Neonatal Intensive Care Unit - Hypoglycaemia Monitoring and Management

Guideline Responsibilities and Authorisation

Department Responsible for Guideline	NICU
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Target Audience	Clinical staff in Waikato NICU

Guideline Review History

Version	Updated by	Date Updated	Summary of Changes
1	Lela Yap	August 2023	Combining multiple guidelines for consensus approach New registration number allocated 6482 Withdrawal of: Diagnosis of hyperinsulinism protocol Ref 1397 Hypoglycaemia evaluation – neonatal procedure Ref 1721 Hypoglycaemia – Management of, protocol Ref 3122 to be reviewed in conjunction with • Postnatal neonatal hypoglycaemia for screening and management Ref. 6483
1.1	Jutta van den Boom	January 2024	Adding in definition of severe and prolonged hypoglycaemia

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Contents

1 Overview

1.1 Purpose

This guideline provides a general management approach for neonatal hypoglycaemia in the NICU with evidence-based recommendations for NICU staff. An individualised approach may be required.

Consider consulting paediatrics endocrinology for persistent or recurrent hypoglycaemia.

1.2 Staff group

Registered nurses and medical staff caring for newborn babies in the NICU, Waikato Hospital.

1.3 Patient group

Both hypoglycaemic neonates and at-risk neonates admitted to the NICU.

1.4 Exceptions / contraindications

Diagnosis and Management of late onset hypoglycaemia i.e. newborn is more than 5 days postnatal (no local guideline at present).

1.5 Definitions and acronyms

BGL	Blood glucose level (mmol/L)
CNS	Clinical Nurse Specialist
DAT	direct antiglobulin test
GDR	Glucose delivery rate
IDM	Infant of diabetic mother
IVF	Intravenous fluid
IVN	Intravenous nutrition
LGA	Large for gestational age - >95th centile on customised calculator
IUGR	Intrauterine growth restriction
Neonatal Hypoglycaemia	Blood glucose concentration < 2.6 mmol/L
NNP	Neonatal Nurse Practitioner
PN	Parenteral nutrition
RN	Registered Nurse
SGA	Small gestational age - <10th centile on customised calculator

SMO	Senior Medical Officer
TFV	Total Fluid Volume (in a 24-hour period)

1.6 Background

Neonatal hypoglycaemia (low blood glucose level (BGL)) is currently defined as a BGL < 2.6mmol/l, regardless of gestational age.

Untreated hypoglycaemia, whether it is transient, severe, or recurring, has been associated with brain injury and unfavourable neurodevelopmental outcomes. The goal is to maintain a safe BGL for all infants. Managing hypoglycaemia involves corrective measures, potential gradual adjustments in glucose delivery rate (GDR) until normal glucose levels are achieved, and ongoing monitoring to ensure stable glucose levels. If glucose infusions are inadequate in maintaining appropriate glucose levels, further investigations, alternative pharmacological interventions, and possible specialist referral are necessary, with the extent determined by the attending Senior Medical Officer (SMO).

Differential causes of Hypoglycaemia

Transient neonatal hypoglycaemia	Due to inadequate substrate stores and/or inability to mobilise these e.g., **prematurity, intrauterine growth retardation,** perinatal asphyxia, delayed or inadequate feeding. Due to increased glucose requirements e.g., birth asphyxia, sepsis, congenital heart disease, hypothermia, neurological problems (periventricular haemorrhage, convulsions).
Hyperinsulinism	**Maternal diabetes** Erythroblastosis faetalis (e.g., severe Rhesus disease) Leucine sensitivity Islet cell hyperplasia or hyperfunction Insulinoma Beckwith-Wiedemann Syndrome Maternal anti-diabetic drugs Neonatal Hyperinsulinaemic Hypoglycaemia (nesidioblastosis)
Endocrine Causes	Panhypopituitarism Hypothyroidism Growth hormone deficiency ACTH unresponsiveness
Inborn Errors of Metabolism	*Carbohydrate metabolism* Galactosaemia Glycogen Storage Disease Type I (Von Gierke's), also III and VI Fructose Intolerance *Amino Acid metabolism* Maple Syrup Urine Disease Proprionicacidaemia Methylmalonicacidaemia Hereditary Tyrosinaemia
Other Issues	Abrupt cessation of glucose infusion Exchange transfusion without glucose replacement Drugs (e.g., THAM, maternal β-blockers)

Presenting Symptoms

Numerous hypoglycaemic infants display no symptoms, and even among infants with symptoms, half may not be hypoglycaemic. Therefore, it is crucial to maintain a high level of clinical suspicion. Consequently, hypoglycaemia must be treated regardless of whether symptoms are present.

Possible signs include:

Signs of Neuroglycopaenia	Signs due to catecholamine response	Cardiac signs due to hypoglycaemia
• Abnormal cry, Jitteriness, Apnoea • Lethargy, apathy, hypotonia • Poor feeding, Convulsions	• Pallor • Sweating • Tachycardia	• Bradycardia, Hypotension • Heart Failure, Cardiac arrest

2 Clinical management

2.1 Competency required

NICU medical staff: Registrar, Neonatal Nurse Practitioner, Clinical Nurse Specialist, Consultant, Registered Nurses.

2.2 Management

Flowsheet – see Appendix A

Assess for:

- SGA/IUGR appearances with low subcutaneous fat
- dysmorphic features
- macrosomia (for infant of diabetic mother (IDM))
- direct antiglobulin test (DAT), blood group (rhesus incompatibility)
- Hepatomegaly, if present, might suggest enzymatic defect

2.3 Additional recommendations

- Monitor serum sodium with increased total fluid volume; particularly intravenous.
- Consider central access if infusion of glucose concentration > 12.5%.
- Consider avoiding glucose intravenous bolus when dealing with known or suspected hyperinsulinism. This may cause exponential release of insulin and subsequent rebound hypoglycaemia.
- Consider continuous feeds for the same reason

2.4 Further management for persistent or severe hypoglycaemia

2.4.1 Definition

A) Prolonged Hypoglycaemia

- Hypoglycaemia beyond 48 hours of birth despite adequate GDR

B) Persistent OR Severe Hypoglycaemia

- Episodes of hypoglycaemia beyond 7 days OR GDR requirement >8mg/kg/min

2.4.2 Calculate glucose delivery rate (GDR)

$$\text{GDR (mg/kg/min)} = \frac{\text{rate (ml/hr) x glucose (\%) X 10}}{\text{weight (kg) x 60 (minutes/h)}}$$

Glucose Calculator Starship Hospital

Cornell University GDR calculator

GDR and Osmolality Local Calculator

2.4.3 Investigations

		Indication as per definition above
Serum Insulin* (pmol/L)	(0.6 ml, plain tube)	A & B
Cortisol (nmol/L)	(0.6 ml, plain tube)	A & B
Growth Hormone (ng/ml)	(0.6 ml, plain tube)	A & B
TSH, fT4	(0.6 ml, plain tube)	B
β-OH butyrate (µmol/L)	(0.4 ml, heparin tube)	B
Lactate (mmol/L)	(0.5 ml in fluoride oxalate tube, on ice)	B
Ammonia (µmol/L)	(1 ml EDTA on ice – ring laboratory before taking sample)	B
(Carnitine profile)	Newborn Testing Card	B
Check urine for ketones	(store urine for organic and amino acids for later analysis).	B

*Hyperinsulinism

This is the most common diagnosis if ketones are negative, and the insulin level *inappropriately* high for a low blood glucose, e.g. BGL <2.2 mmol/L, insulin > 5 pmol/L

In certain at-risk infants the threshold may be moved to a higher BGL (e.g., 3.0 or 3.5 mmol/L) in order to provide substrate for brain metabolism.

2.4.4 Adjuvant therapy

Consider glucagon (glucagon for neonates), diazoxide (Starship, Diazoxide), steroids or surgery. Consider discussing with Starship Paediatric Endocrine Service.

Glucagon or Diazoxide must be discussed with SMO prior to prescribing. Chlorothiazide (Chlorothiazide for Neonates) is to be used with Diazoxide to reduce fluid retention.

2.5 Discontinuing therapy

- Glucose monitoring should continue while IV glucose/glucagon/diazoxide are gradually reduced. Rapid reductions in glucose infusion can cause rebound hypoglycaemia.
- Consider fasting period for babies with severe hyperinsulinism /Beckwith – Wiedemann syndrome for up to 6h with serial BGL measurements (at 3hr, 4hr, 5hr, 6hr) prior to discharge.

2.6 Potential complications

- Extravasation injury in NICU.
- Hyperglycaemia.

3 Patient information

Diazoxide: This medication is a section 29 drug preparation and parents should be informed that it is not registered for oral use in New Zealand.

4 Associated Te Whatu Ora Waikato Documents

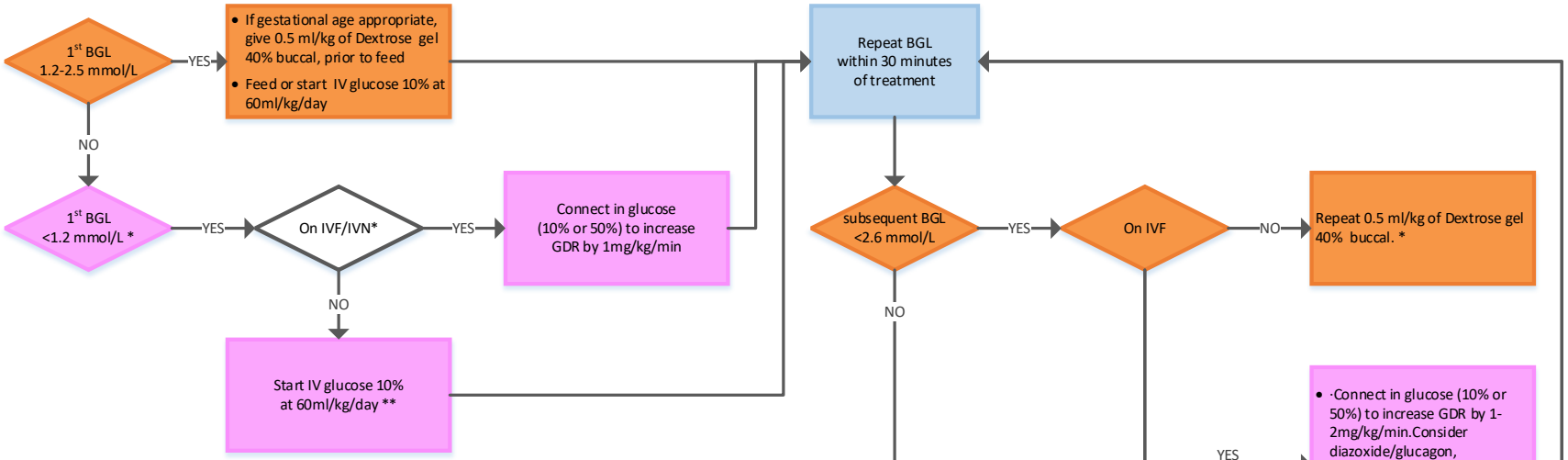
- Glucagon for neonates
- Chlorothiazide for Neonates
- Diazoxide Starship Child Health, Newborn Intensive care, Drug dosage guideline
- Enteral feeding: standardisation of feeding in Newborn Intensive Care Unit (NICU)
- Hypoglycaemia Monitoring and Management – Postnatal Ward

5 Bibliography

- Cornblath MD, Hawdon JM, Williams AF, Aynsley-Green A, WardPlatt MP, Schwartz R, et al. Controversies regarding definition of neonatal hypoglycemia:suggested operational thresholds. Pediatrics 2000;105: 1141-5.
- Lucas A, Morley R, Cole TJ. Adverse neurodevelopmental outcome of moderateneonatal hypoglycaemia. BMJ. 1988;297:1304-8.
- Harris DL, Weston PJ, Harding JE. Incidence of neonatal hypoglycemia in babies identified as at risk. Journal of Pediatrics 2012;161:787-91.

- Kaiser JR, Bai S, Gibson N, Holland G, Lin TM, Swearingen CJ, et al. Associationbetween transient newborn hypoglycemia and fourth-grade achievement test proficiency: A population-based study. JAMA Pediatrics. 2015.
- Kerstjens JM, Bocca-Tjeertes IF, de Winter AF, Reijneveld SA, Bos AF. Neonatal morbidities and developmental delay in moderately preterm-born children. Pediatrics. 2012;130:265-72.
- McKinlay CJD, Alsweiler JM, Anstice NS, Burakevych N, Chakraborty A, Chase JG,et al. Association of neonatal glycemia with neurodevelopmental outcomes at 4.5 years. JAMA Pediatr. 2017;171:972-83.
- McGowan JE, Price-Douglas W, Hay WW. Glucose homeostasis. In: Merenstein GB, Gardner SL, eds. Handbook of neonatal intensive care. 6th ed. St Louis: Mosby Elsevier; 2006. p. 368-90.
- Hay WW, Raju T, Higgins R, Kalhan S, Devaskar S. Knowledge gaps and research needs for understanding and treating neonatal hypoglycaemia: workshop report from Eunice Kennedy Shriver National Institute of Child Health and Human Development. J Pediatr 2009;155:612-7.
- 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. The Lancet. 2013;382:2077-83.
- Weston PJ, Harris DL, Harding JE. Dextrose gel treatment does not impairsubsequent feeding. Arch Dis Child Fetal Neonatal Ed. 2017:539-41.
- Harris DL, Gamble GD, Weston PJ, Harding JE. What happens to blood glucose concentrations after oral treatment for neonatal hypoglycemia? J Pediatr. 2017;190:136-41.
- Oral dextrose gel for the treatment of hypoglycaemia in newborn infants, March 2022, Cochrane database of systematic reviews 2022(3), retrieved 23rd March 2022.
- Hegarty JE, Harding JE, Gamble GD, Crowther CA, Edlin R, Alsweiler JM. Prophylactic Oral Dextrose Gel for Newborn Babies at Risk of Neonatal Hypoglycaemia: A Randomised Controlled Dose-Finding Trial (the Pre-hPOD Study). PLoS Med. 2016 Oct 25;13(10):e1002155. doi: 10.1371/journal.pmed.1002155. PMID: 27780197; PMCID: PMC5079625.
- Pediatric Endocrine Society - (http://dx.doi.org/10.1016/j.jpeds.2015.03.057
- NHS - https://www.clinicalguidelines.scot.nhs.uk/nhsggc-guidelines/nhsggc-guidelines/neonatology/persistent-or-refractory-hypoglycaemia-in-the-neonate-a-guideline-for-management/

Appendix A – Management of Hypoglycaemia in the NICU



Considerations:

- 2 X BGL <2.6mmol/L despite Dextrose Gel and Feeding ->start glucose 10%, 60ml/kg/day
- May continue to feed in addition to all interventions
- Monitor serum sodium for dilutional hyponatraemia
- *D10 and D50 are the current available dextrose concentrations at Te Whatu Ora, Waikato.

* Consider IV gluclose 10% bolus, 2ml/kg

** If fluid restricted, consider "connect in" Dextrose 50% (requires central venous access)

*** 3 consecutive results are required, this does not mean over three consecutive feeds. Consider spacing BGL monitoring based on clinical picture to cover a recommended 24 hours.

**** recommended maximum total fluid volume day 0/1 is 90ml/kg/day