Use of Lispro Insulin Diluted with Normal Saline to 10 U/ml in an Insulin Pump: Case Report

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In very young children with type 1 diabetes mellitus (T1DM), insulin dose is often below 5–10 U/day, which necessitates infusion of volumes lower than 0.05–0.1 ml/day of 100 U/ml insulin. Some children require as little as 0.2–0.3 U of bolus insulin (0.002–0.003 ml of 100 U/ml) to cover 10 g of meal carbohydrates. These factors pose a challenge for precise and stable continuous subcutaneous insulin delivery as well as for occlusion alarm triggering in insulin pumps. As T1DM diagnosis is made at an increasingly younger age, the problem of low dose delivery may concern more and more patients.[1] Lispro insulin diluted with a dedicated diluent has been used in neonates or young children on pump therapy.[2–4] We present our first experience with 10 U/ml lispro diluted in normal saline used in an insulin pump.

A 2.5-year-old boy with a 12-month history of T1DM had been on pump therapy since diagnosis [Paradigm 722®, Quick-set® 6 mm, Medtronic MiniMed, Northridge, CA; aspart (NovoRapid®, Novo Nordisk A/S, Bagsvaerd, Denmark) followed by lispro (Humalog®, Eli Lilly Nederland B.V., Houten, The Netherlands)]. He was a poor eater, and his weight and height were <3rd percentile for age and sex. His glycated hemoglobin A1c (HbA1c) levels were 6.4–6.7%; however, removal of air bubbles from the tubing was necessary several times per week, cannula occlusions were frequent, and technical problems made it difficult to use the infusion sets for more than 2 days. Blood glucose (BG) fluctuations were high (mean ± standard deviation, 173 ± 92.6 mg/dl; 10–17 BG measurements per day). Insulin dose equaled ~4.0–6.5 U/day (0.41–0.62 U/kg/day), with ~18–25% given as a basal rate (most 0.05 U/h, selected hours 0.00 U/h). Steel infusion sets were tried without improvement. In addition to dedicated insulin diluents not being readily accessible, the patient's bilirubin and biliary acids were temporarily elevated, which potentially could make him more vulnerable to preservatives (i.e., metacresol/phenol). Therefore, we decided to try insulin diluted in normal saline. The Local Ethics Committee approved this modification of therapy, and the parents signed informed consent.

After detailed instructions were given concerning insulin dilution and pump settings (settings 10 times higher than actual insulin doses), the parents started to use 10 U/ml dilution of lispro in normal saline on an outpatient basis. Infusion sets were changed, and a new 10 U/ml lispro dilution was prepared every 3 days.

During the first days of 10 U/ml lispro therapy, technical problems with insulin delivery subsided and BG levels became lower and more predictable (average BG, 138 ± 70.8 mg/dl; 13–14 measurements per day; **Figure 1**).

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Abbreviations: (BG) blood glucose, (HbA1c) glycated hemoglobin A1c, (T1DM) type 1 diabetes mellitus

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Throughout the 20-month-long follow-up, tubing/cannula occlusion was suspected only three times. One episode of severe hypoglycemia necessitating glucagon injection occurred (BG 22 mg/dl), manifesting in impaired consciousness for 2–3 min, without seizures. His HbA1c levels equaled 6.3–6.9% during the first 15 months but increased to 7.3–7.5% during the last 5 months of follow-up (when respiratory tract infections recurred). Insulin dose on 10 U/ml lispro equaled from 4.6 to 2.8 U/day (0.37–0.20 U/kg/day), with percentage of basal rate ~35–55%, depending on infections and appetite. The boy is still an unpredictable, extremely poor eater, which unfavorably affects his glucose control, but he has developed well and has caught up in weight (at 3rd percentile) and height (at 10th percentile). Bilirubin and biliary acids decreased to normal. As technical problems with insulin delivery were definitely minimized, the parents are satisfied with this modification of insulin therapy, and they opposed a switch back to 100 U/ml.

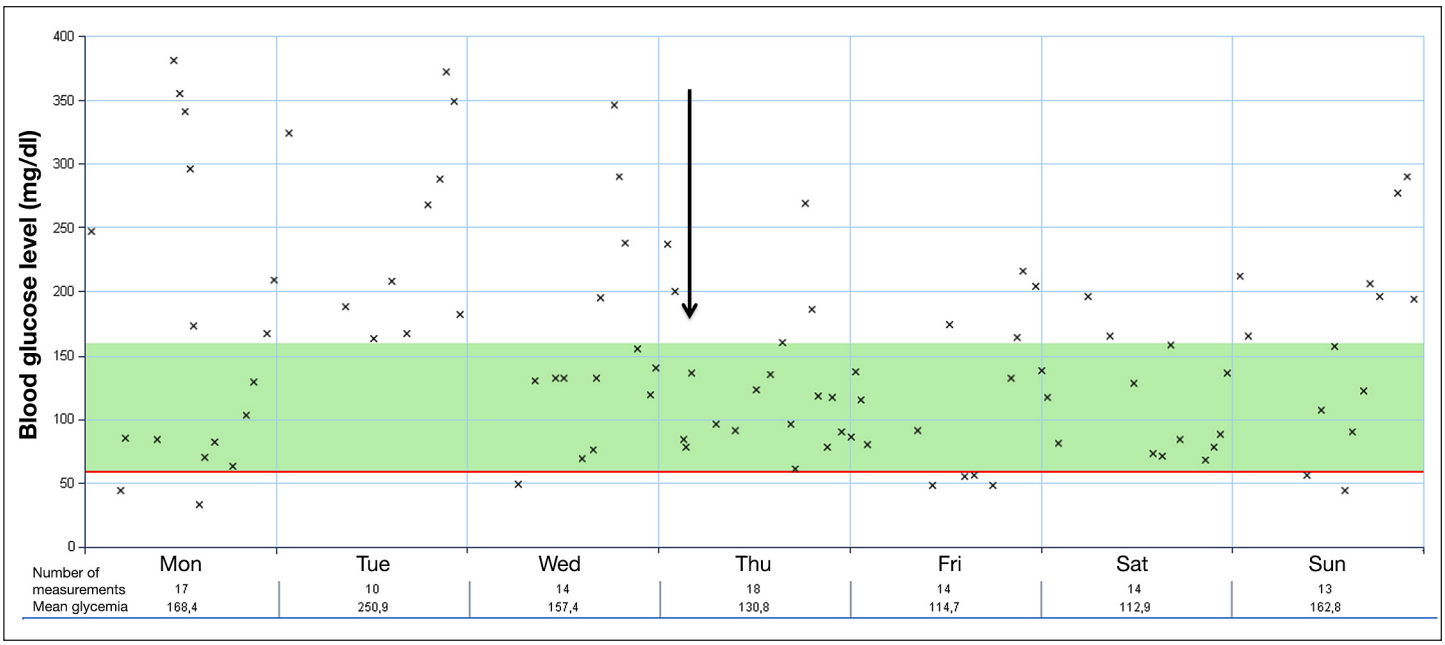

Figure 1. Blood glucose levels recorded in the patient's BG meter during the week of switch from 100 U/ml lispro to 10 U/ml lispro in the insulin pump (the arrow shows the time of the switch).

Despite this case report being rather anecdotic, this revealed important clinical implications. We suggest that the 10 U/ml dilution of lispro in an insulin pump may help to overcome technical problems with continuous insulin delivery, and this treatment seemed to be safe in our reported child who required a very low insulin dose. Strict parental cooperation and careful supervision of the child is crucial during such therapy. Insulin pump software allowing setting actual doses for diluted insulin could facilitate its use in young children. Insulin dilution could be considered in the development of "closed-loop" insulin delivery systems for the youngest age group. Further studies and input from insulin manufacturers are needed to draw final conclusions.

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