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Title - Guideline Review: Identification and Management of Neonatal Hypoglycaemia in the Full Term Infant (British Association of Perinatal Medicine - Framework for Practice)

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Guideline Review

Identification and Management of Neonatal Hypoglycaemia in the Full Term Infant (British Association of Perinatal Medicine - Framework for Practice)

Background:

Hypoglycaemia was the third most common reason for admission of term babies to neonatal units in England in the period 2011-2013.[1] Of those babies admitted with 'hypoglycaemia', one third had a blood glucose level higher than the WHO threshold of 2.6mmol/l, while half did not require intravenous dextrose.[1] These findings suggest that a significant number of babies may be separated from their mothers inappropriately. There is also significant variability in defining at-risk groups and intervention thresholds.[1] Guidance should seek to minimise the risk of potentially devastating brain injury that can result from severe neonatal hypoglycaemia, without exposing large numbers of babies to the harm of unnecessary interventions, separation from their mothers, and neonatal unit admission.

The British Association of Perinatal Medicine (BAPM) published its framework for identification and management of hypoglycaemia in term newborns in April 2017.[2] The working group was made up of neonatologists, midwives, an infant feeding coordinator, officers from NHS Improvement and the Unicef Baby Friendly Initiative, and a parent representative. They reviewed published literature, and used national audit data and themes arising from cases of litigation to formulate the guidance. Professional consensus was used when there was insufficient evidence.

Previous guidelines
There are many consensus guidelines covering neonatal hypoglycaemia including World Health Organisation (WHO) guidance (1997),[3], an American Academy of Pediatrics (AAP) clinical report (2011)[4] and the 2015 National Institute for Health and Care Excellence (NICE) guideline[5] (Table 1).

Table 1: Key guidance prior to BAPM framework for practice

	WHO[3]	AAP[4]	NICE[5]
Population to screen	Infants of diabetic mothers, small and large for gestational age (with caveats)	Late preterm (≥34 weeks), infants of diabetic mothers, small and large for gestational age	N/A (guidance covers only infants of diabetic mothers)
Threshold for treatment of asymptomatic hypoglycaemia	2.6mmol/l	35mg/dl (approx. 2.0mmol/l)	2.0mmol/l at two consecutive readings

What does the guideline recommend?

1. Prevention of hypoglycaemia in at-risk babies
Newborns at risk of hypoglycaemia are identified in Table 2. They should be managed proactively to prevent hypoglycaemia. This includes providing thermal care, regular monitoring and intensive breastfeeding support with a maximal feed interval of three hours. The first feed should be offered within the first hour of life and the first blood glucose level checked before the second feed, 2-4 hours after birth.

For at-risk babies who do not show signs of effective breastfeeding:

- Encourage continuous skin-to-skin contact with mother
- Teach mother to hand express and give resulting colostrum to the baby

- Advise mother to hand express at least 8 times per 24 hours, and continue intensive feeding support until breastfeeding is established
- If no colostrum is available, or when there is informed maternal choice not to express, consider 10-15ml/kg formula per feed until feeding is effective or colostrum available

Table 2: Babies at risk of neonatal hypoglycaemia

Birth weight <2nd centile, or clinically wasted
Infants of diabetic mothers (regardless of type or treatment used during pregnancy)
Infants of mothers taking beta-blockers (in third trimester and/or at time of delivery)
Moderate and late preterm babies (noted in the guidance to avoid confusion, but this guideline is aimed at term babies and further advice does not necessarily apply to this subset of babies)

2. Special cases for assessment outside 'at-risk' categories

Table 3 shows other situations when newborns should have a blood glucose measurement.

Long feed intervals in the first 24-48 hours of life can be a normal pattern.[3,6] However, reluctance to feed may also be a sign of an underlying medical problem. Babies who are not latching to the breast, not suckling effectively or not waking for feeds should have:

- Clinical assessment for signs of underlying illness within 6 hours of birth
- Clinical status monitored 4 hourly
- Intensive breastfeeding support as outlined above in the section on babies at-risk and feeding ineffectively
- Check blood glucose level only if there are abnormal clinical signs, or the period of reluctance to feed follows a period of normal feeding

Table 3: Clinical presentations triggering blood glucose measurement

Perinatal acidosis (cord arterial/infant pH <7.1 and base deficit ≤ -12.1mmol/l)
Hypothermia (<36.5) not attributed to environmental factors
Suspected or confirmed early onset sepsis*
Cyanosis or apnoea
Altered level of consciousness, seizures, hypotonia, excessive lethargy or high pitched cry
Reluctance to feed, only with abnormal clinical signs or if reluctance follows a period of normal feeding

*during the consultation process the guideline authors were asked if suspected sepsis included babies with risk factors for sepsis but no clinical signs of sepsis. The authors replied that it would be prudent to measure a blood glucose level on any baby starting intravenous antibiotics

3. Blood glucose level thresholds for intervention

Intervention is required for blood glucose:

- <1.0mmol/l at any time
- <2.0mmol/l in a baby at risk for hypoglycaemia
- <2.5mmol/l with abnormal clinical signs (this includes all infants with hypoxic-ischaemic encephalopathy)
- <3.0mmol/l in infants with suspected hyperinsulinism in the first 48 hours (<3.5mmol/l thereafter)

If blood glucose level is <1.0mmol/l, arrange urgent medical review and treat with intravenous 10% glucose bolus and infusion. Use post intervention blood glucose levels to guide increasing glucose delivery rate until blood glucose levels are >2.5mmol/l. Enteral feeds, including breastfeeding, should continue if possible.

If blood glucose level is 1.0-1.9mmol/l, 40% buccal dextrose gel can be used alongside intensive feeding support. Urgent medical review is needed if more than two doses of dextrose gel are required consecutively.

Note, the guidance suggests applying the 'suspected hyperinsulinism' threshold when:

- Blood glucose level remains <2.0mmol/l on three or more occasions in the first 48 hours despite adequate energy provision
- OR if a glucose infusion rate greater than 8mg/kg/min is required

How would this guidance change practice?

What would I do differently?

- Use 40% buccal dextrose gel 200mg/kg alongside intensive breastfeeding support for at-risk babies who are asymptomatic with blood glucose levels 1.0-1.9mmol/l in the first 48 hours of life (multiple readings at this level require further investigation and escalation in management)
- Rechecking blood glucose level should usually occur before the next feed – 'post-feed' levels are not required. Post intervention glucose level (after 30 mins) is only required after intravenous dextrose bolus or increase in intravenous dextrose volume or concentration
- At-risk babies can stop blood glucose monitoring once they have had two consecutive values ≥2.0mmol/l

What would I continue doing as before?

- Use clear criteria to define babies at risk of hypoglycaemia, and manage proactively to prevent hypoglycaemia
- Encourage breastfeeding in all babies and be aware of intensive breastfeeding support techniques before suggesting infant formula feeding plans
- Provide verbal and written information to parents about hypoglycaemia and its management

What would I stop doing?

- Do not define at-risk babies by a generic weight cut off – exact gestation and sex-specific 2nd centile values should be used (table provided in the guidance)
- Do not define and treat large for gestational age babies as at risk for hypoglycaemia, unless there are dysmorphic features suggestive of Beckwith-Wiedemann or there is evidence of maternal diabetes
- Do not check blood glucose level purely because of jitteriness, as this is common and, when present on its own, is not a sign of hypoglycaemia
- Do not check blood glucose level in an asymptomatic, term baby purely because of reluctance to feed in the first 48 hours of life. Consider doing so if reluctance to feed follows a period of normal feeding, or there are clinical signs suggestive of underlying illness
- Do not treat blood glucose levels ≥2.0mmol/l, unless the baby is symptomatic, or has suspected hyperinsulinism
- Do not rely on low blood glucose measurement on a handheld glucometer, as they have a possible error of ±0.8mmol/l for values <5.5mmol/l. If a handheld glucometer is used, confirm low values with a ward based blood gas biosensor
- Do not treat breast milk and formula feed volumes as interchangeable – formula feed has been associated with lower availability of alternative cerebral fuels such as ketone bodies. No specific volume target is required for expressed colostrum, whereas formula feeds should be 10-15ml/kg per feed

Unresolved controversies:

The guidance mentions that further evidence is awaited to advise on antenatal expression of colostrum when risk of hypoglycaemia is known before birth, and on the use of dextrose gel as a prophylactic measure to avoid hypoglycaemia. The working party did not feel that they could offer advice on the use of donor breast milk due to the absence of data in this population. In addition, there is a move to consider alternative cerebral fuels such as lactate and ketones when making decisions about hypoglycaemia treatment. This emerging research was not considered in the guidance.

Box 1: Critical Review

- Choosing a threshold blood glucose level for intervention is controversial, in part due to the lack of available evidence. Two opinions on this area accompany this article.
- Suspected sepsis is listed as a condition requiring blood glucose level. However many clinically well babies have investigation soon after birth for 'suspected sepsis' due to risk factors such as prolonged rupture of membranes, maternal group B streptococcus carriage and maternal sepsis/chorioamnionitis. These babies would therefore have a blood glucose measurement at or near the physiological nadir, which could lead to overtreatment. An alternative would be to request midwifery staff to do a one-off blood glucose level at 3-4 hours of age, rather than checking the blood glucose at the time of other blood tests.
- The guideline does not give a suggested or acceptable volume for colostrum given orally to babies not feeding well, due to lack of robust evidence on this topic. This is welcome, as it will reduce the demand for physiologically impossible volumes of colostrum, which currently happens when babies are commonly placed on 'feeding plans' of 60ml/kg/day on day 1. Colostrum intake has been estimated at 6-10ml/kg/day on day 1 and 13-25ml/kg/day on day 2 in healthy newborns,[7,8] which would equate to approximately 0.5-1ml/kg per feed on day 1 and 1-3ml/kg per feed on day 2, depending on feed frequency. However, according to the guidance, a low birthweight baby not feeding effectively at the breast and with a blood glucose of 1.1mmol/l could be given as little as 0.2ml colostrum, if this is all that the mother can express, and not have another blood glucose measurement for 3 hours. This could then potentially lead to several hours of significant hypoglycaemia if this amount of colostrum is not sufficient. Some clinical judgement will be necessary for applying guidelines to individual infants when colostrum volumes are low. The guidance also advises that dextrose gel can be given alongside colostrum
- The guidance recommends the use of dextrose gel when blood glucose level is 1.0-1.9mmol/l based on the 'Sugar Babies' trial[9]; however, it should be noted that this trial used a treatment threshold of 2.6mmol/l so dextrose gel has not been tested at the threshold recommended in this guidance

Clinical bottom line

- Proactive management of babies at risk of hypoglycaemia includes thermal care, skin-to-skin contact and breastfeeding support
- First line management of ineffective feeding is intensive breastfeeding support and frequent breast expression with administration of colostrum
- A threshold for intervention of blood glucose level 2.0mmol/l can be used unless there is suspected hyperinsulinism or symptoms suggesting neurological dysfunction
- 40% dextrose gel is the first line intervention, alongside intensive feeding support, in an asymptomatic baby when blood glucose level is 1.0-1.9mmol/l

Competing Interests

IL is a trustee of a small charity providing community breastfeeding support (Oxfordshire Breastfeeding Support)

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