What is already known on this topic:

- Hypoglycaemia is frequently diagnosed in newborn infants and prolonged hypoglycaemia has been associated with adverse neurodevelopmental outcome
- Management of hypoglycaemia involves supplemental feeds, failing which NICU admission and mother-infant separation is indicated for more invasive treatment
- Evidence is accumulating to use dextrose gel in the treatment of neonatal hypoglycaemia

What this paper adds:

- Dextrose gel reduces NICU admission for hypoglycaemia and mother-infant separation without prolonging the hospital stay
- Dextrose gel can be used to treat neonatal hypoglycaemia in the postnatal ward setting

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Abstract

Aim: To evaluate dextrose gel in the management of neonatal hypoglycaemia in the postnatal wards at an Australian tertiary level perinatal centre.

Methods: An audit was performed before and after implementation of dextrose gel. Pre-implementation, neonatal hypoglycaemia was managed with feed supplementation alone, and dextrose gel was used in addition to feed supplementation in the post-implementation phase. Outcomes included admission to neonatal intensive care (NICU) for management of hypoglycaemia, proportion of neonates who achieved normoglycaemia (defined as blood glucose ≥ 2.6 mmol/L with no clinical signs after ≤ 2 treatment attempts) and proportion of neonates with hypoglycaemia recurrence after normoglycaemia and ≤ 2 treatment attempts.

Results: NICU admission for treatment of hypoglycaemia reduced significantly post-implementation of dextrose gel [29/100 (29%) vs. 14/100 (14%); $p=0.01$]. No significant difference was seen in the proportion of neonates achieving normoglycaemia [71/100 (71%) vs. 75/100 (75%), $p=0.52$], but hypoglycaemia recurrence was higher in the post-implementation group [22/71 (31%) vs. 37/75 (49%), $p=0.02$].

Conclusions: Dextrose gel is effective in the management of neonatal hypoglycaemia in the postnatal setting, reducing admission to NICU and mother-infant separation.

Key Words (MeSH terms):

Hypoglycaemia

Glucose

Guideline

Infant, Newborn

Introduction

Neonatal hypoglycaemia is common, affecting 5-15% of otherwise healthy newborns and up to 50% with risk factors for hypoglycaemia.⁽¹⁾ Infants of diabetic mothers, infants of obese mothers, those born with low birth weight (LBW; < 2500g), small for gestational age (SGA; <10th centile), macrosomic or large for gestational age (LGA; >90th centile), preterm (<37 weeks' gestation), and those with concurrent illnesses (e.g. respiratory distress, sepsis, polycythaemia) are considered most at risk for significant hypoglycaemia after birth.^{(2) (3)} Prolonged neonatal hypoglycaemia is associated with brain injury, presenting with encephalopathy and seizures, with subsequent long-term neurocognitive sequelae.^{(4) (5)}

Whilst uncertainty persists regarding what actual blood glucose concentration constitutes significant hypoglycaemia, clinical guidelines recommend the operational threshold of a true blood glucose (TBG; measured by the glucose oxidase method) <2.6mmol/L to guide the treatment of neonatal hypoglycaemia in clinical practice.^{(4) (6)} This cut-off is not associated with adverse neurodevelopmental outcome.^{(7) (8)}

Until recently, treatment options for hypoglycaemia consisted only of supplemental feeds [expressed breast milk (EBM) or infant formula (IF)], failing which intravenous glucose was administered.⁽⁹⁾ Many of these babies, especially those requiring intravenous glucose, were admitted to a newborn intensive care unit (NICU) resulting in mother-infant separation, disrupting bonding and establishment of breastfeeding.^{(6) (10)} Dextrose gel has been shown to reduce hypoglycaemia, rebound hypoglycaemia and NICU admission for hypoglycaemia,⁽¹¹⁾ with a possible reduction in supplementary feed volume.⁽¹²⁾

The aim of this study was to implement and evaluate dextrose gel in the management of neonatal hypoglycaemia in the postnatal wards at a large Australian tertiary perinatal hospital.

Materials and Methods

A prospective audit of a sample of convenience of 200 sequential neonates ≥ 36 weeks' gestation at risk and treated for hypoglycaemia was conducted before (n=100) and after (n=100)

the implementation of 40% dextrose gel (July 2014) in the management of neonatal hypoglycaemia in the postnatal wards at the Royal Women's Hospital (RWH), Victoria, Australia. Excluded infants were those born <36 weeks' gestation and/or admitted to NICU for reasons other than hypoglycaemia. Data were abstracted from each baby's clinical notes and the Clinical Lookup and Results Acknowledgement (CLARA) pathology system.

Prior to the implementation of the dextrose gel, neonatal hypoglycaemia (pre-feed TBG <2.0 mmol/L in the first 24 hours of life and <2.6 mmol/L thereafter) in the postnatal ward was managed with supplementary feeds of EBM or 5-10mL of IF per low TBG. From July 2014, 40% dextrose gel (Glucose 15^{TM}) was administered in addition to the same supplementary feeds. Neonates with TBG of 1.5-1.9mmol/L (first 24 hours), or 1.5-2.5mmol/L thereafter with no clinical signs of hypoglycaemia, were given 200mg/kg (0.5 mL/kg) 40% dextrose gel via buccal administration; all neonates with clinical signs of hypoglycaemia and TBG <2.6mmol/L were admitted to the NICU. Blood glucose concentration was measured prior to the next feed (≤ 3 hours post administration of dextrose gel), with a maximum of six doses of dextrose gel that could be administered in the first 48 hours of life in the postnatal wards. Blood glucose concentrations continued to be measured before each 3 hourly feed until 3 consecutive readings ≥ 2.6 mmol/L were achieved.

The primary outcome of the audit was admission to the NICU for the management of hypoglycaemia. Secondary outcomes comprised i) proportion of neonates achieving normoglycaemia (defined as TBG ≥ 2.6 mmol/L with no clinical signs) after ≤ 2 treatment attempts (supplementary feeds before implementation of dextrose gel or dextrose gel and supplementary feeds after implementation of dextrose gel) and; ii) proportion of neonates with recurrence of hypoglycaemia, defined as any pre-feed TBG <2.0mmol/L in the first 24 hours or <2.6mmol/L after 24 hours of life, after having a normal TBG achieved with prior treatment.

Data analyses were performed using SPSS for Windows version 19.0 (SPSS Inc., Chicago, IL, USA). Categorical data were compared between groups using χ^2 tests and continuous data with independent *t*-tests.

The study was approved by the RWH Human Research Ethics Committee as meeting the National Health and Medical Research Council requirement for quality assurance for audit projects.

Results

Between October 2013 to May 2015, 200 neonates treated for hypoglycaemia in the postnatal wards at RWH were included in the study. Table 1 demonstrates that maternal and neonatal baseline characteristics were broadly comparable between groups, with no significant differences in risk factors for hypoglycaemia. The post-implementation group had statistically more males and were of later gestational age.

Inclusion of dextrose gel in the management of hypoglycaemia resulted in a significant reduction in NICU admissions for hypoglycaemia treatment [29/100 (29%) vs. 14/100 (14%); $p=0.01$]. However, the proportion of neonates achieving normoglycaemia with ≤ 2 treatment attempts in the postnatal wards did not differ (Table 2), with most neonates receiving only one dose of dextrose gel [54/72 (75%)]. The remaining 11 infants in the post-implementation group received more than 2 treatment attempts with dextrose gel and supplementary feeds to achieve normoglycaemia. Although hypoglycaemia recurrence was higher in the post-implementation group ($p=0.02$), the length of hospital stay was comparable.

No difference was seen in feeding outcomes - breastfeeding (BF), expressed breast milk (EBM) and infant formula (IF), [BF alone, 94 (94%) vs. 95 (95%); BF and EBM, 5 (5%) vs. 2 (2%); or IF only, 1 (1%) vs 3 (3%), $p=0.32$] and the length of hospital stay in all infants treated for hypoglycaemia in the postnatal wards was also similar (Table 2).

Discussion

Dextrose gel reduced NICU admissions for hypoglycaemia management, compared with supplementary feeds alone. Although supplementary feeds were not reduced, dextrose gel allowed more babies treated for hypoglycaemia to be managed in the postnatal wards with their

mothers. Reduced NICU admissions also means that invasive therapies were avoided, with potential reductions in costs and resources.

The reduction in NICU admissions with dextrose gel in hypoglycaemia management is consistent with findings of previous observational studies,^{(13) (14)} the Sugar Babies double-blind, placebo-controlled randomised trial of 200mg/kg 40% dextrose gel treatment for neonatal hypoglycaemia⁽¹¹⁾ and the recent Cochrane systematic review.⁽¹⁵⁾ Our audit supports recommendations to include dextrose gel in hypoglycaemia management guidelines for babies born ≥ 36 weeks' gestation in the postnatal ward setting.⁽⁶⁾⁽¹⁵⁾ This accumulating evidence for dextrose gel treatment of neonatal hypoglycaemia also supports the investigation of dextrose gel in the prevention of neonatal hypoglycaemia.⁽¹⁶⁾

The Sugar Babies randomised controlled trial reported a significant reduction in the number of infants with TBG < 2.6 mmol/L after ≤ 2 doses of dextrose gel (14% vs 24%; relative risk 0.57, $P=0.04$)⁽¹¹⁾ Our study, however, found that the proportion of neonates achieving normoglycaemia with ≤ 2 treatment attempts was similar in the pre- and post-implementation groups. With the onset of action of oral glucose occurring within 10 minutes and the time to peak concentration of 40 minutes,⁽¹⁷⁾ buccal administration of the dextrose gel is also expected to reach maximum effect at approximately 40 minutes post administration. Therefore, the difference in findings may be due to the prompt absorption and utilization of the dextrose gel, together with the differences in supplementary feeding policies and in repeat TBG measurement between the Sugar Babies Study and our audit. TBG was measured 30 minutes after the second of the 2 dextrose gel doses in the Sugar Babies Study and babies were encouraged to feed and only given EBM or IF if feeding was poor. In our audit, babies received only one dextrose gel dose with TBG measured prior to the next feed (up to 3 hours after dextrose gel dose) and all babies were supplemented with EBM or IF with each TBG < 2.6 mmol/L as per the RWH hypoglycaemia guideline.

Another limitation is the non-parallel design of the study, although both groups had comparable maternal and neonatal baseline characteristics. The retrospective data abstraction may limit the

stringency and robustness of data quality, and was dependent on the accuracy of documentation by clinical staff. However, wherever possible, information was confirmed against the CLARA pathology system (e.g. TBG readings) and neonatal medicine charts.

In conclusion, 200mg/kg of 40% dextrose gel is effective in the management of neonatal hypoglycaemia in the postnatal setting, reducing NICU admission and mother-infant separation.

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Conflicts of interest: The authors have no conflicts of interest to declare.

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Tables

Table 1. *Baseline maternal and neonatal characteristics of 200 neonates treated for hypoglycaemia*

	Pre-implementation (n=100)	Post-implementation (n=100)	p-value
Maternal			
Maternal BMI, mean (SD)	26.4 (± 5.8)	27.1 (± 7.0)	0.49
Maternal diabetes status, n (%)			0.25
Non-diabetic	66 (66%)	74 (74%)	
Diet-controlled DM	11 (11%)	5 (5%)	
Insulin-dependent DM	23 (23%)	21 (21%)	
Neonatal			
Male, n (%)	43 (43%)	62 (62%)	0.01
Multiple, n (%)	13 (13%)	10 (10%)	0.51
Gestation in weeks, mean (SD)	37.8 (± 1.4)	38.3 (± 1.5)	0.02
Birth weight (g), mean (SD)	3178.7 (± 823.0)	3113.2 (± 726.6)	0.55
Birth weight, n (%)			0.25
<2500g	26 (26%)	20 (20%)	

SGA (<10 th centile)	8 (8%)	14 (14%)	
LGA >90 th centile	24 (24%)	17 (17%)	
10 th -90 th centile	42 (42%)	49 (49%)	
Prematurity (<37 weeks), n (%)	20 (20%)	13 (13%)	0.18
Suspected sepsis, n (%)	6 (6%)	12 (12%)	0.14

* standard deviation (SD), number (n), percentage (%), and DM (diabetes mellitus); Body Mass Index (BMI)

Table 2. Outcomes in all neonates following dextrose gel implementation

	Pre-implementation (n=100)	Post-implementation (n=100)	p-value
Admissions to NICU, n (%)	29 (29%)	14 (14%)	0.01
Normoglycaemia after ≤ 2 treatment attempt(s) in postnatal wards, n (%)	71 (71%)	75 (75%)	0.52
Normoglycaemia after > 2 treatment attempt(s) in postnatal wards, n (%)	0	11 (11%)	
Length of hospital stay, days, mean (SD)	4.4 (2.9)	4.1 (4.5)	0.55

*SD (Standard deviation), number (n), percentage (%), Neonatal Intensive Care unit (NICU)

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