A feed-centric hypoglycaemia pathway ensures appropriate care escalation in at-risk infants

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ABSTRACT

Background There is a lack of clarity of what constitutes the starting point of a clinical pathway for infants at risk of hypoglycaemia. Glucose-centric pathways (GCP) identify low glucose in the first 2 hours of life that may not represent clinical hypoglycaemia and can lead to inappropriate glucose management with infusions and medications.

Objective To study the impact of a feed-centric pathway (FCP) on the number of admissions for hypoglycaemia to level 2 special care nursery (SCN) and the need for parenteral glucose/medications, compared to GCP.

Methods This project was conducted over 2 years, before and after switching from a GCP to FCP in our institution. FCP involves skin-to-skin care, early breast feeding, checking glucose at 2 hours and use of buccal glucose. The primary outcome was the number of SCN admissions for hypoglycaemia. Secondary outcomes include the number of infants needing intravenous glucose, medications and length of SCN stay.

Results Of 23,786 live births, 4,438 newborns were screened. We screened more infants at-risk for hypoglycaemia using the FCP (GCP: 1462/11969, 12.2% vs FCP: 2976/11817, 25.1%) but significantly reduced SCN admissions (GCP: 246/1462, 16.8% vs FCP: 102/2976, 3.4%; p<0.001). Fewer but proportionally more FCP newborns required intravenous glucose (GCP: 136/246, 55% vs FCP: 88/102, 86%; p<0.001). Compared with GCP, FCP reduced the total duration of stay in SCN by 104 days per annum, reducing the cost of care. However, the mean length of SCN stay for FCP was higher (GCP: 2.43 days vs FCP: 3.49 days; p=0.001). There were no readmissions for neonatal hypoglycaemia to our institution.

Conclusion The use of FCP safely reduced SCN admissions, averted avoidable escalation of care and helped identify infants who genuinely required intravenous glucose and SCN care, allowing more efficient utilisation of healthcare resources.

INTRODUCTION

Hypoglycaemia is the most common biochemical abnormality in neonates affecting 15%–30% of newborns, of whom 10% require more intensive and expensive care.1,4 Neonatal hypoglycaemia can lead to long-term neurodevelopmental morbidity and claims for injury.5,6 Compared with term well neonates, infants of diabetic mothers, large and small-for-gestational-age and preterm infants are at greater risk for metabolic maladaptation. Additionally, co-occurrence of maternal obesity with these risk factors may potentiate hypoglycaemia.2

Existing screening guidelines lack clarity due to the paucity of data and differing interpretations of available literature.8–15 What constitutes the starting point of a hypoglycaemia pathway remains unclear. There is no study that looks specifically at the optimal timing and interval for glucose screening. Several protocols test glucose levels following a feed,8–11 some test soon after birth, prior to first feed,12–14 while others do not clearly specify the timing of testing in relation to feeds.15 The starting point is important given that there is a physiological glucose nadir in well babies where glucose levels may drop to a nadir as low as 1.5 mmol/L by 1 hour of age and rise with feeds and hormone responses to more than 3 mmol/L by 2 hours.16 Untimely, glucose testing within the nadir may uncover transitional hypoglycaemia that does not require intervention. Starting invasive measures in asymptomatic infants during the nadir may lead to more intensive measures to normalise glucose.

In a glucose-centric hypoglycaemia pathway (GCP), glucose levels determine the immediate next management steps. This may lead to inappropriate infusions and medications to correct physiological hypoglycaemia. Performing glucose checks at 0 and 1 hour of life, when infants are transitioning, may lead to unnecessary escalation of care. Unlike GCP, a feed-centric pathway (FCP) recognises the nadir and encourages skin-to-skin care and breast feeding soon after birth. This facilitates bonding, deferring testing to after the first 2 hours of life. Skin-to-skin care improves glucose homeostasis by stabilising temperature regulation, heart rate and respiration, and promotes/prolongs breast feeding and duration of latching.17–19 In the FCP, buccal
glucose with a supplementary feed instead of intravenous glucose is used as a first-line intervention for hypoglycaemia. Buccal glucose has been used effectively to facilitate the glucose transition in infants ≥35 weeks gestation and is more effective than milk feeds alone in reversing hypoglycaemia in at-risk infants.

In this project, our primary objective was to determine if the FCP safely reduces the number of admissions to special care nurseries (SCN) for hypoglycaemia compared with GCP. We also compared the need for glucose infusion and the use of medications to control hypoglycaemia among GCP and FCP infants and determined the respective total duration of SCN stay.

METHODOLOGY
Setting
The study was conducted from 1 February 2015 to 31 January 2017 (GCP study period: 1 February 2015 to 31 January 2016, FCP study period: 1 February 2016 to 31 January 2017). Our institution is a large women and children’s hospital with eleven thousand births per year. A 40-bed level 4 neonatal intensive care unit and 60-bed level 2 SCN and postnatal nurseries are in service to manage the neonates. If intravenous fluid is required, the baby will be transferred to SCN from the postnatal nursery. Parents of newborns were not involved in the design or reporting of this initiative but received home care training (on hypo and hyperglycaemia plans) before discharge.

The GCP was in practice from 1 November 2007 to 31 January 2016. Infants with initial capillary glucose ≤2.5 mmol/L obtained at 0 and 1 hour of life were directly transferred to SCN. The priority of the GCP was to correct hypoglycaemia within 6 hours by increasing the volume of oral feeds, followed by intravenous dextrose and intravenous glucagon, where necessary. To improve the existing pathway, an interdisciplinary hypoglycaemia workgroup was formed in 2015 to review the management of infants at-risk of hypoglycaemia and establish a specialised team for infants with refractory hypoglycaemia due to hyperinsulinism. Hypoglycaemia team members received training at the Institute of Child Health, University College London. Thereafter, the multidisciplinary team of neonatologists, endocrinologists and nurses representing all areas of neonatal care took the initiative to develop a model of improvement. We utilised the Best Practices Research quality approach and adopted a ‘smart practice’ methodology and SQUIRE (Standards for Quality Improvement Reporting Excellence) guidelines. We identified the glucose nadir as mechanically critical and took advantage of the availability of buccal glucose to improve the management process. We based the glucose norms in our FCP guideline on recommendations from the Paediatric Endocrine Society. We confirmed all capillary glucose values <3 mmol/L with plasma glucose levels, as there is glucometer variability in estimating glucose at lower levels.

Figure 1 Glucose-centric pathway (1 November 2007 to 31 January 2016). BW, birth weight; FBC, full blood count; IDM, infant of diabetic mother; IM, intramuscular; IUGR, intrauterine growth retardation; IV, intravenous; LGA, large for gestational age; NBM, nil by mouth; NEC, necrotising enterocolitis; SC, subcutaneous.

Glucose-centric pathways
In the GCP, hypoglycaemia was defined as capillary glucose ≤2.5 mmol/L. Figure 1 describes the GCP process, and Table 1 shows the criteria of at-risk infants who received screening. At-risk infants were identified at birth and had capillary glucose monitored at 0, 1, 3, 6, 12 and 24 hours of age. Subsequent care depended on the glucose levels at 0 and 1 hour. All infants were directly admitted to SCN if capillary glucose was ≤2.5 mmol/L at 0 and 1 hour of life. Plasma glucose was performed for verification if capillary glucose was suggestive of hypoglycaemia. For all asymptomatic infants who were unable to maintain capillary glucose >2.5 mmol/L, formula feeds were offered as the first intervention. Term infants, large for gestational age and infants of diabetic mothers, were offered a supplementary feed and care was escalated to intravenous glucose if capillary glucose remained ≤2.5 mmol/L. All preterm infants were given intravenous glucose when capillary glucose was ≤2.5 mmol/L. In addition, parenteral gluconon was also offered to infants weighing >2500 g if they remained hypoglycaemic. Intravenous glucose was indicated in any at-risk infant with glucose levels <1 mmol/L, even when asymptomatic. Capillary glucose was tested within 60 min after any intervention, such as an increase in feed volume, commencement of intravenous fluids, change in glucose infusion rate, or administration of parenteral gluconon. All infants of diabetic mothers were admitted to SCN irrespective of glucose metre results.
Feed-centric pathway

The FCP was formally introduced into clinical practice on 1 February 2016. Nurses and doctors in all neonatal areas received training on FCP and the use of glucose gel. Parents were encouraged to participate at the bedside to recognise and manage hypoglycaemia in their infants under medical supervision. Mothers were taught how to administer glucose gel with the aid of an instructional video. The hypoglycaemia team provided oversight on the smooth implementation of the FCP in the delivery room and postnatal wards. Random safety audits were conducted at intervals to monitor compliance with the protocols. Educational activities to reinforce the clinical pathway included regular lectures and workshops for nurses and doctors, including junior medical staff rotating through the department. We adopted 3–6 essential practices for sustainable improvement by (1) standardising the pathway, (2) having the hypoglycaemia team be accountable and (3) integrating the FCP across departments in our institution.28

In the FCP, hypoglycaemia was defined as capillary glucose <3 mmol/L in the first 48 hours of life. Figure 2 describes the FCP process, and table 1 shows the criteria of at-risk infants who received screening. At-risk infants were identified at birth and had capillary glucose monitored at 2, 6, 12, 18 and 24 hours of age for appropriate and large for gestational age infants. Small-for-gestational-age infants, defined as term infants <2600 g, had an additional screening check at 36 hours. Plasma glucose was performed for verification if capillary glucose was suggestive of hypoglycaemia. Before the first glucose check at 2 hours, all infants were allowed skin-to-skin care and latched on to the mother’s breast. Infants were left on the mother’s chest as long as required and later sent to the postnatal nursery, emphasising adequate feeding within the first 2 hours of life. These initial measures were the responsibility of the attending medical officer, labour ward (LW) and operation theatre (OT) nurses. Mothers were encouraged to breast feed on demand. When glucose levels were suboptimal, offered feed supplements with either own mother’s milk, pasteurised donor human milk or ready-to-feed formula milk following glucose gel administration before considering a transfer to SCN. Intravenous glucose was indicated if capillary glucose levels in asymptomatic infants were <1.5 mmol/L at 2 hours after having received feeds in the first hour of life. Asymptomatic infants with borderline glucose levels between 1.5–2.9 mmol/L received buccal administration of glucose gel (0.5 mL/kg of buccal glucose gel 40% dextrose—Rapilose, Penlan Healthcare, UK) followed by an extra feed. In some cases, up to six further doses of glucose gel was offered within 48 hours of life. Intravenous fluids were only necessary if glucose levels remained persistently low despite glucose gel and

![Table 1](http://bmjopenquality.bmj.com/)

<table>
<thead>
<tr>
<th>Hypoglycaemia threshold</th>
<th>≤2.5 mmol/L</th>
<th>&lt;3 mmol/L</th>
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</thead>
<tbody>
<tr>
<td>Screening eligibility criteria</td>
<td>Infants of diabetic mothers. LGA (BW ≥4000 g). Term ≥37 weeks with BW ≥2270 g. Preterm 35–37 weeks with BW ≥1800 g.</td>
<td>Infants of diabetic mothers. LGA (BW &gt;4000 g or &gt;90th centile). Term ≥37 weeks with &lt;2600 g. Preterm 35–37 weeks with BW ≥1800 g. Infants of obese mothers (&gt;85 kg or BMI &gt;33 kg/m²).</td>
</tr>
<tr>
<td>Timing of capillary glucose monitoring</td>
<td>0, 1, 3, 6, 12 and 24 hours of age.</td>
<td>2, 6, 12, 18 and 24 hours of age for AGA and LGA infants. SGA infants have an additional test at 36 hours.</td>
</tr>
<tr>
<td>Approach to intervention</td>
<td>Formula feeds, then IV dextrose, then IV glucagon and/or hydrocortisone.</td>
<td>Skin-to-skin care and breast feeding soon after birth. Emphasis on feeding in the first 2 hours. First glucose check at 2 hours of life. When glucose levels were suboptimal, glucose gel followed by feeding.</td>
</tr>
<tr>
<td>Admission to SCN criteria</td>
<td>Infants of diabetic mothers irrespective of capillary glucose levels. Infants with capillary glucose ≤2.5 mmol/L irrespective of feeding status.</td>
<td>Infants who are unable to maintain glucose ≥3 mmol/L after glucose gel and feeds. Infants born to a diabetic mother on insulin therapy and with weight &gt;4000 g (or &gt;90th centile).</td>
</tr>
<tr>
<td>Excluded infants</td>
<td>Infants with birth weight &lt;1800 g. Infants &lt;35 weeks gestation. Infants requiring direct level 4 care. Infants who are out born. Infants admitted to SCN for non-hypoglycaemia reasons.</td>
<td>Infants requiring direct level 4 care. Infants with birth weight &lt;3500 g. Infants &lt;35 weeks gestation. Infants who are out born. Infants admitted to SCN for non-hypoglycaemia reasons.</td>
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AGA, appropriate for gestational age; BMI, body mass index; BW, birth weight; FCP, feed-centric pathway; GCP, glucose-centric pathway; IV, intravenous; LGA, large for gestational age; SCN, special care nursery; SGA, small-for-gestational-age.
infusion requirement, use of medications and length of stay in SCN). The process measures were screening and admission rates of infants at-risk of hypoglycaemia in the FCP and GCP. A run chart was developed to examine changes in trends with the transition from GCP to FCP. Outcome measures included the use of buccal glucose among FCP infants and the need for glucose infusion and intravenous medications among FCP and GCP infants. Structural measures were mean length of stay in SCN and total SCN utilisation days. The key balancing measure was the number of readmissions to the hospital for hypoglycaemia.

Data were analysed using SPSS V.22.0. We compared differences in admissions during the GCP and FCP periods using Fischer’s exact test and weight status at birth using the χ² test. For statistical significance, the probability was set at <5%.

RESULTS

We screened a total of 4438 at-risk infants out of 23786 live births (18.6%) during the 2-year period, which included 1462 GCP (1462/11969, 12.2%) and 2976 FCP infants (2976/11817, 25.2%) (table 2). There was twice the number of infants screened in FCP due to the addition of infants of obese mothers, revision of small-gestational-age criteria and greater pathway enforcement.

The characteristics of the infants admitted to SCN for hypoglycaemia are shown in table 3. There is no difference in the sex, weight-for-age status, and proportion of infants of diabetic mothers between GCP and FCP. The median gestational age for GCP and FCP was 37.5 and 38.1 weeks (p=0.002). Of those screened, significantly fewer FCP infants required admission to SCN compared with GCP (3.4% vs 16.8%; p=0.000) (figure 3). Admissions from LW/OT were markedly reduced, 119 in GCP vs 10 in FCP (p=0.000). Admissions from postnatal wards were also significantly reduced, 127 in GCP vs 92 in FCP (p=0.002) (table 2). Fewer but proportionally more FCP infants required intravenous glucose (GCP: 136/246, 55% vs FCP: 88/102, 86%; p=0.000). Although there was no statistical difference in the number of infants admitted

Table 2  GCP versus FCP: screening and SCN admission rates of infants at-risk of hypoglycaemia

<table>
<thead>
<tr>
<th>Type of pathway</th>
<th>No of infants in pathway/ total infants</th>
<th>SCN admissions/ total infants on pathway</th>
<th>Source of admission</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCP</td>
<td>1462/11969 (12.2%)</td>
<td>246/1462 (16.8%)</td>
<td>LW/OT: 119, FCP: 127</td>
</tr>
<tr>
<td>FCP</td>
<td>2976/11817 (25.2%)</td>
<td>102/2976 (3.4%)</td>
<td>LW/OT: 10, FCP: 92</td>
</tr>
</tbody>
</table>

P value  <0.000  0.000  0.002

FCP, feed-centric pathway; GCP, glucose-centric pathway; LW, labour ward; OT, operation theatre; PW, postnatal ward; SCN, special care nursery.
to SCN who required medications (glucagon, hydrocortisone or diazoxide) (GCP: 14/246, 5.7% vs FCP: 4/102, 4%; p=0.497), there was a sevenfold percentage reduction among screened FCP infants vs GCP infants (GCP: 14/1462, 0.96% vs FCP: 4/2976, 0.13%; p=0.000).

Although the mean length of stay for FCP infants was longer compared with GCP (GCP: 2.43d vs FCP: 3.49d, p=0.001), there was a reduction in the total number of days of SCN stay by 104 days, from 458 days in GCP to 354 days in FCP, due to numerically fewer FCP admissions. The average cost savings of US$500 per day in SCN translated to an estimated cost saving of US$52,000 per year. No readmissions for neonatal hypoglycaemia to our hospital were observed.

**DISCUSSION**

Our results demonstrate that a feed-centric approach to glucose monitoring of neonates at-risk of hypoglycaemia significantly reduced admissions to SCN, need for glucose infusion or pharmacological intervention and total SCN utilisation days, compared with a glucose-centric approach. The defining feature of the FCP is avoidance of measuring asymptomatic physiological hypoglycaemia prior to feeding within the first 2 hours of life, averting unnecessary intravenous glucose exposure as the newborn transitions to enteral nutrition. A second key feature of the FCP is the utilisation of buccal glucose as an intermediate step in asymptomatic hypoglycaemia management, deferring the use of intravenous glucose in the treatment algorithm. Our results show that early oral feeding and buccal glucose, as opposed to early glucose testing and intravenous glucose, can facilitate physiological stabilisation of blood glucose levels within 48–72 hours of life, in line with current recommendations.25 26

Our findings are a reminder to adopt a phased and physiological approach to neonatal hypoglycaemia.29 as, unlike in symptomatic babies, there is limited evidence to guide the management of the asymptomatic neonate. The definition of hypoglycaemia is controversial, and there is uncertainty over the intensity of hypoglycaemia that leads to neuronal consequences.5 30 Fear of neurological sequelae and litigation can lead to the practice of early testing and intervention.5 6 When mindsets and systems are primarily glucose-centric, at-risk neonates with asymptomatic hypoglycaemia may be prematurely treated, leading to inappropriate infusions and medications to correct physiological hypoglycaemia. This leads to unnecessary admissions to secondary/tertiary care, maternal separation and bonding, delayed breast feeding, delayed discharge and added cost.
We adopted systems thinking in the design implementation of the FCP.\textsuperscript{31} We first established that the primary purpose of the FCP was to facilitate the safe metabolic transition of newborn infants at-risk of hypoglycaemia to extrauterine life, and not merely the prompt identification and treatment of hypoglycaemia. We determined that transition includes an appreciation of the physiological nadir, early skin-to-skin care and breast feeding, the establishment of enteral nutrition and stabilisation of glucose levels. We included maternal obesity as a risk factor as it is associated with complications in pregnancy and increases fetal morbidity and mortality.\textsuperscript{7} Additionally, increasing insulin resistance has been independently shown in both gestational diabetes mellitus and obesity.\textsuperscript{32} Insulin resistance causes high maternal-fetal glucose levels, which produces excess fetal insulin that can result in varying degrees of hypoglycaemia.\textsuperscript{33,34} A meta-analysis showed that the risk of developing gestational diabetes is two, four and eight times higher among overweight, obese and severely obese mothers, respectively, with increased risk of adverse outcomes.\textsuperscript{35-37} Macroscopic infants (birth weight $\geq 4000$ g) are twice more likely to be born to obese compared with normal weight mothers ($16.8\%$ vs $8.4\%$, $p<0.02$).\textsuperscript{38}

We introduced buccal administration of 40\% dextrose gel as initial management, which transferred care to the bedside while avoiding invasive interventions.\textsuperscript{21} We recognised the need for training and education since the pathway involved stakeholders across multiple domains, including obstetricians, paediatricians and endocrinologists, as well as nursing professionals across various clinical areas. The expanded inclusion criteria, greater buy-in by care teams and strict adherence to the FCP may explain the doubling of babies screened.

Despite twice the numbers screened, we observed twofold lowering in FCP admissions (248, 16.8\% GCP vs 102, 3.4\% FCP), with reductions particularly from LW/OT (119 GCP vs 10 FCP; $p=0.000$), and from primary care wards (127 GCP vs 92 FCP; $p=0.002$). Reductions were achieved despite a higher PES recommended hypoglycaemia threshold in the FCP (capillary glucose levels, GCP: $\leq 2.5$ mmol/L vs FCP: $< 3$ mmol/L). These observations suggest that testing glucose shortly after birth in the LW/OT may identify glucose nadirs that lead to SCN admissions and the use of intravenous glucose. We propose that the system of feeding within 1 hour, testing from 2 hours and use of buccal glucose allows primary care wards to retain autonomy to identify, treat and escalate care appropriately.

Compared with GCP admissions to SCN, a higher percentage of FCP admissions required intravenous glucose (GCP: 136/246, 55\% vs FCP: 88/102, 86\%), indicating that infants who required therapeutic glucose were correctly identified. Among FCP infants, we also observed the reduced need for pharmacotherapy (14/246, 5.7\%, GCP vs 4/102, 4\%, FCP) and fewer total SCN utilisation days (458, GCP vs 354, FCP). By appropriately identifying at-risk infants needing care escalation, it is unsurprising that the mean length of stay in the hospital was longer for FCP infants (2.43d GCP vs 3.49d FCP, $p=0.001$).

### Strengths and limitations

We conducted this project in a maternity hospital with levels 1, 2 and 4 neonatal care units where care was provided to pregnancies and babies ranging from low to high risk, which helps the generalisability of our results. All screening tests were performed using a single brand of glucose metre that employs the glucose dehydrogenase enzyme method. Although emergency readmissions typically reach our institution, we acknowledge that babies with hypoglycaemia may be admitted elsewhere. We also acknowledge that our project would have been enhanced by collecting user satisfaction data, especially from primary care wards, LW/OT and SCN. As the expanded small-for-gestational-age criteria increased screening numbers, further balancing measures including studying cost-effectiveness and parental anxiety would have been helpful. Other limitations include a significantly lower number of infants screened in the GCP due to less stringent enforcement and narrower inclusion criteria for screening. Although GCP and FCP glucose data were both obtained from the hospital’s Quality Safety Risk Management Unit, clinical data in the GCP was collected retrospectively through a medical records review, which might result in missing data. In contrast, FCP data was collected through an organised audit.

### CONCLUSION

A carefully administered hypoglycaemia pathway that respects the physiological nadir can significantly reduce SCN admissions and promote better utilisation of resources. Being feed-centric rather than glucose-centric through early feeding and use of buccal glucose resulted in the safe transfer of care to the bedside, reduced the need for escalation to glucose infusions and pharmacotherapy, and thereby enabled care to be provided to babies who truly needed it.

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### Contributors

SC: conception and design of the study and wrote the manuscript; JXS: prepared the preliminary draft of the manuscript including appropriate references; VSR: contributed substantially to the design of the study and interpretation of the data; RWSL: acquisition and analysis of the data; MCC: conception and design of the study and interpretation of the data; FY: contributed substantially to the conception and design of the study, interpretation of the data; writing and editing the final manuscript. All authors critically revised the manuscript, agree to be fully accountable for ensuring the integrity and accuracy of the work, and read and approved the final manuscript. SC accepts full responsibility for the work, conduct of the study, access to data and controlled the decision to publish.

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### Competing interests

None declared.
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