Oral dextrose gel for prevention of neonatal hypoglycaemia

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AUCKLAND DISTRICT HEALTH BOARD
Te Toka Tumai

hPOD
hypoglycaemia Prevention with Oral Dextrose

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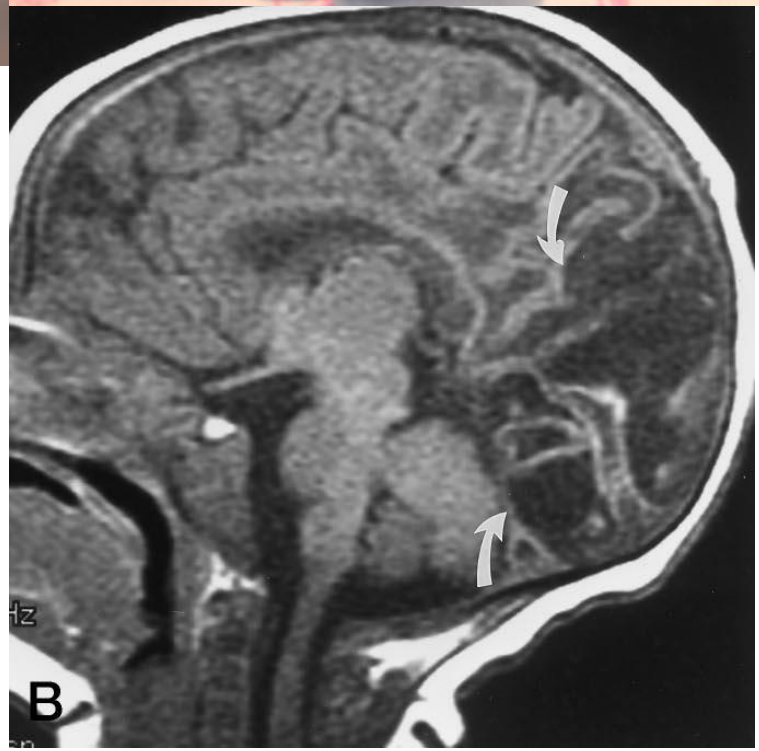

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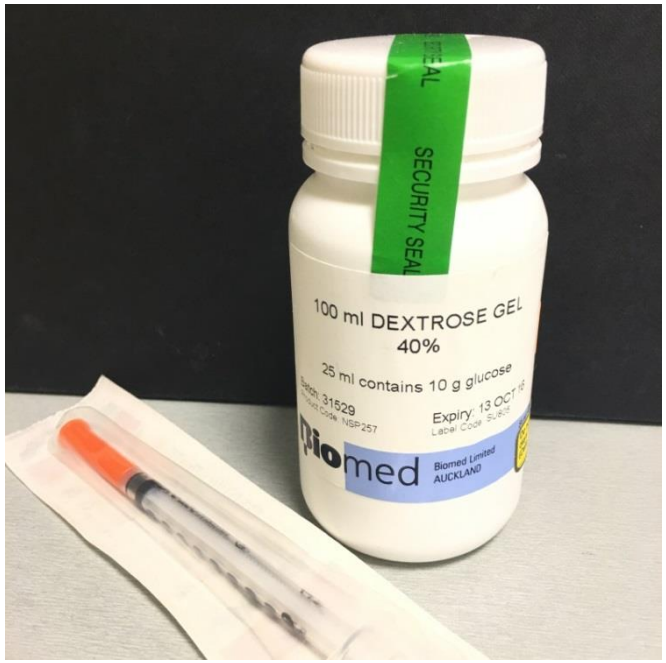
Canadian Paediatric Society

NICE National Institute for Health and Care Excellence

Baby - www.flickr.com/photos/radloff/
MRI - Barkovich AJNR Am J Neuroradiol 19:523–528, March 1998
Heel prick – Bethan Jones, hPDD Research Nurse

the sugar babies study

a randomised controlled trial



Dextrose gel for neonatal hypoglycaemia (the Sugar Babies Study): a randomised, double-blind, placebo-controlled trial

Deborah L Harris, Philip J Weston, Matthew Signal, J Geoffrey Chase, Jane E Harding

Summary

Background Neonatal hypoglycaemia is common, and a preventable cause of brain damage. Dextrose gel is used to reverse hypoglycaemia in individuals with diabetes; however, little evidence exists for its use in babies. We aimed to assess whether treatment with dextrose gel was more effective than feeding alone for reversal of neonatal hypoglycaemia in at-risk babies.

Methods We undertook a randomised, double-blind, placebo-controlled trial at a tertiary centre in New Zealand between Dec 1, 2008, and Nov 31, 2010. Babies aged 35–42 weeks' gestation, younger than 48 h old, and at risk of hypoglycaemia were randomly assigned (1:1), via computer-generated blocked randomisation, to 40% dextrose gel 200 mg/kg or placebo gel. Randomisation was stratified by maternal diabetes and birthweight. Group allocation was concealed from clinicians, families, and all study investigators. The primary outcome was treatment failure, defined as a blood glucose concentration of less than 2·6 mmol/L after two treatment attempts. Analysis was by intention to treat. The trial is registered with Australian New Zealand Clinical Trials Registry, number ACTRN12608000623392.

Findings Of 514 enrolled babies, 242 (47%) became hypoglycaemic and were randomised. Five babies were randomised in error, leaving 237 for analysis: 118 (50%) in the dextrose group and 119 (50%) in the placebo group. Dextrose gel reduced the frequency of treatment failure compared with placebo (16 [14%] *vs* 29 [24%]; relative risk 0·57, 95% CI 0·33–0·98; p=0·04). We noted no serious adverse events. Three (3%) babies in the placebo group each had one blood glucose concentration of 0·9 mmol/L. No other adverse events took place.

Interpretation Treatment with dextrose gel is inexpensive and simple to administer. Dextrose gel should be considered for first-line treatment to manage hypoglycaemia in late preterm and term babies in the first 48 h after birth.

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Introduction

Neonatal hypoglycaemia is important because it is a common disorder, which is associated with brain injury and poor neurodevelopmental outcome.[1-3] Although the definition of neonatal hypoglycaemia is controversial,[4] thresholds for treatment have been established[5] and are used in clinical practice.[6] Neonatal hypoglycaemia affects as many as 5–15% of otherwise healthy babies[6,7] and is widespread in resource-poor countries.[8,9] Furthermore, prevalence of the disorder is increasing because of the increasing incidence of preterm birth[10] and maternal factors, such as diabetes[11] and obesity,[12] which can predispose babies to hypoglycaemia. Little evidence exists to guide treatment and repeated calls have been made to develop evidence-based guidelines for the treatment of neonatal hypoglycaemia.[6,7,13,14]

Treatment choices vary dependent on the baby's birthweight and gestational age. In late preterm and term babies, initial management focuses on feeding and increased monitoring, requiring repeated and painful blood tests. If blood glucose concentration remains low, admission to the newborn intensive-care unit for intravenous glucose is usually indicated.[15] Such admission usually means that mother and baby are separated, which can delay the establishment of breastfeeding.

In addition to intravenous glucose, 40% dextrose gel is another less commonly used treatment. Potential advantages of dextrose gel are that it keeps mother and baby together while treatment is provided, is easy to administer, and is low cost. Oral carbohydrate is first-line treatment for low blood glucose concentrations in the conscious diabetic child or adult,[16] and sublingual glucose is as effective as intravenous glucose for treatment of hypoglycaemic children with malaria.[17] Two small observational studies[18,19] in babies aged between 28 weeks' and 42 weeks' gestation have reported improvement in blood glucose concentrations after massaging of 200 mg/kg dextrose gel into the buccal mucosa. However, a randomised trial,[20] in which 75 babies with hypoglycaemia were randomly assigned to a feed or feed plus 400 mg/kg dextrose gel on the first day after birth, showed no differences in blood glucose concentrations at 15 min and 30 min after treatment. Furthermore, formula-fed babies assigned to the dextrose-gel group suckled a smaller volume during the subsequent feed than did those in the feed-alone group.[20] Therefore, the role of dextrose gel in the management of neonatal hypoglycaemia remains unclear.

We assessed whether treatment with 40% dextrose gel was more effective than feeding alone for reversal of

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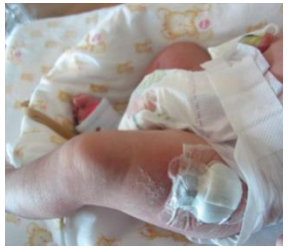
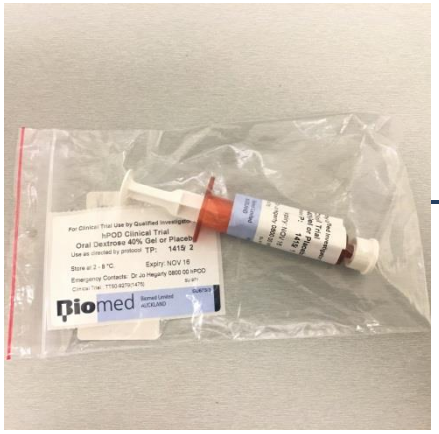
Pre-hPOD (dosage trial)

To determine the dose of prophylactic oral dextrose gel which will prevent neonatal hypoglycaemia when administered to newborn babies at risk of hypoglycaemia.





pre-hPOD

Eligible babies

Single dose arm

multiple dose arm

At 1 hour

200mg/kg (0.5 ml/kg) glucose

400mg/kg (1 ml/kg) glucose

0.5 ml/kg placebo

1 ml/kg placebo

200mg/kg (0.5 ml/kg) glucose

400mg/kg (1 ml/kg) glucose

0.5 ml/kg placebo

1 ml/kg placebo

Prefeed x 3 doses

200mg/kg (0.5 ml/kg) glucose

0.5 ml/kg placebo

Inclusion criteria

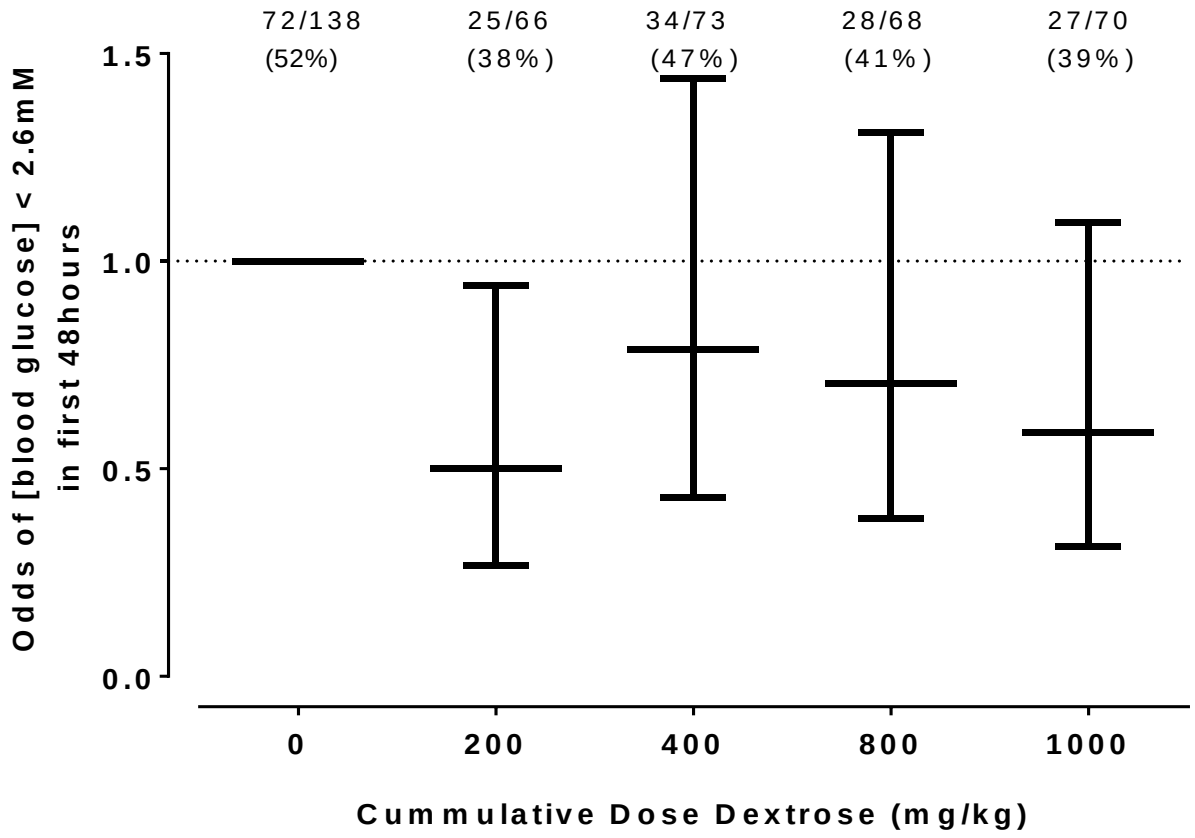
At risk of hypoglycaemia; **at least ONE** of:

- Infants of diabetic mothers (any type)
- Preterm (< 37 weeks)
- Small (< 2.5 kg or < 10th centile, population or customised)
- Large (> 4.5 kg or > 90th centile, population or customised)
- Other

AND satisfy **ALL** of the following:

- ≥ 35 weeks' gestation
- Birth-weight ≥ 2.2 kg
- < 1 hour old
- No apparent indication for NICU/SCBU admission at time of randomisation
- Unlikely to require admission to NICU/SCBU for any other reasons e.g. respiratory distress
- Mother intending to breast-feed

Results


72/138
(52%)
25/66
(38%)
34/73
(47%)
28/68
(41%)
27/70
(39%)
1.5
1.0
0.5
0.0
Odds of [blood glucose] < 2.6mM
in first 48hours
0
200
400
800
1000
Cummulative Dose Dextrose (mg/kg)

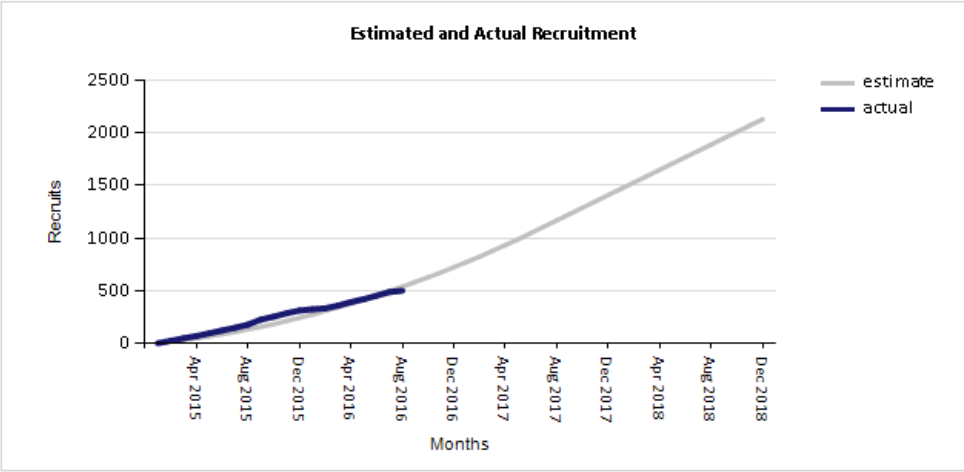
Results

OVERALL: any dose of dextrose gel vs placebo
RR 0.79; 95% CI 0.64-0.90, P = 0.03
NNT = 10, 95% CI 5-115

Prophylactic oral dextrose gel in babies at risk reduced the incidence of hypoglycaemia

The most effective dose was a single dose of 0.5 ml/kg

main-hPOD



- 2,129 babies
- Primary outcome: Admission to NICU
- Commenced randomisation January 2015
- Currently 8 centres recruiting in NZ
- CTA/ethics Australia – additional 14 sites
- 503 recruited as of 18 Aug
- MCNZ - 5 professional activity points for significant contribution

Te Tatau o te Whare Kahu
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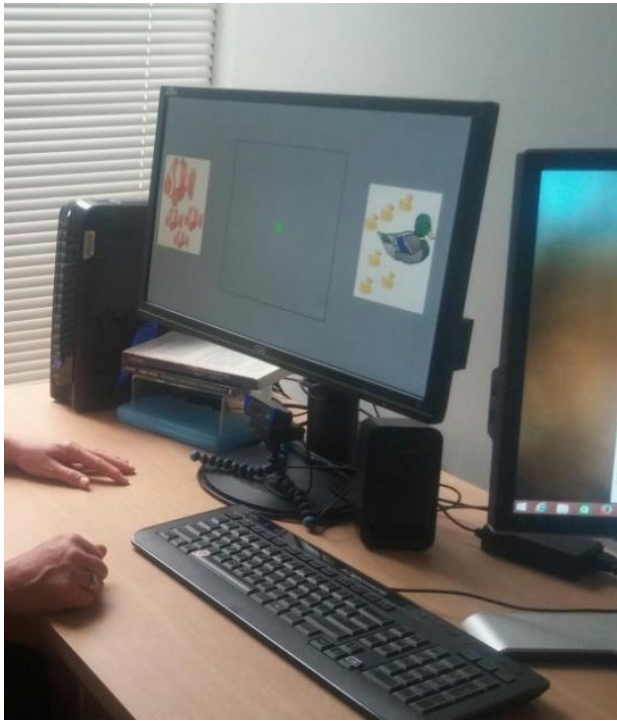
Follow-Up Study: hPOD-FU@2

Primary outcomes

Neurosensory impairment

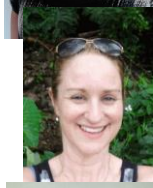
Processing difficulty
(motion coherence
and executive function)

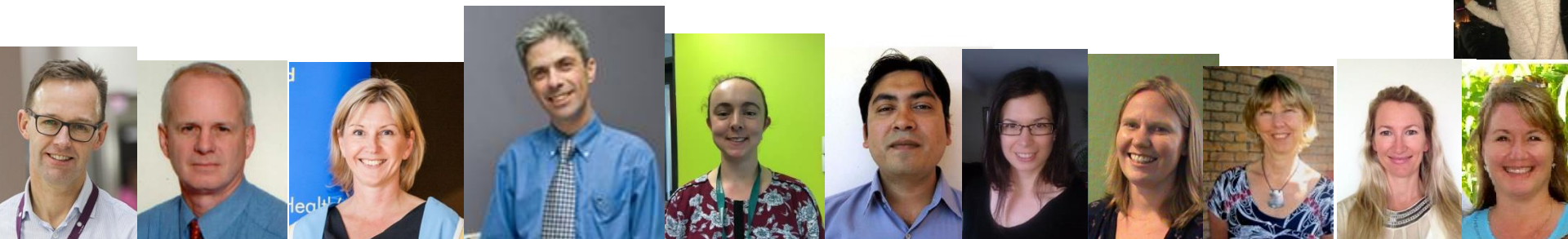


Progress

- 259/415 seen
- 91% retention rate

Thank you!





Extra slides

Results

	Placebo	Dextrose 0.5ml/kg	RR (CI)	p	Dextrose 1ml/kg	RR (CI)	p
SINGLE dose n=209	70	66			73		
Hypoglycemia	41 (59)	25 (38)	0.65 (0.45,0.93)	**0.02**	34 (47)	0.80 (0.58,1.09)	0.15
NICU admission	10 (14)	3 (5)	0.32 (0.09,1.11)	0.07	3 (4)	0.29 (0.08,1.00)	0.05
for hypoglycemia	9 (13)	1 (2)	0.12 (0.02,0.90)	**0.04**	3 (4)	0.32 (0.09,1.13)	0.08
Formula at 6wks	32/66 (48)	28/61 (46)	0.95 (0.65,1.37)	0.77	32/70 (46)	0.94 (0.66,1.35)	0.75
	Placebo	**Dextrose 0.5ml/kg x 4**	**RR (CI)**	**p**	**Dextrose 1ml/kg x 1 0.5ml/kg x 3**	**RR (CI)**	**p**
MULTIPLE dose n=206	68	68			70		
Hypoglycemia	35 (51)	28 (41)	0.80 (0.55,1.15)	0.23	28 (40)	0.78 (0.54,1.12)	0.18
NICU admission	4 (6)	8 (12)	2.00 (0.63,6.33)	0.24	4 (6)	0.97 (0.25,3.73)	0.97
for hypoglycemia	3 (4)	4 (6)	1.33 (0.31,5.73)	0.70	2 (3)	0.65 (0.11,3.76)	0.63
Formula at 6 wks	28/63 (44)	22/61 (36)	0.81 (0.53,1.25)	0.34	29/65 (45)	1.00 (0.68,1.48)	0.98