

Case Study: Experience in Insulin Pump Therapy During the Neonatal Period

Jahanara Begum-Hasan, MD, PhD, FAAP, Aisha A.K. Bruce, MD, and JoAnn Koster, RN, CDE, CPT

PRESENTATION

T.C., a 4-day-old baby girl born at 36 weeks, was brought to the emergency department with a history of poor feeding and lethargy. She was small for gestational age, with a birth weight of 4.6 lb. The pregnancy was complicated with oligohydroamnios.

On examination, she appeared emaciated and dehydrated, with sunken eyes and depressed anterior fontanelle. Her capillary refill was 4 seconds, and she weighed 4 lb. Her laboratory tests results were significant for elevated blood glucose at 765 mg/dl, and she was diagnosed with neonatal diabetes.

T.C. was admitted to the pediatric intensive care unit for the initial management of diabetes with intravenous (IV) insulin infusion (0.01–0.05 units/kg of body weight/hour). After 6 days on IV insulin, she was switched to subcutaneous (SC) insulin injection therapy with NPH and aspart insulin, 2–3 times a day. The insulin doses were titrated frequently to control blood glucose levels (0.5–1 units/kg/day). Because of wide excursions of blood glucose levels with one episode of severe hypoglycemia, her NPH was changed to ultralente insulin. T.C.'s blood glucose remained difficult to manage with SC insulin injections. She required IV insulin infusion again to stabilize her glucose levels.

QUESTIONS

1. What is the best way to optimize diabetes management for an infant

with difficult-to-control neonatal diabetes?

2. What considerations are necessary to develop a safe discharge plan for such a patient?

COMMENTARY

Initiating CSII

To better control her blood glucose levels, physicians treating T.C. considered initiating insulin pump therapy. After parental consent was obtained and diabetes education was provided, continuous subcutaneous insulin infusion (CSII) therapy was started via an insulin pump (Medtronic 512) on day 27 of T.C.'s

life. She was started with an initial basal infusion rate of 0.05 units/hour using lispro insulin in 10x dilution (Humalog U10/ml, Eli Lilly and Co.). For a consistent feeding regimen (every 2–3 hours), four to six basal rates were used without any mealtime boluses. The target blood glucose was set for premeal (108–144 mg/dl) and postmeal (162–216 mg/dl). The pump was tucked in a slipper attached to the outside of the infant's diaper.

The pump insertion site (thighs) was changed every 3–4 days. T.C. was discharged home after 7 days of insulin pump therapy with the following basal rates: midnight, 0.04

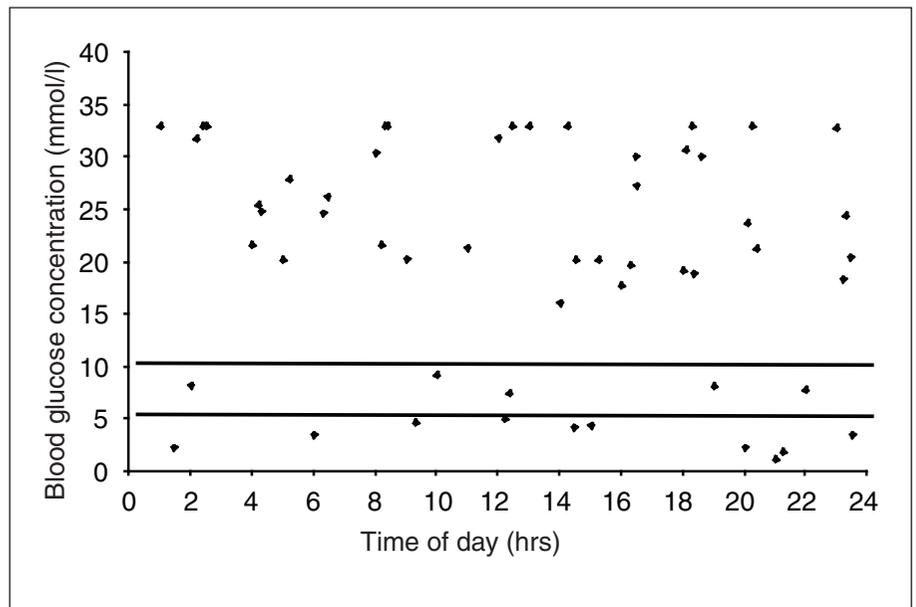


Figure 1. Glycemic pattern on SC insulin injection therapy with NPH (or ultralente) and aspart. Blood glucose levels varied widely, ranging from 1.3 to 35 mmol/l (23.4–630 mg/dl) with most of the readings in the high teens (16.6–22.2 mmol/l; 300–400 mg/dl).

units/hour; 3:00 a.m., 0.055 units/hour; 6:00 a.m., 0.065 units/hour; noon, 0.045 units/hour; 4:00 p.m. 0.05 units/hour; and 8:00 p.m., 0.06 units/hour. The total dose of insulin was 0.7 units/kg/day.

T.C. was followed monthly at the outpatient clinic with telephone contacts between visits. CSII was continued until she reached the age of 4 months, when her transient diabetes resolved.

CSII results

T.C.'s initial high blood glucose levels at diagnosis gradually normalized (90–144 mg/dl) with IV insulin infusion. With SC injections (NPH and aspart or ultralente and aspart), her blood glucose levels varied widely (23.4–630 mg/dl), with most of the readings in the high 300 mg/dl range (Figure 1) During the first week of CSII therapy (day 27 to day 34 of T.C.'s life), her blood glucose levels ranged from 54 to 360 mg/dl, with 40% of the readings within the target range (90–144 mg/dl) (Figure 2a). However, after initial stabilization on CSII, her blood glucose variability decreased significantly, with 90% of the readings within the target range. Figure 2b shows a sample of blood glucose data when T.C. was 2 months old and still using the pump. On CSII, the frequency of hypoglycemia (< 54 mg/dl) and hyperglycemia (> 200 mg/dl) was decreased to < 10%, as observed in Figure 2b. No severe hypoglycemia (< 36 mg/dl) was documented or reported by the mother while T.C. was on CSII.

The frequency of blood glucose monitoring decreased from 8 to 12 times per day on SC insulin injection therapy to 4–6 times per day on CSII therapy. No adverse effects, including soiling of the pump with feces or urine, were reported. With the replacement of two to three SC insulin injections daily by one catheter insertion every 3–4 days on CSII, the

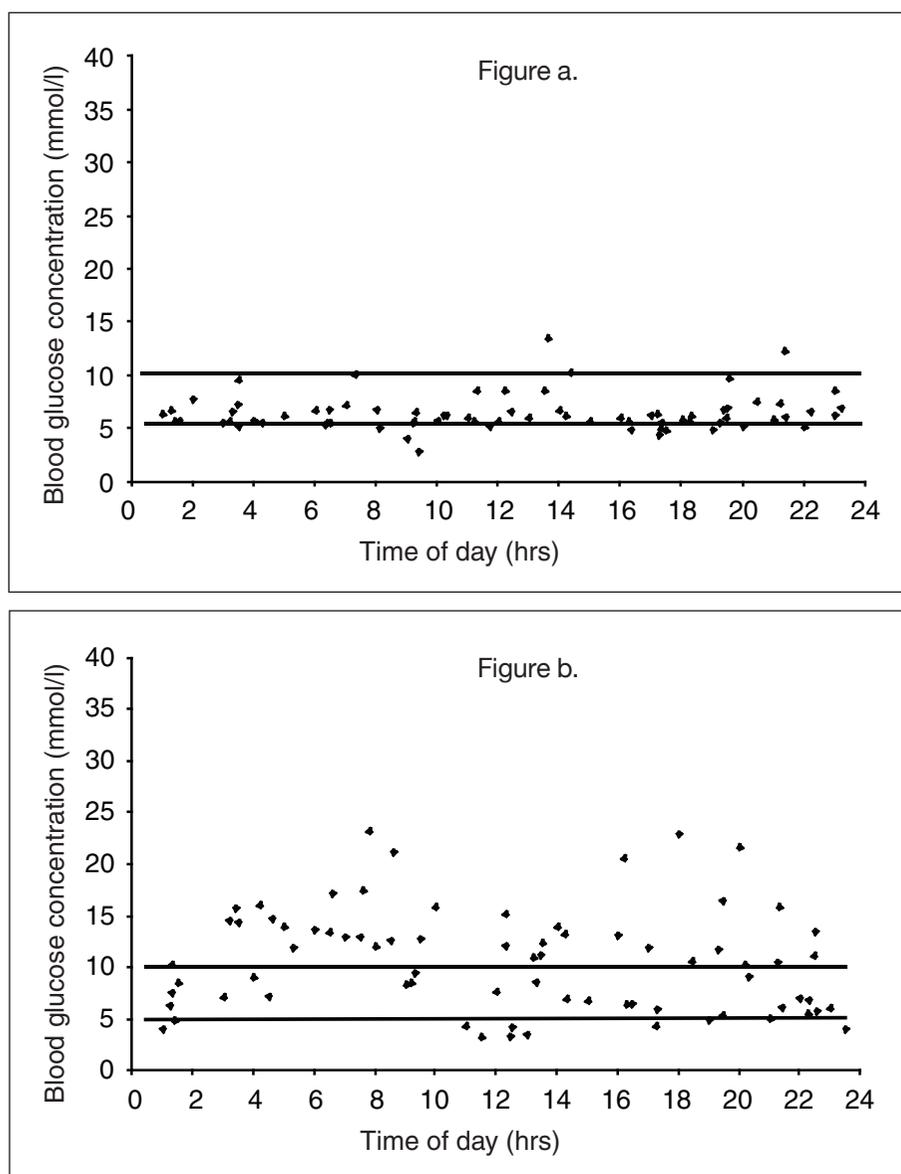


Figure 2. Glycemic pattern on CSII therapy during initial period (day 27 to day 34) of pump initiation (a) and at the age of 2 months after initial stabilization (b). The Y axis represents the range of blood glucose 0–40 mmol/l (0–720 mg/dl).

parents reported a greater level of satisfaction in their child's diabetes management.

Initial blood samples were negative for serum ketones and for autoimmune markers of type 1 diabetes. Cytogenetic analysis identified a duplication of chromosome 6 consistent with a known cause of transient neonatal diabetes. T.C.'s initial A1C was at 3% and remained within the reference range at 4

months of age (5.9%). The level of serum C-peptide was low at diagnosis (< 166 pmol/l) but increased (560 pmol/l) at 4 months.

Further discussion

In this case, we describe a case of transient neonatal diabetes in which insulin pump therapy was used efficiently during the neonatal period. To our knowledge, this case is the second-youngest baby reported in the

literature who was treated successfully with insulin pump therapy.

The difficulty of diabetes management in young infants is well known.¹ In our patient, after initial stabilization on CSII, blood glucose levels demonstrated less variability and eventually approached the target range without any significant hypoglycemia or hyperglycemia.

A number of studies have also demonstrated the safety and efficacy of CSII in children with type 1 diabetes.²⁻⁴ None of these studies included children younger than 1 year of age.

To date, CSII therapy has been used sporadically in neonatal diabetes. This issue is likely exacerbated by the infrequency of the disease. One such case study describes an infant with permanent neonatal diabetes with a Kir6.2 mutation,⁵ who was treated effectively with CSII therapy from age 4 months to 9 months, when the therapy was switched to glybenclamide.⁶

Recently, Bharucha et al.¹ reported their experience with the use of CSII in two cases of neonatal diabetes; insulin pump therapy had been started on day 43 in one case and on day 30 in the other. Consistent with our experience, the traditional approach of SC insulin injection therapy with NPH or ultralente and a rapid-acting insulin analog failed to control glycemic excursions. Transition to CSII provided better glucose control and made diabetes management easier.

We believe that the single-source of carbohydrate during early infancy made glycemic control with only basal rates easier and simpler for the parents than attempting to provide mealtime boluses. Specific instructions were given to disconnect or suspend the pump and contact the physician when the baby's blood glucose was < 72 mg/dl. The treatment of hypoglycemia with glucose

water or formula was recommended, and the parents were taught how to administer a glucagon injection in case of a hypoglycemic emergency.

However, the use of diluted insulin helped us titrate the basal rate to as low as 0.01–0.03 units/hour, particularly during the period of weaning from insulin pump therapy.

Pump insertion in this young infant with limited subcutaneous fat was a great challenge. In addition, with 6–8 wet diaper changes per day, there was potential risk of site infection. However, with careful site change, we did not encounter such problems. In our experience, the upper outer part of the thigh provided a suitable area for pump insertion.

Early discharge from the hospital would not have been possible without CSII because of T.C.'s wide blood glucose fluctuations on SC insulin injection therapy. With CSII, we reached our therapeutic goal of providing T.C.'s parents a means to manage their infant's diabetes in a comfortable and safe environment and to promote growth of the infant. In the absence of current guidelines, we believe our experience in the management of diabetes by insulin pump therapy in a neonate will be a helpful addition to this limited literature.

CLINICAL PEARLS

Guidelines on CSII during the neonatal period are lacking. We have described our experience of insulin pump therapy in a 27-day-old neonate with transient neonatal diabetes. Our patient is the second youngest among the infants reported in the literature with a history of successful use of the insulin pump. The following recommendations for insulin pump therapy during the neonatal period are made from our experience:

- Careful assessment of parental support and motivation for CSII is crucial.
- Written instructions must be provided for an insulin regimen using diluted insulin.
- Clear directions must be given to suspend the insulin pump for hypoglycemic emergencies.
- Successful CSII therapy in this age-group requires around-the-clock health care professional support.

ACKNOWLEDGMENTS

The authors wish to thank Medtronic, Inc., for their generous loan of the insulin pump used for this patient. This study was presented in part as a poster at the ENDO 2007 Conference (89th Annual Meeting of Endocrine Science), 2–5 June 2007, in Toronto, Canada.

REFERENCES

- ¹Bharucha T, Brown J, McDonnell C, Gebert R, McDougall P, Cameron F, Werther G, Zacharin M: Neonatal diabetes mellitus: insulin pump as an alternative management strategy. *J Pediatr Child Health* 41:522–526, 2005
- ²Doyle EA, Steffen AT, Tamborlane WV: Case study: challenges of insulin pump therapy in a toddler and adolescent with type 1 diabetes. *Diabetes Educ* 31:584–590, 2005
- ³Weinzimer SA, Ahern JH, Doyle EA, Iincen MR, Dziura J, Steffen AT, Tamborlane WV: Persistence of benefits of continuous subcutaneous insulin infusion in very young children with type 1 diabetes: a follow-up report. *Pediatrics* 114:1601–1605, 2004
- ⁴Berhe T, Postellon D, Wilson B, Stone R: Feasibility and safety of insulin pump therapy in children aged 2 to 7 years with type 1 diabetes: a retrospective study. *Pediatrics* 117: 2132–2137, 2006
- ⁵Sagen JV, Raeder H, Hathout E, Shehadeh N, Gudmundsson K, Baevre H, Abuelo D, Phornphutkul C, Molnes J, Bell GI, Gloyn AL, Hattersley AT, Molven A, Søvik O, Njølstad PR: Permanent neonatal diabetes due to mutations in KCNJ11 encoding Kir6.2: patient characteristics and initial response to sulfonylurea therapy. *Diabetes* 53: 2713–2718, 2004
- ⁶Zung A, Glaser B, Nimri R, Zadik Z: Glibenclamide treatment in permanent neonatal diabetes mellitus due to an activating mutation in Kir6.2. *J Clin Endocrinol Metab* 89:5504–5507, 2004

Jahanara Begum-Hasan, MD, PhD, FAAP, is an associate professor in the Department of Pediatrics at the Virginia Tech Carilion School of Medicine in Roanoke, Va. Aisha

A.K. Bruce, MD, is a resident physician in the Department of Pediatrics at Queen's University in Kingston, Ontario, Canada. JoAnne Koster, RN, CDE, CPT, is a certified diabetes

nurse educator and certified insulin pump trainer at Hotel Dieu Hospital in Kingston, Ontario, Canada.