Guideline

Hyperglycaemia Management of Preterm Infants in NICU

Key points

Neonatal hyperglycaemia is:

- defined as a true blood glucose concentration (TBG) ≥ 10 mmol/L
- associated with mortality and morbidity, especially sepsis
- treated when TBG ≥ 10mmol/L for more than 4 hours or TBG ≥ 10mmol/L in association with ≥ 2+ glycosuria, with a reduction in glucose delivery, or insulin infusion to maintain TBG 5 - 9 mmol/L

1. Purpose

This clinical guideline outlines the approach in management of hyperglycaemia in preterm babies at the Women's.

Hyperglycaemia occurs frequently in extremely low birthweight (ELBW) preterm infants[1,2]. The aetiology is multifactoral, but includes secretion of inactive proinsulin by an immature pancreas[3], inability to suppress hepatic gluconeogenesis in the presence of intravenous (IV) glucose administration[4], and a paucity of insulin-sensitive peripheral tissues[5]. Hyperglycaemia is associated with neonatal mortality and a number of neonatal morbidities (including IVH, white matter injury, retinopathy of prematurity and sepsis)[6-8]. Hyperglycaemia may also disrupt the normal development of the endocrine pancreas[9]. Insulin treatment to control hyperglycaemia in critically ill adults and children is associated with increased survival and decreased rates of sepsis[10].

2. Definitions

Hyperglycaemia: True blood glucose (TBG) ≥ 10mmol/L

There is continued uncertainty as to what constitutes a level of hyperglycaemia that is likely to result in an adverse outcome and thus justifies specific intervention[11]. Once the renal tubular threshold is breached, glucose is lost into the urine, and glucose content of lower and upper airway secretions increases with a linear relationship once blood glucose concentrations > 8mmol/L[12]. Excreted glucose provides a substrate for bacterial and fungal growth and promotes polyuria, which may worsen electrolyte imbalance and metabolic acidosis in fragile ELBW infants[13]. In preterm infants with hyperglycaemia, controlling blood glucose concentrations to a target of < 10 mmol/L is associated with school-age neurodevelopmental outcomes that are similar to those of preterm infants without hyperglycaemia[14].

3. Responsibilities

Staff caring for ELBW infants with hyperglycaemia in Neonatal Intensive Care.

4. Guideline

4.1 Prevention

Neonatal hyperglycaemia occurs in ELBW infants on or after postnatal day 3. This is often in association with an iatrogenic increase in IV carbohydrate delivery. Small, early enteral feeds of expressed breast milk (EBM) are associated with a reduced incidence of hyperglycaemia[15].

4.2 Indication for treating hyperglycaemia:

- TBG ≥ 10mmol/L for more than 4 hours or TBG ≥10mmol/L in association with ≥ 2+ glycosuria.

It may be reasonable to continue current management if the hyperglycaemia occurs within the first 3 days of postnatal life, or if the hyperglycaemia is known to be associated with a short-term stressor (such as surgery or pulses of postnatal corticosteroids); however the risk of sepsis in these situations should be considered.

4.3 Management

4.3.1 Reduce glucose intake

If infused glucose levels are high (> 8-10mg/kg/min), reduction of glucose intake alone may be sufficient to decrease TBG to an acceptable level (< 10 mmol/L). However, it is important not to restrict total energy intake to ELBW infants who are at risk of postnatal growth failure, a condition associated with adverse neurodevelopmental outcome[16]. High glucose infusion rates are more likely in infants where multiple medications are made up in 10% glucose, or the total daily fluid intake has been rapidly increased (this may have been in response to early hypoglycaemia, or hypernatraemia).

The process includes the following:

- Aim for TBG < 10mmol/L
- Do not reduce glucose intake below 4mg/kg/min
- Do not reduce total fluid intake below that required to maintain hydration
- Ensure maximal lipid and IVN allowances are being given within the TFI. Change infusion solutions containing 10% glucose to 5% glucose, 0.9% sodium chloride or 0.45% sodium chloride (if compatible) before decreasing total fluid intake
- Document glucose infusion rates for all infants with hyperglycaemia

Glycosuria alone should not initiate reduction of glucose intake if TBG is <10 mmol/L.

4.3.2 Insulin infusion

If glucose intakes cannot be reduced, or reduction does not control blood glucose concentrations < 10 mmol/L, insulin infusion should be started. When using insulin to control blood glucose concentrations:

- Aim to maintain TBG between 5 - 9 mmol/L
- Avoid hypoglycaemia (TBG < 2.6 mmol/L)
- Insulin infusion is provided to allow maximal utilisation of nutrition and should NOT be included in the daily fluid intake
- For safety, where IVN is being provided, insulin should always run in the SAME line
- Insulin infusion - starting dose: 0.05 units/kg/hour (usual range 0.01 – 0.2 Units/kg/hr).
- Check TBG no more than 2 hours after commencing insulin infusion in case of a rapid response. Aim for a rate of decrease no more than 3 - 4 mmol/L/hr.
- Titrate insulin rate gently (i.e. steps of 0.01 - 0.02 units/kg/hour) with sufficient time between adjustments to monitor effects (approx. 4 hours)
- If TBG drops below 5.0 mmol/L, halve insulin infusion rate and re-check TBG in 1 - 2 hours.

- If TBG drops below 2.6 mmol/L, give bolus of 2ml/Kg of 10% glucose and consider stopping insulin infusion. Rarely, glucagon may be considered if there is no response (discuss with neonatal consultant).
- If feeds are stopped, or fluids changed, re-calculate glucose intake. Small adjustments of insulin infusion and more frequent TBG monitoring may be required.
- Maintenance insulin infusion rate is likely to be less than that required to decrease initial TBG concentration.

Some infants are very sensitive to rapid changes in insulin infusion rates with unpredictable responses, thus care is needed when increasing infusion rates. Extra care should also be taken with infants who are hyperglycaemic secondary to medications such as corticosteroids, as they are likely to be relatively more insulin resistant and require higher insulin doses, but with a risk of rapid changes in insulin sensitivity.

4.4 Monitoring

Timing of TBGs:

- Use the NICU Blood Gas Analyser to measure TBG
- Once stabilised, TBG can be tested 4 - 6 hourly
- Check TBG more frequently if:
  - rate of administration of infused insulin and/or maintenance glucose / feed is changed
  - medication mixed with glucose and/or an insulin infusion is disrupted
  - new insulin infusion mix is commenced

4.5 Other information

4.5.1 Variability of insulin infusate

Insulin binds to plastic syringes and lines, which can result in a lower concentration of insulin reaching the infant when an infusion is first commenced. The concentration of insulin in the infusion as it enters the infant may then increase over time as binding sites in the plastic become saturated[17,18]. The method of flushing and sitting lines is designed to promote saturation of binding sites prior to commencing the infusion and thus reduce variability in the concentration of the solution over the infusion period. Regular TBG monitoring also assists in preventing hypoglycaemia, which is potentially more likely toward the end of a 24 hour period as saturation occurs and infusate concentration increases.

For more information regarding insulin infusion, refer to the Neonatal Pharmacopoeia

4.5.2 Sepsis

Sepsis is commonly associated with hyperglycaemia, therefore when hyperglycaemia occurs, infection should be considered as a cause, particularly if onset of hyperglycaemia is beyond the first week of postnatal life, or in infants > 32 weeks' gestational age.

4.5.3 Persistent Hyperglycaemia

Hyperglycaemia in preterm infants tends to be a transitory phenomenon and insulin treatment can usually be stopped after a few days. If hyperglycaemia persists for more than 2 weeks, or hyperglycaemia occurs in a term infant in the absence of sepsis or severe asphyxia, consider alternative diagnoses such as neonatal diabetes (1:400,000); investigations include serum insulin, C-peptide and ketones and urine ketones. Consult an Endocrinologist after discussion with neonatal consultant.

5 Evaluation, monitoring and reporting of compliance to this guideline

Compliance to this guideline will be monitored via clinical incident reporting through Victorian Health Incident Management System (VHIMS).

6 References

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19. Online glucose calculator (access via the following website): www.nicutools.org.

7 Legislation/Regulations related to this guideline

Not applicable.

8 Appendices

Not applicable.