Neonatal Hyperglycemia

Definition:
An elevated blood glucose concentration >8.3 mmol/L (>150 mg/dL) occurs frequently in VLBW infants, especially during the first days after birth.\(^1\)

Risk factors
The risk of hyperglycemia is inversely related to gestational age and birth weight and increases with the severity of accompanying illnesses.\(^2,3\) Review of trials of postnatal corticosteroids for prevention of chronic lung disease found an increased risk of hyperglycaemia (14 studies, 1192 infants; RR 1.5, 95% CI 1.3, 1.8; NNT 10) and glycosuria (2 studies, 48 infants; RR 8.0, 95% CI 2.4, 26.5) from use of mostly dexamethasone.\(^4\) Late onset bacterial\(^5\) and fungal infection\(^6,7\) has also been a reported association with hyperglycemia.

The mechanisms of neonatal hyperglycemia are probably multifactorial including high rates of exogenous glucose given to preterm neonates in infusions and TPN exceeding the reported endogenous rates of glucose production (4-7mg/kg/min)\(^8,9\); a reduced ability of the preterm infant to suppress endogenous glucose production\(^9\); low quantities of insulin-dependent tissues (fat and muscle) and a limited insulin response to glucose.\(^10\)

Consequences
Adverse clinical outcomes associated with neonatal hyperglycemia include death,\(^1,5,11\) intraventricular hemorrhage grades 3 and 4,\(^1\) retinopathy of prematurity,\(^2,12,13\) necrotizing enterocolitis,\(^5\) bronchopulmonary dysplasia and prolonged length of hospital stay (LOS).

The threshold for these outcomes is unclear. Various studies have reported adverse outcomes at varying thresholds of blood glucose level including >8.3 mmol/L,\(^1,2,11\) >8.5 mmol/L,\(^13\) >10.0 mmol/L,\(^5\) and >12.0 mmol/L.\(^6\) More severe outcomes were reported when the hyperglycemia was prolonged.\(^1,7,11\)

Diagnosis
The following infants should be screened for hyper- (and hypo-) glycaemia:

- Infants born <35 weeks gestation
- Infants receiving IV fluids or TPN
- Sick infants
- Infants with glycosuria

Screening blood glucose level = SBGL: performed on Accu-Check® Advantage Meter\(^14,15\)

Formal blood glucose level = FBGL: to confirm high SBGL before commencing treatment. Performed in laboratory on serum specimen preferably using calcium oxalate tubes \(\text{Â–note: use of lithium heparin tubes with delay in assay results in falsely low BGL. Repeated FBGL are not necessary for monitoring of treatment.}\)

Definitions:
- Hyperglycaemia that has been associated with adverse outcomes in observational studies is defined
Trials that reported treatment of hyperglycemia was associated with improved non-protein energy intake and short term growth most commonly enrolled infants with a persistent BGL 8.9 mmol/l or >9.9 mmol/L.

**Treatment**

**Prevention:**

Glucose administration to preterm infants should start at 4-8mg/kg/min (or 5.8g/kg/day to 11.5g/kg/day), and should not exceed 13mg/kg/min (or 18g/kg/day) for full term neonates as this tends to induce net lipogenesis. Premature infants are often relatively intolerant with glycosuria (not always with an osmotic diuresis).

Systematic review of trials of early insulin infusion for prevention of neonatal hyperglycemia found that use of an insulin infusion reduced hyperglycemia but increased death before 28 days and increased the risk of hypoglycemia. The reduction in hyperglycemia was not accompanied by significant effects on major morbidities; effects on neurodevelopment are awaited.

**Treatment:**

Systematic review of trials of insulin infusion for treatment of neonatal hyperglycemia found that use of an insulin infusion obviates the need to decrease the concentration of dextrose prescribed, and optimised the utilisation of calories by the infant resulting in significant increases in non-protein energy intake, glucose intake, and short-term weight gain. However, Insulin infusion had no significant effect on death, severe intraventricular hemorrhage, retinopathy of prematurity, bacterial sepsis, fungal sepsis, or necrotizing enterocolitis; effects on other major morbidities were not assessed. These trials did not report an excess of hypoglycaemia, possibly due to the more liberal target BGLs (4.4 – 9.9 mmol/L and 5.5-9.9 mmol/L).

**What we do at RPA:**

- Significant hyperglycemia = persistent BGL >10mmol/L
- **If BGL >10 mmol/L assess infant for possible underlying cause including:**
  - Sepsis
  - Excess glucose intake
  - Other illness
  - Exogenous corticosteroid
  - Growth restriction
- **Step 1:** If BGL persists >10mmol/L for >12 hours:
  - Consider change to 7.5% Dextrose Preterm TPN;
  - Plan to return to Standard Preterm TPN by 48 hours. The goal is short term treatment of hyperglycemia.
- **Step 2:** If BGL still persists >10mmol/L despite change to 7.5% Dextrose Preterm TPN and is expected to persist for next 24 hours; OR after 48 hours if unable to return to TPN with 10% Dextrose due to persistent hyperglycemia:
  - Consider insulin infusion (see insulin — hyperglycemia policy), **AND**
  - Change back to TPN with 10% Dextrose. The goal is now improved growth.
- **Target BGL = 5.5 - 9.9 mmol/L**

**Other considerations:**

- Initially BGL should be monitored closely when infusion is first commenced - at 30 minutes and then at 1 hour post infusion. Once stabilised BGL may be measured 4-6th hourly.
- Check BGL more frequently if maintenance solution, and/or medication mixed with glucose and/or an insulin infusion is disrupted or rate of administration is changed.
References


18. ESPGHAN Guidelines on Paediatric Parenteral Nutrition. 5. Carbohydrates *J Pediatr Gastroenterol*