



Topic Expert Group: Medical care and clinical practice

Hypoglycaemia in at risk term infants

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Target group

Term newborn infants and parents

User group

Healthcare professionals, neonatal units, hospitals, and health services

Statement of standard

Measures are taken to identify, prevent, and manage hypoglycaemia in newborn infants who are at risk for impaired metabolic adaptation, including those with growth restriction, maternal diabetes, asphyxia, maternal beta-blocker medication.

Rationale

The goal is to prevent the adverse effect of hypoglycaemia while minimising unnecessary separation of mother and the newborn infant.

Hypoglycemia in newborn infants is associated with risk for brain damage and neurodevelopmental sequelae. (1) At birth, the discontinuation of nutrients from the mother results in a decline in plasma glucose level during the first two hours of postnatal life to as low as 1.1-1.4 mmol/L (20-25 mg/dL) that is considered to be part of normal adaptation to postnatal life. (2,3) Many newborn infants tolerate these initially low blood glucose levels even though glucose is the major oxidative fuel of the brain, because the neonatal brain also has the capacity to oxidise ketone bodies and lactate. After the first two postnatal hours, glucose concentration rises to more stable concentrations. During this period, endogenous production of glucose is promoted by glycogenolysis and gluconeogenesis. Enhancement of fat oxidative metabolism also contributes to the production of ketone bodies. Metabolic neonatal transition is integrated under the influence of a postnatal hormonal surge and timely production of key regulatory enzymes. (4)

In addition to the risk categories listed above, perturbations of adaptive responses can occur in preterm infants and those with, sepsis, haemolytic disease and specific inborn errors of metabolism. They can also occur in term infants with congenital disorders that prevent infants from mounting an adequate counter-regulatory metabolic and endocrine response, such as hyperinsulinism. (5)

Benefits

Short-term benefits

- Reduced exposure to potentially harmful hypoglycemia in at risk infants (6)
- Reduced unnecessary investigations and interventions (7)
- Minimised separation of mother and infant (consensus)
- Increased rate of diagnoses of infants with hypoglycemic disorders before discharge (8)



Long-term benefits

- Improved neurologic outcome (consensus)

Components of the standard

Component	Grading of evidence	Indicator of meeting the standard
For parents and family		
1. Parents are informed by healthcare professionals about the importance of early energy provision and blood glucose monitoring. (9)	A (Low quality) B (High quality)	Patient information sheet
For healthcare professionals		
2. A unit guideline on identification, prevention, and management of hypoglycaemia is adhered to by all healthcare professionals.	B (High quality)	Guideline
3. Training on identification, prevention, and management of hypoglycaemia is attended by all responsible healthcare professionals.	B (High quality)	Training documentation
4. Risk factors for hypoglycaemia are identified at birth. (10)	A (Moderate quality)	Clinical records, guideline
5. An early feed, within one hour, is provided. (11,12)	A (High quality)	Clinical records, guideline
6. Thermal care, ideally given by skin-to-skin positioning, is provided. (13)	A (Moderate quality)	Clinical records, guideline
7. Blood glucose is measured at predetermined times. (6)	A (Moderate quality)	Clinical records, guideline
8. Observation of well-being and feeding documentation is conducted. (14)	B (High quality)	Clinical records, guideline
9. Interventions are administered according to operational thresholds approach. (15)	B (High quality)	Clinical records, guideline



For neonatal unit

10. A unit guideline based on an operational threshold approach using values advocated by professional bodies is available and regularly updated in all maternity and neonatal units. (16)	A (Low quality) B (High quality)	Guideline
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For hospital

11. Training on identification, prevention, and management of hypoglycaemia is ensured.	A (High quality) B (High quality)	Training documentation
12. Equipment suitable for immediate and reliable blood glucose measurements is provided. (17)	A (High quality) B (High quality)	Audit report
13. Training in awareness of the limitations of the devices used for blood glucose monitoring is ensured. (17)	A (High quality) B (High quality)	Training documentation

For health service

14. A national guideline based on an operational threshold approach using values advocated by professional bodies is available and regularly updated.	B (High quality)	Guideline
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Where to go – further development of care

Further development	Grading of evidence
For parents and family N/A	
For healthcare professionals N/A	
For neonatal unit N/A	
For hospital N/A	
For health service	
<ul style="list-style-type: none">• Prioritise scientific studies investigating impaired metabolic adaptation, and the long term consequences of hypoglycaemia with or without clinical symptoms.	B (Moderate quality)



Getting started

Initial steps

For parents and family

- Parents are verbally informed by healthcare professionals about the importance of early energy provision and blood glucose monitoring.

For healthcare professionals

- Attend training on identification, prevention, and management of hypoglycaemia.
- Promote early skin-to-skin contact and breastfeeding as standard care.

For neonatal unit

- Develop and implement a unit guideline on identification, prevention, and management of hypoglycaemia, based on an operational threshold approach using values advocated by professional bodies.
- Develop information material about the importance of early energy provision and blood glucose monitoring for parents.

For hospital

- Support healthcare professionals to participate in training on identification, prevention, and management of hypoglycaemia.

For health service

- Develop and implement a national guideline on prevention, diagnosis and management of hypoglycaemia, based on an operational threshold approach using values advocated by professional bodies.

Description

Glucose thresholds for intervention

- It is currently unknown at which glucose concentrations and after what duration neurologic injuries occur in newborn infants.
- Blood glucose levels below 1.0 mmol/L (18 mg/dL) that are associated with acute neurological dysfunction present the greatest risk of cerebral injury. (18–21)
- The tolerance to low glucose levels probably varies due to the newborn infant's ability to produce alternative substrates. (22)

→ Need to implement practices that prevent harm that results from unrecognised or untreated hypoglycemia whilst minimising unnecessary interventions and admission in neonatal unit.

- Measures to prevent and detect hypoglycaemia should be undertaken after birth in infants at risk, including: thermal care with skin-to-skin; support of breastfeeding; early energy provision and monitoring of blood glucose starting within the first hours of life.
- Feeding should be observed and abnormal feeding (not waking for feeds, not latching at the breast, not sucking effectively, appearing unsettled) should be recorded by the healthcare team.
- Glucose monitoring should be initiated before the second feed and no later than four hours after birth in asymptomatic infants, or at any time if there are abnormal clinical signs.



- Blood glucose concentration should be measured with validated devices. Local guidelines should be based on the operational threshold approach, using values advocated by professional bodies in their own country.

The lack of a clear evidence base for defining cerebral energy sufficiency is reflected in the contrast of recommendations between different organisations. (23)

1. Cornblath Operational Thresholds (2000), updated on review of the literature subsequently (14), and used by the British Association of Perinatal Medicine (2017). The suggested operational threshold concentrations at which clinicians should consider intervention are (15):
 - Blood glucose level <2 mmol/L (36 mg/dL) in an asymptomatic baby, that remains below the same value at next measurement.
 - A single measurement <2.5 mmol/L (45 mg/dL) in a newborn with abnormal clinical signs.
 - A very low concentration of blood glucose <1.0 mmol/L (<18 mg/dL) indicates the need for intravenous glucose infusion aimed at raising plasma glucose concentration above 2.5 mmol/L. (45 mg/dL)

In symptomatic newborn infants with documented profound recurrent or persistent hyperinsulinic hypoglycaemia, therapeutic levels of 3.5 mmol/L (60 mg/dL) are recommended. (15) Infants with hypoxic ischemic encephalopathy have abnormal clinical signs by definition and the threshold of 2.5 mmol/L (45 mg/dL) should be used. (24)

2. The American Academy of Pediatrics (AAP) (2011)
The American Academy of Pediatrics (AAP) proposed an algorithm with suggested thresholds for intervention in at risk newborn infants at ≥ 34 weeks' gestation depending upon postnatal age: 1.4-2.2 mmol/L (25-40 mg/dL) in the first 4 hours, 1.9-2.5 mmol/L (35-45mg/dL) from 4-24 hours and 2.5 mmol/L (45 mg/dL) after 24 hours. (11)
3. The Paediatric Endocrine Society (2015)
Recently, the Paediatric Endocrine Society (PES) recommended higher plasma glucose levels to be considered safe in newborn infants: plasma glucose should be kept above 2.8 mmol/L (50 mg/dL) during the first 48 hours and above 3.3 mmol/L (60 mg/dL) for infants older than 48 hours. (8)

Measurement of glucose levels

- Accurate measurement of blood glucose level is essential for diagnosis and management of neonatal hypoglycaemia.
- The ward-based blood gas biosensor should be considered the reference standard for measuring blood glucose based on accuracy and speed of result availability.
- Blood gas analysers will produce glucose results as a calculated 'plasma glucose equivalent' concentration that should agree with laboratory plasma glucose results in the majority of cases.
- Most handheld glucometers also report results as 'plasma glucose equivalents', some devices are available that measure true whole blood glucose by rupturing the blood cells and measuring combined plasma and cellular glucose.
- This true whole blood glucose may be 10-15% lower than the corresponding plasma glucose. Practitioners should be aware that all current cot side



technologies are prone to some inaccuracy, particularly in the range 0-2.0 mmol/l.

- If handheld glucometers are being used to screen for low blood glucose, only those devices conforming to the ISO 15197:2013 standard should be used and their limitations should be understood: possible error of +/- 0.8 mmol/l (14.4 mg/dL) for values <5.5 mmol/l (<99 mg/dL).
- If a handheld glucometer is used, low values should be confirmed using an accurate method. (17)

Other considerations

- Oral dextrose gel may be considered as an adjunct to a feeding plan in newborn infants at risk of hypoglycaemia.
- Newborn infants presenting with clinical signs of hypoglycaemia or with very low glucose levels should be treated with intravenous dextrose (an intravenous bolus of 2.5 ml/kg 10% glucose) as soon as possible, followed by constant rate infusion of glucose.
- Newborn infants with risk factors should not be discharged until at least two adequate-level consecutive pre-feed blood glucose measurements have been made, and effective feeding has been established over several fast-feed cycles.
- Hypoglycemia that persists beyond 72 hours after birth might have a different etiology than “transitional neonatal hypoglycemia” and requires specific investigations. (8)

Source

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