



Brief Report

Switching to insulin lispro U-200 in a pregnant woman using a 780G advanced hybrid closed-loop led to a rapid improvement in glucose metrics

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ABSTRACT

Maintaining tight glucose levels during pregnancy is crucial and challenging. We describe a pregnant woman with type 1 diabetes and obesity, treated with an advanced hybrid closed-loop MiniMed 780G since pre-pregnancy, who displayed a sustained improvement in her glucometrics after switching to lispro U-200.

Maintaining tight glucose levels during pregnancy is crucial for women with pre-existing diabetes to reduce adverse outcomes [1] in the context of changing insulin requirements [2]. Diabetes technology has proven beneficial in this respect. The CONCEPTT trial showed improved glycemic control and pregnancy outcomes with use of real-time continuous glucose monitoring [3] and advanced hybrid closed-loop (AHCL) systems have demonstrated to be safe and effective during pregnancy [4,5,6,7]. Still, none of current therapies provide the glycemic regulation required to achieve the Saint Vincent Declaration aspiration for no diabetes unwarranted effects.

Concentrated insulins are available commercially with the aim to reduce injection volume and number in patients with high insulin requirements [8]. While generally concentrated insulins are not approved for pumps, there are reports of patients with insulin resistance displaying improved glycemic regulation after switching to U-200 or U-500 in pumps [9,10]. There are also limited reports of pregnant women with type 2 diabetes using U-500 in pumps [11,12].

We present a woman with type 1 diabetes (T1DM), treated with the AHCL Medtronic 780G® pre-pregnancy, who experienced worsening glucose levels in the 2nd trimester that improved and maintained after switching to lispro U-200. Written consent was provided. She was 43 years old, diagnosed at 3 years of age, had a diabetic ketoacidosis at 12 years and a severe hypoglycemia at 34 years while on treatment with labetalol [13]. G5P1041. She had background diabetic retinopathy, chronic hypertension, dyslipidemia and obesity (pre-pregnancy body mass index (BMI) of 46.5 kg/m²). During her first pregnancy she was

treated with multiple daily injections. She aimed for a second child, initiated treatment with sensor-augmented pump in 2017, and in 2021 started AHCL Medtronic MM780G™ with fast aspart insulin (FiAsp). When she became pregnant, she opted to continue with the system after discussing the lack of data in pregnancy, at that time. Additional treatment included metformin, alpha-methyl-dopa, and folic acid initiated pre-pregnancy.

Pump was programmed with the optimal settings of 5.5 mmol/l (100 mg/dl) glucose target and 2:00 h active insulin duration. On the last month pre-pregnancy, hemoglobin A1c (HbA1c) was 6.7 % (50 mmol/mol), total daily insulin dose (TDID) 46.9 IU (0.43 IU/kg/d) and time in range (TIR, 3.9–7.8 mmol/l (70–140 mg/dl)) 69 %. At 11 weeks' gestation HbA1c was 6.3 % (45 mmol/mol). Glucometrics were on target during the first trimester (average glucose 6.8 mmol/l (122 mg/dl), 73 % TIR for pregnancy target (TIRp 3.5–7.8 mmol/l (63–140 mg/dl), 1 % time below range for pregnancy target (TBRp) and began to deteriorate despite frequent adjustments.

At 17 weeks of gestation, insulin was switched to off-label lispro U-200 (TDID before switch 70.1 IU). Active insulin duration was increased to 3:30 h and all pump settings modified to those equivalent to U-100 (Supplementary Table 1), without additional modifications. Changes in glucose profile were observed immediately, especially at night. Compared to 2 weeks before, 2 weeks after switch, average glucose decreased 0.78 mmol/l (14 mg/dl) and TIRp increased by 10 % (Fig. 1). For the 4 am–8 am period, median glucose decreased from 6.1 to 5.4 mmol/l (112 to 94 mg/dl) ($p < 0.01$). Remarkably, TDID increased by

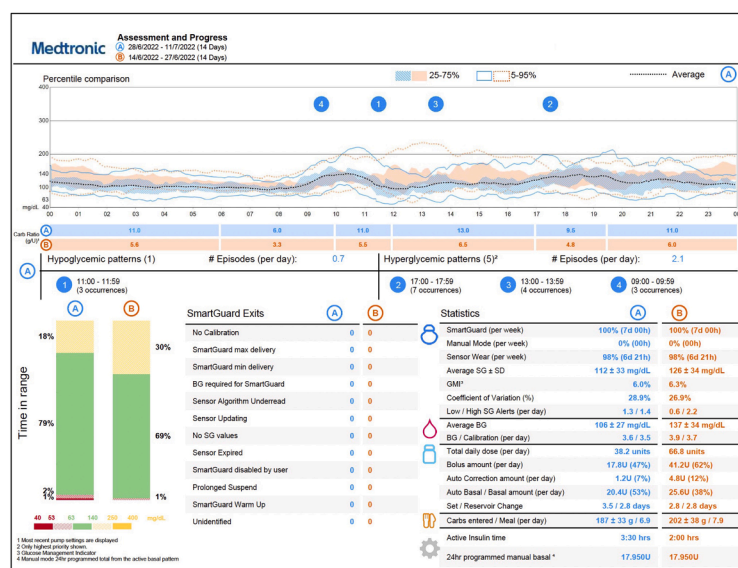
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Doses shown in the figure are for U-200.
 U-100 doses will be **twice** as high.



Fig. 1. Comparison of glucose and insulin metrics 2 weeks before and after switch to U-200 (A). Daily profile 3 days before and after switch to U-200 (B). Footnote: *The switch is indicated by the blue arrow.

14 % in the second period, mainly due to basal dose while correction boluses decreased (Fig. 1). Active insulin duration was progressively decreased to 2:00 h at 26 weeks.

The patient remained in target ($TIR_p > 70\%$) until delivery. TIRp progressively increased throughout pregnancy, without significant increase in TBRp (Supplemental figures S1 and S2). TDID before delivery was 49.3 U-200 units (98.6 IU). Assisted carbs were not required at meals and used occasionally to push for corrections (Supplemental figure S3).

At 37 + 1 weeks she underwent a C-section and delivered a healthy girl weighing 3680 gr (98 centile). No neonatal complications occurred.

Postpartum insulin dose was calculated as 60 % of the pre-pregnancy TDID, considering the U-200 conversion. Glucose target remained unchanged and insulin duration was set at 4 h. The patient switch back to insulin U-100 after hospital discharge.

To our knowledge this is the first detailed report of U-200 use in an AHCL system in pregnancy. U-200 lispro was chosen because it was the only concentrated short-acting insulin analog available in Spain at the time. It is considered a U-100 bioequivalent [14], recommended for patients requiring meal boluses > 20 units [15]. While most available evidence on U-200 insulin comes from studies in type 2 diabetes, its use in a pump has been reported in a patient with T1DM and marked insulin resistance [10], who displayed improvements in glycemic regulation following the switch.

In the CRISTAL trial, evaluating the use of MiniMed 780G [5] in pregnancy overall TIRp did not improve in the intervention arm, but TBR and nocturnal glucometrics did. No unanticipated safety events were observed and the authors concluded that system is safe for pregnancy use.

In this report of a woman with pre-pregnancy obesity and high insulin requirements for a 780G system, glucometrics started to worsen during the second trimester. The switch to insulin U-200 allowed to lower carb/insulin ratios with no issues with safe insulin boluses. Longer insulin duration could be expected with U-500 insulin [16], but to a

much lower extent with U-200 [15]. Nevertheless, apparent duration of U-200 lispro was longer than that of FiAsp (improved nocturnal glucose with a 3.5 h active insulin duration for U-200 lispro vs. that for FiAsp with 2.0 h active insulin duration), and this allowed for more intense algorithm adjustments.

This is a case report and cannot establish safety. U-200 use in the MiniMed 780G AHCL is off-label. Therefore, it should be limited to well-trained health providers and consenting experienced users, as in this case. AHCL algorithms vary, so our observations may only apply for the 780G. However, this experience can be basis for further studies and algorithm development to improve glucose regulation in patients with high insulin requirements.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: L. M reports receiving non-financial support for travel from Ypsomed and Medtronic. R.C reports receiving non-financial support for travel from Ypsomed, Medtronic, Roche and Novalab, and research support from Ypsomed and Medtronic. O.C and V.S are Medtronic employees.

Appendix A. Supplementary material

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.diabres.2025.112047>.

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