NETS
Part of the Sydney Children's Hospitals Network

HYPOGLYCAEMIA OF THE NEWBORN

PRACTICE GUIDELINE ©

DOCUMENT SUMMARY/KEY POINTS

- Consider the risk of hypoglycaemia in any retrieved baby.
- In a baby at increased risk of hypoglycaemia a BGL is mandatory prior to transport.

CHANGE SUMMARY

- Updated reference papers
- Added glucose gel to the recommended treatments

READ ACKNOWLEDGEMENT

- All NETS clinical staff are to read and acknowledge they understand the contents of this guideline.

Approved by:	SCHN Policy, Procedure and Guideline Committee	NETS Executive
Date Effective:	1st June 2017	**Review Period**: 3 years
Team Leader:	Staff Specialist	**Area/Dept**: NETS

Rationale

- Glucose is an essential nutrient for the brain. Abnormally low levels can cause an encephalopathy and have the potential to produce long term neurological sequelae [1,2]
- Neurological sequelae have been reported in infants with recurrent or persistent BGL < 2.6 mmol/L[1].
- Hypoglycaemia is most commonly due to excessive insulin secretion and the clinician needs to be cognisant of this when planning therapy. Only occasionally is it due to lack of substrate.
- Neonates at increased risk of hypoglycaemia include:
    - Infants with a birth weight < 2.5 kg or > 4.5 kg
    - Macrosomic infants – these infants have increased subcutaneous fat, are plethoric and appear to have a small head in relation to their body size
    - Infants with polycythaemia Hb>200g/dL or HCT>65%
    - SGA/ IUGR infants
    - Premature infants – preterm infants have an impaired ability to produce a ketone (an alternative brain fuel) response to low glucose levels and low non protein energy stores
    - Infants of diabetic mothers – particularly if there is recent poor control, an elevated HBA_1C (> 6%) or Type 1 diabetics
    - Perinatal asphyxia
    - Sepsis
    - Haemolytic disease
    - Respiratory distress syndrome
    - Congenital heart disease
    - Infants with clinical signs of wasting – these infants have loose skin folds on the upper arms and thighs. The umbilical cord is often thin and there is loss of Wharton's Jelly. The birth weight can fall within the normal range.
    - Inborn errors of metabolism
    - Hypopituitarism or congenital adrenal hyperplasia

Management strategy

- Identify the newborn at risk and ensure a BGL is obtained at first contact with the referring hospital

- Offer clinical advice to the referring hospital; including specimens to be obtained on an hypoglycaemic sample ('critical bloods'), calculation of glucose requirement and clinical management. Note that critical bloods are less valid on a non-hypoglycaemic sample
- Note time of last blood glucose reading. The NETS team should repeat the blood glucose test if the last reading was low or if three hours have elapsed since last recording
- A BGL of < 2.6mmol/L is considered hypoglycaemia and requires appropriate management
- Hypoglycaemia requires a three-layered response – immediate elevation of BGL, prevention of rebound hypoglycaemia and an escalation in background therapy to prevent further hypoglycaemic episodes
- Infants with a history of or at risk of hypoglycaemia must have at least one functional intravenous cannula maintained throughout retrieval
- Check fluid rate and determine the concentration of glucose. Rectify any identified problems
- If BGL < 2.6 mmol/L give 2 mL/kg of 10% glucose over 5 minutes intravenously and increase maintenance fluids by 10-20 mL/kg/day. If the baby has perinatal asphyxia, you may consider increasing your total glucose concentration to 12.5% rather than increasing total maintenance fluid volume. Consult with the receiving and/or NETS consultant
- Repeat a BGL 15 mins after the bolus of glucose has been delivered
- If BGL normal, continue maintenance fluid and repeat BGL in one hour
- If BGL low at any time, and critical bloods not already obtained, obtain samples for insulin, cortisol and growth hormone and then repeat 2mL/kg of 10% glucose over 5 minutes intravenously and prevent further hypoglycaemia by adding one or more of the following:
  - increasing maintenance fluids – volume or concentration of glucose
  - commencing a glucagon infusion
  - treating with intravenous hydrocortisone.
- Recheck BGL within 30 minutes
- If hypoglycaemia persists, discuss with receiving neonatologist and/or NETS consultant
- Central venous access is necessary for delivery of glucose concentrations > 12.5%
- As a rule, premature babies with low gestation or IUGR (i.e. babies with low substrate) who have persistent hypoglycaemia require an increase in the IV concentration of glucose to 12.5% or 15%
- Conversely, babies who are LGA or whose hypoglycaemia is secondary to maternal diabetes are best managed with Glucagon, which helps to release substrate from the liver and muscles. Note that glucagon is available as a 1mg "Hypokit" in NSW hospitals.
- Calculate newborn's total Glucose intake in **milligrams/kg/minute**:

$$\textbf{Glucose in mg/kg/min} = \frac{\textbf{\% concentration x hourly rate}}{\textbf{Weight x 6}}$$

For example: 2kg newborn with IV 10% Glucose at 5mL/hour (60mL/kg/day)

Infusion rate = 10 x 5/2 x 6
= 4.2mg/kg/minute

- Further tests that maybe required include FFA, βOH butyrate and NH_3 (all on ice) along with electrolytes, liver function tests and urine metabolic screen – these can usually be performed at the tertiary hospital
- The calculation of glucose intake, recommended treatment doses and rates and summary of critical bloods is available via the NETS' Song Sheet. This can be used to guide referring hospitals as well as NETS' teams
- Optimise thermoregulation and respiratory support to minimise excessive utilisation of glucose

Education Notes

- Glucose is an essential nutrient for the developing brain.
- Koh[3] *et al* showed reversible disturbance in evoked potentials at glucose levels below 2.6 mmol/L in asymptomatic term infants. Therefore the definition of hypoglycaemia is a BGL of < 2.6 mmol/L
- Hypoglycaemia that is allowed to go unchecked leads to occipital parenchymal changes and can lead to blindness and cerebral palsy
- Recurrent moderate hypoglycaemia or a single episode of severe hypoglycaemia can result in impaired psychomotor development in growth restricted infants
- Symptoms of hypoglycaemia in the newborn include; jitteriness, tremors, hypotonia, apnoea, bradycardia, cyanosis, weak or high pitched cry and seizures
- Hypoglycaemia is often associated with hypothermia
- BGL measurement can be done from different sample types, e.g. whole blood or plasma. Samples measured at point-of-care by rapid indicator, are whole blood and can be 15% lower than plasma samples measured in laboratory. Hence, the importance of confirming point-of-care samples with laboratory testing. In retrieval, practice is not to wait for these results and treat from the glucose meter or portable blood analyser
- Critical samples and storage:

Test	Medium	Volume	Tube Type
Insulin, Cortisol, Growth Hormone	Room temperature	2mL	Lithium heparin tube usually green or red / gold top serum tube

Whenever sampling for laboratory blood glucose, it is important to ensure immediate analysis of the specimen. The laboratory should be informed the sample is imminent. Undue delay will result in falsely low BGLs and inappropriate management.

- FFA, beta hydroxybutyrate, lactate and amino acids maybe collected should hypoglycaemia be persistent following arrival at a tertiary hospital.

- Only use 10% Glucose to give a bolus, **NOT 25 - 50%**, to avoid refractory hypoglycaemia (high glucose infusion causes hyperglycaemia, which stimulates a surge in insulin secretion, and leads to hypoglycaemia when the bolus is completed). 50% Glucose is a hyperosmolar solution and is an irritant to veins
- Glucose concentrations of >12.5% should preferably be administered via central vein (e.g. UVC) as extravasation of a high concentration of glucose administered through a peripheral cannula may result in irritation and damage
- Persistent hypoglycaemia, requiring more than 10-12mg/kg/min glucose infusion, may need further investigation looking for metabolic or pancreatic disease. Investigations that should be performed in these instances include:

  - Serum ammonia
  - Serum lactate
  - Serum and urine ketones
  - Serum and urine amino acids
  - Urine reducing substances
  - Newborn screening test
  - Urine metabolic screen

- Recommended doses for pharmacological agents:
  - **HYDROCORTISONE:** 1– 2 mg/kg/dose IV every 6 hours for persistent hypoglycaemia after 2 days of glucose infusion rate of 12 mg/kg/min or more
  - **GLUCAGON:** Continuous IV infusion: 5 - 20 micrograms/kg/hour. Note: Glucagon is not recommended in IUGR babies as they are short of substrate
    - **Glucagon may be given IM in emergencies where IV access is difficult at 40micrograms/kg**
  - **10% Glucose solution** can also be given via gastric tube at 2mLs/kg
  - **Glucose oral gel** is effective in maintaining BGL whilst establishing breastfeeding in well babies
- Making higher glucose concentrations (percentage) in 50mL syringes, using added 50% glucose

  Formula = (Concentration (%) required – concentration in stock) x 1.25

  i.e. to make up 15% Glucose in 50 mL = (15% - 10%) x 1.25 = 5 x 1.25 = 6.25mL
  Therefore, add 6.25mL of 50% glucose to 43.75mL of 10% glucose to get final concentration of 15% Glucose

References

1. Boluyt N, van Kempen A, Offringa M. Neurodevelopment after neonatal hypoglycemia: a systematic review and design of an optimal future study. Pediatrics. 2006 Jun;117(6):2231-43. Review. PubMed PMID: 16740869.
2. Committee on Fetus and Newborn., Adamkin DH. Postnatal glucose homeostasis in late-preterm and term infants. Pediatrics. 2011 Mar;127(3):575-9. doi:1542/peds.2010-3851. Review. PubMed PMID: 21357346.
3. Stanley CA, Rozance PJ, Thornton PS, De Leon DD, Harris D, Haymond MW, Hussai K, Levitsky LL, Murad MH, Simmons RA, Sperling MA, Weinstein DA, White NH, Wolfsdorf JI. Re-evaluating "transitional neonatal hypoglycemia": mechanism and implications for management. J Pediatr. 2015 Jun;166(6):1520-5.e1. doi: 10.1016/j.jpeds.2015.02.045. Review. PubMed PMID: 25819173; PubMed Central PMCID:PMC4659381.
4. Adamkin DH, Polin R. Neonatal hypoglycemia: is 60 the new 40? The questions remain the same. J Perinatol. 2016 Jan;36(1):10-2. doi: 10.1038/jp.2015.125. Review. PubMed PMID: 26707690.
5. Güemes M, Hussain K. Hyperinsulinemic Hypoglycemia. Pediatr Clin North Am. 2015 Aug;62(4):1017-36. doi: 10.1016/j.pcl.2015.04.010. Review. PubMed PMID: 26210630.
6. Adamkin DH. Metabolic screening and postnatal glucose homeostasis in the newborn. Pediatr Clin North Am. 2015 Apr;62(2):385-409. doi: 10.1016/j.pcl.2014.11.004. Review. PubMed PMID: 25836704.
7. Boardman JP, Hawdon JM. Hypoglycaemia and hypoxic-ischaemic encephalopathy.Dev Med Child Neurol. 2015 Apr;57 Suppl 3:29-33. doi: 10.1111/dmcn.12729. Review. PubMed PMID: 25800489.
8. Mitanchez D, Burguet A, Simeoni U. Infants born to mothers with gestational diabetes mellitus: mild neonatal effects, a long-term threat to global health. J Pediatr. 2014 Mar;164(3):445-50. doi: 10.1016/j.jpeds.2013.10.076. Review. PubMed PMID: 24331686.
9. Rozance PJ. Update on neonatal hypoglycemia. Curr Opin Endocrinol Diabetes Obes. 2014 Feb;21(1):45-50. doi: 10.1097/MED.0000000000000027. Review. PubMed PMID: 24275620; PubMed Central PMCID: PMC4012366.
10. Tin W. Defining neonatal hypoglycaemia: a continuing debate. Semin Fetal Neonatal Med. 2014 Feb;19(1):27-32. doi: 10.1016/j.siny.2013.09.003. Review. PubMed PMID: 24148999.
11. Datye KA, Bremer AA. Endocrine disorders in the neonatal period. Pediatr Ann. 2013 May;42(5):67-73. doi: 10.3928/00904481-20130426-08. Review. PubMed PMID: 23641880.
12. Boardman JP, Wusthoff CJ, Cowan FM. Hypoglycaemia and neonatal brain injury. Arch Dis Child Educ Pract Ed. 2013 Feb;98(1):2-6. doi: 10.1136/archdischild-2012-302569. Review. PubMed PMID: 23086597.
13. Beardsall K. Measurement of glucose levels in the newborn. Early Hum Dev. 2010 May;86(5):263-7. doi: 10.1016/j.earlhumdev.2010.05.005. Review. PubMed PMID: 20542649.
14. Harris DL, Alsweiler JM, Ansell JM, Gamble GD, Thompson B, Wouldes TA, Yu TY, Harding JE; Children with Hypoglycaemia and their Later Development (CHYLD) Study Team. Outcome at 2 Years after Dextrose Gel Treatment for Neonatal Hypoglycemia: Follow-Up of a Randomized Trial. J Pediatr. 2016 Mar;170:54-9.e1-2. doi: 10.1016/j.jpeds.2015.10.066. PubMed PMID: 26613985; PubMed Central PMCID: PMC4769950.
15. McKinlay CJ, Alsweiler JM, Ansell JM, Anstice NS, Chase JG, Gamble GD, Harris DL, Jacobs RJ, Jiang Y, Paudel N, Signal M, Thompson B, Wouldes TA, Yu TY, Harding JE; CHYLD Study Group.. Neonatal Glycemia and Neurodevelopmental Outcomes at 2 Years. N Engl J Med. 2015 Oct 15;373(16):1507-18. doi: 10.1056/NEJMoa1504909. PubMed PMID: 26465984; PubMed Central PMCID: PMC4646166.
16. Thornton PS, Stanley CA, De Leon DD, Harris D, Haymond MW, Hussain K, Levitsky LL, Murad MH, Rozance PJ, Simmons RA, Sperling MA, Weinstein DA, White NH, Wolfsdorf JI; Pediatric Endocrine Society.. Recommendations from the Pediatric Endocrine Society for Evaluation and Management of Persistent Hypoglycemia in Neonates, Infants, and Children. J Pediatr. 2015 Aug;167(2):238-45. doi: 10.1016/j.jpeds.2015.03.057. PubMed PMID: 25957977.
17. Harris DL, Weston PJ, Signal M, Chase JG, Harding JE. Dextrose gel for neonatal hypoglycaemia (the Sugar Babies Study): a randomised, double-blind, placebo-controlled trial. Lancet. 2013 Dec 21;382(9910):2077-83. doi: 10.1016/S0140-6736(13)61645-1. PubMed PMID: 24075361.
18. Harris DL, Weston PJ, Harding JE. Incidence of neonatal hypoglycemia in babies identified as at risk. J Pediatr. 2012 Nov;161(5):787-91. doi: 10.1016/j.jpeds.2012.05.022. PubMed PMID: 22727868.
19. Harris DL, Battin MR, Weston PJ, Harding JE. Continuous glucose monitoring in newborn babies at risk of hypoglycemia. J Pediatr. 2010 Aug;157(2):198-202.e1. doi: 10.1016/j.jpeds.2010.02.003. PubMed PMID: 20338573.

Harris DL, Weston PJ, Battin MR, Harding JE. A survey of the management of neonatal hypoglycaemia within the Australian and New Zealand Neonatal Network. J Paediatr Child Health. 2014 Oct;50(10):E55-62. doi: 10.1111/j.1440-1754.2009.01599.x. PubMed PMID: 19863712.