CASE REPORT

Perioperative continuous glucose monitoring in a preterm infant

Pratyasha Saha, Kathryn Beardsall

Department of Paediatrics,
University of Cambridge School
of Clinical Medicine, Cambridge,
UK

Correspondence to
Pratyasha Saha,
pratyashasaha@doctors.org.uk

Accepted 16 June 2018

SUMMARY

Surgery in the neonatal period presents challenges, especially in preterm infants weighing <1 kg. Their small size, minimal reserves and physiological immaturity means attention to detail and careful monitoring is critical to avoid cardiovascular instability; maintaining fluid balance and metabolic stability is also problematic due to often limited vascular access and small blood volumes. Developments in technology have meant that cardiovascular parameters such as heart rate, blood pressure and oxygen saturations are all routinely and continuously monitored before and during surgery. We have been exploring the role of continuous glucose monitoring (CGM) for metabolic monitoring and management of glucose control in very preterm infants (24–32 weeks gestation). In this paper, we report on a preterm infant who uniquely underwent surgery while wearing a continuous glucose monitor, blinded to the clinical team. This case highlights the metabolic vulnerability of these babies and a possible role for real-time CGM during surgical procedures.

BACKGROUND

Preterm infants are at high risk of both hyperglycaemia and hypoglycaemia, both of which have been associated with poorer health outcomes. The risk of hypoglycaemia persists in preterms, until at least term-equivalent age.¹ Hypoglycaemia has also been associated with neurodevelopmental impairment later in life that can be identified at, and persist beyond, 4 years of age.^{2,3}

Surgery is a high-risk period for babies due to their limited reserves, immature physiology and small size; these risks are further amplified when preterm. Preterm infants are thus monitored extensively both within neonatal intensive care units and during neonatal surgery; this includes blood pressure, heart rate, oxygen and fluid balance. While umbilical arterial lines when available can provide access for blood sampling, the desire to limit blood loss means samples are taken infrequently.

The case reports on a baby who was recruited as part of a study investigating the use of continuous glucose monitoring (CGM) in very preterm infants during the first week of life. The baby had been randomised to the control study arm, which simply required blinded collection of CGM data from a subcutaneous glucose sensor. During the study period, the baby became unwell and required surgery for suspected necrotising enterocolitis (NEC). We report on the data obtained from the

blinded CGM in this baby and consider that real-time CGM may have helped to limit his exposure to hypoglycaemia.

CASE PRESENTATION

This male baby was born with a birth weight of 810 g, following a spontaneous vaginal delivery at 29+1 weeks of gestation. A 21-week ultrasound had identified a dysplastic right kidney but otherwise the pregnancy had been uncomplicated.

He was intubated immediately after birth and had Apgar scores of 3 and 5 at 1 and 5 min. Vascular access was obtained through an umbilical venous catheter (UVC), and as his blood glucose level at birth was 1.3 mmol/L, he was given a bolus of 10% dextrose and started on maintenance fluids at 90 mL/kg/day. His parents consented to participation in a trial of CGM in the preterm infant, and having been randomised to the control study arm, he had an Enlite sensor (Medtronic Watford, UK) inserted subcutaneously in his thigh; the sensor was connected to an Ipro2 monitor (Medtronic Watford) for blinded data collection. The clinical team relied on intermittent blood glucose monitoring (IGM), the current standard of care for glucose monitoring and management in these babies. The CGM data was only available after downloading at the end of the study period. Blood glucose levels were measured on the Novostat point of care device (Novobiomedical, Massachusetts, USA) or blood gas analyser (Cobas b221, Roche, Indiana, USA).

The baby remained stable and was extubated on day 2, but became unwell on day 3 with irritability and a rigid abdomen. An abdominal radiograph suggested NEC with perforation, requiring surgical intervention due to clinical deterioration. He was intubated for surgery and in anticipation of removal of the UVC, an additional peripheral venous line (PVL) was sited. At surgery, an isolated bowel perforation was identified 15 cm from the ileocaecal valve, signifying a diagnosis of spontaneous ileal perforation rather than NEC; this was resected with ileostomy formation.

Figure 1 shows the IGM blood glucose levels (red dots) that relate to a preoperative reading of 7.9 mmol/L, an intraoperative reading of 3.8 mmol/L and a postoperative reading of 1.6 mmol/L 1 hour after surgery. This constitutes a drop of 6.3 mmol/L in 3.5 hours. During the surgery, the PVL, as the sole intravenous access, had tissue and left the baby without vascular access. After the operation, intravenous access was restored and a 10%

To cite: Saha P, Beardsall K.
BMJ Case Rep Published
Online First: [please
include Day Month Year].
doi:10.1136/bcr-2018-
224728

Figure 1 Comparison of intermittent blood glucose monitoring (IGM) and continuous glucose monitoring (CGM) in a surgical preterm infant.

dextrose bolus was given, followed by a dextrose infusion at a rate of 5 mg/kg/min.

OUTCOME AND FOLLOW-UP

Figure 1 shows the blinded CGM data, downloaded at the end of the study period (blue lines) alongside the clinical IGM data (red dots). Both methods demonstrate a notable perioperative episode of hypoglycaemia.

The CGM data (blue lines) highlights the persistent and rapid decline of glucose levels from 8.4 mmol/L preoperatively to 2.4 mmol/L postoperatively, as well as the rapid rise in glucose levels on restarting the dextrose infusion. Levels then peak at 9 mmol/L before falling again over the subsequent 10–20 hours.

The infant recovered from this surgery and underwent a reversal of the ileostomy 2 months later. He is now a healthy boy with mild learning difficulties.

DISCUSSION

Clinicians aim to avoid neonatal hypoglycaemia due to its effects on the developing brain. Neuroimaging studies have shown that in the short term, early hypoglycaemia causes diffuse cerebral cortical and subcortical white matter damage.⁴ Long-term data from ‘well’ newborns at risk of hypoglycaemia and monitored using CGM demonstrates an association between episodes of clinically ‘silent’ hypoglycaemia and longstanding difficulties with executive function.³ To monitor these avoidable hypoglycaemic episodes, recent studies have demonstrated the potential of CGM in premature neonates; technology originally developed for monitoring individuals with diabetes mellitus.⁵ Furthermore, studies in very preterm infants have shown reductions in glycaemic variability with CGM determined computer-guided glucose infusion rates.⁶ CGM has therefore been shown to be effective in both the monitoring and management of hypoglycaemia.

This case highlights the physiological vulnerability of preterm babies undergoing surgical procedures, where there are risks from loss of venous access and the ability to maintain nutritional support. It also demonstrates the potential utility of CGM in raising the awareness of rapidly falling glucose levels

and clinically silent episodes of hypoglycaemia. In this infant, this data was not available to the clinical team, but the development of real-time CGM which provides glucose monitoring as a continuous variable could have forewarned the clinical team of the impending hypoglycaemia.

Physiologically, CGM may prove to be particularly relevant in preterm babies, as they are known to be vulnerable to rapid fluctuations in glucose levels due to immaturity. The clearly documented precipitous and persistent decline of glucose in this case is highlighted by the CGM, in contrast to the large step changes seen using IGM glucose readings. Existing studies using CGM in well infants have highlighted longer untreated periods of hypoglycaemia, in comparison to IGM alone.¹ Surgery is a time in which it is often challenging to notice loss of intravenous access, and CGM may also help to identify failing access before a baby becomes significantly compromised. In this case, where the PVL was tissue, CGM levels could have acted as an early warning sign to facilitate more rapid clinical intervention.

This case report is an important addition to the limited evidence surrounding CGM in neonatal surgery; previous studies have predominantly related to older children undergoing cardiac surgery.⁷ Studies have raised concerns regarding the potential accuracy of CGM readings in the presence of oedema, dehydration and vasopressors and due to differences between tissue and blood glucose measurements.⁸ The impact of surgery itself on the accuracy of glucose levels has not been explored in this population. These devices are, however, well tolerated by babies and we would suggest that CGM could be viewed as an adjunct to IGM, rather than a replacement for it. This is in keeping with other continuous monitoring in neonatal care, where minimal handling and reduction in blood sampling is associated with improved outcomes.

Surgery in preterm neonates is a common but high-risk event, and the extremes of glycaemia are the most common metabolic abnormalities in the newborn.⁹ Introduction of new technology needs to be justified as efficacious and cost-effective. The use of CGM to support the need for IGM would bring potential added costs but with the potential benefits of reduced need for invasive blood sampling, earlier identification of hypoglycaemic risk and

reduction of the preventable long-term costs of neurocognitive impairment.

Learning points

- ▶ Hypoglycaemia is a common metabolic abnormality in newborns that can result in future neurodevelopmental impairment.
- ▶ Continuous glucose monitoring (CGM) is a presently underutilised technology that can identify clinically silent episodes of hypoglycaemia and failing intravenous access.
- ▶ Surgery in preterm neonates is a specific setting in which the use of CGM is particularly beneficial, as neonates are more prone to hypoglycaemia due to their immature physiology and limited reserves.

Acknowledgements This patient was part of Improving Glucose Control in Preterm Infants Trial (IMPP NHS East of England Committee 11/EE/0455), which had ethical approval for the use of a CGM device and informed consent was signed by the parents before inclusion. We would like to thank Lynn Thomson, Research Nurse, Addenbrooke's Hospital.

Contributors PS had substantial contributions in the design and writing of the case report, with KB responsible for the identification of the patient, the conception of the work and its drafting.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors

Competing interests None declared.

Patient consent Parental/guardian consent obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- 1 This patient was part of Improving Glucose Control in Preterm Infants Trial (IMPP NHS East of England Committee 11/EE/0455), which had ethical approval for the use of a CGM device and informed consent was signed by the parents before inclusion.
- 2 Pertierra-Cortada A, Ramon-Krauel M, Iriando-Sanz M, *et al.* Instability of glucose values in very preterm babies at term postmenstrual age. *J Pediatr* 2014;165:1146–53.
- 3 Duvanel CB, Fawer CL, Cotting J, *et al.* Long-term effects of neonatal hypoglycemia on brain growth and psychomotor development in small-for-gestational-age preterm infants. *J Pediatr* 1999;134:492–8.
- 4 McKinlay CJD, Alsweiler JM, Anstice NS, *et al.* Association of neonatal glycemia with neurodevelopmental outcomes at 4.5 years. *JAMA Pediatr* 2017;171:972.
- 5 Kim SY, Goo HW, Lim KH, *et al.* Neonatal hypoglycaemic encephalopathy: diffusion-weighted imaging and proton MR spectroscopy. *Pediatr Radiol* 2006;36:144–8.
- 6 Uettwiller F, Chemin A, Bonnemaïson E, *et al.* Real-time continuous glucose monitoring reduces the duration of hypoglycemia episodes: a randomized trial in very low birth weight neonates. *PLoS One* 2015;10:e0116255.
- 7 Galderisi A, Facchinetti A, Steil GM, *et al.* Continuous glucose monitoring in very preterm infants: a randomized controlled trial. *Pediatrics* 2017;140:e20171162.
- 8 Piper HG, Alexander JL, Shukla A, *et al.* Real-time continuous glucose monitoring in pediatric patients during and after cardiac surgery. *Pediatrics* 2006;118:1176–84.
- 9 McKinlay CJD, Chase JG, Dickson J, *et al.* Continuous glucose monitoring in neonates: a review. *Matern Health Neonatol Perinatol* 2017;3:18.
- 10 Pierro A. The surgical management of necrotising enterocolitis. *Early Hum Dev* 2005;81:79–85.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow