulin delivery. The MM670G "auto mode" normally uses a target of 6.7 mmol/L (120 mg/dL) to adjust the insulin delivery every 5 minutes in response to the RT-CGM readings, although an optional target of 8.3 mmol/L (150 mg/dL) can be set. Users must still manually deliver bolus doses to cover meals or correct for residual hyperglycemia.[6] MM670G has not been formally studied in pregnancy. Until now, only a small series of 3 pregnant patients with T1DM have been reported to be treated with commercialized HCL systems.[7] In fact, MM670G has not been approved for use during gestation.

Case Report

We present a case of a 36-year-old primiparous woman diagnosed with T1DM at the age of 9 years who suffered from no chronic complications of diabetes. Associated comorbidities included autoimmune primary hypothyroidism, celiac disease, and prothrombin gene heterozygous mutation. She was treated with insulin detemir at 0.6 UI/kg/day and insulin aspart at 0.5 UI/kg/day when she became pregnant in autumn 2018. This unplanned

Table
Real-Time Continuous Glucose Monitoring Evolution

	16 wks (before auto mode)	20 wks	28 wks	32 wks	36 wks
RT-CGM adherence, % of time	96	93	91	97	95
Automode adherence, % of time	0	96	95	96	98
MIG, mmol/mol (mg/dL)	7.6 (137)	7.7 (139)	7.4 (133)	7.5 (135)	8.0 (144)
CV, %	38	31	31	30	24
TAR, %	50.2	47.6	47.6	46.5	35.1
TIR, %	46.8	51.3	50.3	52.8	63.5
TUR, %	3.0	1.1	2.1	0.7	1.4

Abbreviations: RT-CGM = real-time continuous glucose monitoring; MIG = mean interstitial glucose; CV = MIG coefficient of variation; TAR = time above range (>7.8 mmol/mol, >140 mg/dL); TIR = time in range (3.7-7.8 mmol/mol, 63-140 mg/dL); TUR = time under range (<3.7 mmol/mol, <63 mg/dL).
The table shows the improvement of glycemic control measured using RT-CGM based on the initiation of the Minimed Medtronic 670G device until the end of pregnancy.

pregnancy coincided with a glycated hemoglobin (HbA1c) level of 8.7 mmol/L (7.1%). She was using a self-financed flash glucose monitoring system (FreeStyle Libre) and spent 20% of the time at <3.9 mmol/L (70 mg/dL) and 5% at <3.0 mmol/L (54 mg/dL) in sensor readings.

After explaining the involved risks and benefits to the patient, an off-label indication for HCL MM670G used during pregnancy was settled. The patient signed properly informed consent and started using the MM670G system at the 13th week of gestation with the goal of improving the glycemic control and reducing the time spent in hypoglycemia. Subsequently, the "auto mode" was activated at the 16th week of gestation when her HbA1c level was 52 mmol/mol (6.9%). Predictive suspend was set before a low glucose limit of 3.3 mmol/L (60 mg/dL) was reached. During the second and third trimesters of the pregnancy, she achieved better glycemic control, with the HbA1c levels at 46 mmol/mol (6.4%), 49 mmol/mol (6.6%), 45 mmol/mol (6.3%), and 49 mmol/mol (6.6%) at weeks 20, 28, 32, and 36, respectively. RT-CGM data evolution during pregnancy according to the International Consensus on Time in Range (TIR) can be seen in Table.[8] After auto mode initiation, TIR (3.7-7.8 mmol/mol, 63-140 mg/dL) increased by 4.5% and time under range (TUR) decreased by 1.9%. The glucose control remained stable during the second and third trimesters. Moreover, with the use of the HCL function, the patient achieved an optimal TUR of <4% until the end of the pregnancy. The patient did not use the optional RT-CGM target of 8.3 mmol/L (150 mg/dL) during her pregnancy. Severe hypoglycemia or diabetes ketoacidosis events were not detected.

At week 37 + 4, she was admitted to a hospital because of a scheduled end of the pregnancy. The patient continued the use of the closed-loop system to control her diabetes after admission. She underwent an epidural anesthesia procedure, induction with prostaglandins and oxytocin, and a low-transverse cesarean section because of lack of labor progression. Finally, a healthy male baby was born; his weight was 3920 g (large-for-gestational age), and Apgar scores at 1 and 5 minutes were 8/10 and 9/10, respectively. He presented with 1 hypoglycemia episode (50 mg/dL), which was treated with oral glucose. The patient decided not to continue with the MM670G treatment after the cesarean section and returned to multiple daily insulin injections. Breastfeeding was started and maintained without complications.

Discussion

We present the case of a female patient with T1DM using an off-label HCL system during pregnancy, with excellent glycemic and obstetrical results. To our knowledge, only a small case series has been previously reported on the use of a commercial HCL artificial pancreas during pregnancy.[7] The use of closed-loop insulin delivery systems to control T1DM during pregnancy has been previously reported.[4,5,7,8] Stewart et al[4] and Stewart et al[5] from the University of Cambridge (United Kingdom) have described the use of an HCL artificial pancreas

(Florence D2A) in which the automated insulin delivery was calculated using an algorithm to achieve an RT-CGM target of 5.8 to 7.3 mmol/L (104-131 mg/dL), allowing stable glycemic control. The use of this system was associated with comparable glucose control and significantly less hypoglycemia than sensor-augmented pump therapy. Here, we used MM670G, which uses a target of 6.7 mmol/L (120 mg/dL), an average glucose value that correlates with an estimated HbA1c level of 40 mmol/mol (5.8%). The United Kingdom National Institute for Health and Care Excellence guidance and American Diabetes Association recommend a target HbA1c level of 42 to 48 mmol/mol (6.0%-6.5%) or <53 mmol/mol (7%) in patients who are susceptible to hypoglycemia.[9] A small published case series has reported 3 pregnancies in patients with T1DM using MM670G. Only 1 of them corresponded to the initiation of a MM670G device during pregnancy (18 weeks). The other 2 cases were unplanned pregnancies in patients using MM670G before their gestations. Improvement of glycemic control was detected until the end of the 3 pregnancies. Our patient remained close to an HbA1c level of 47 mmol/mol (6.5%), with a clinically significant reduction in the time in hypoglycemia (20% before MM670G 20% vs 1.5% with MM670G). Automated insulin delivery adjusted in response to the RT-CGM readings can explain these results and their superiority to achieve better glycemic control (an additional 5% in TIR) in adult patients compared with conventional sensor-augmented pumps.[10] Unfortunately, we were not able to compare our international consensus on TIR-adjusted data to previously reported small series in which the authors could not change CareLink Clinical Software standard reports. Finally, MM670G in auto mode does not allow, by definition, to achieve tight glycemic control during pregnancy because of its fixed glycemic target (ie, 120 mg/dL). Hence, well-validated pregnancy glycemic targets may not be obtained through this HCL system. Moreover, data from randomized controlled trials validating the use of HCL systems during pregnancy are not yet available. However, in our individual case, MM670G proved to be useful in achieving better glycemic control, especially in the reduction of TUR.

Conclusion

As the use of HCL insulin delivery models (MM670G, T Slim X2 with Control-IQ) is increasing, and new automated insulin delivery systems, such as MM780G, have been recently introduced, the artificial pancreas will be more frequently present in gestational scenarios. Future HCL systems with adjustable targets may prove to be more useful in pregnancy. More studies, particularly randomized controlled trials, are needed in order to determine the efficacy and safety of HCL systems during pregnancy.

Disclosure

The authors have no multiplicity of interest to disclose.

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