Newborn Critical Care Center (NCCC) Clinical Guidelines

Hyperglycemia and the Use of Insulin

BACKGROUND

Multiple studies in neonates have indicated that persistently elevated serum glucose concentrations (>150 mg/dL) are correlated with adverse clinical outcomes and/or increased mortality.¹ One study demonstrated a prevalence of hyperglycemia (>180 mg/dL) of 30% during the first 2 postnatal weeks in infants born <27 weeks.² In this cohort, insulin treatment during the first 28 postnatal days was associated with lower 28- and 70-day mortality (even after adjusting for clinical illness).² In a trial of early insulin replacement in very low birth weight infants (<1500 grams), the use of insulin within the first week of life did not decrease mortality and increased the risk of hypoglycemia.³

Studies have also demonstrated that the use insulin for tight glycemic control (blood glucose of 72-108 mg/dL) compared to standard practice (blood glucose of 144-180 mg/dL) was shown to double the risk of hypoglycemia, and increase weight gain and head growth at the expense of linear growth. The authors concluded that this likely represents increases in fat mass rather than lean mass.^{4, 5}

CRITERIA

For glucose 220-320 mg/dL:

ELBW's: check triglyceride level (see ELBW guidelines). Consider continuous insulin infusion if blood glucose 220 - 320 mg/dL despite reduction in GIR to 4 mg/kg/min.

For glucose >320 mg/dL and not receiving insulin:

- 1. Reduce GIR by 2-3 mg/kg/min (minimum GIR of 4 mg/kg/min)
- 2. Consider IV insulin bolus (**MUST** be approved by attending or fellow):
 - a. < 1,000 g = 0.1 units
 - b. >1,000 g = 0.1 0.2 units/kg

Concentration of insulin infusion is 0.5 units/mL

(25 units regular insulin in 50 mL $\frac{1}{2}$ NS = 0.5 units/mL)

MANAGEMENT

- 1. Orders for an insulin infusion must be approved by attending or fellow.
- 2. All drips are to start at 0.05 units/kg/hr, and titrated up each hour by 0.05 units/kg/hr to maintain goal blood glucose but not exceed maximum insulin dose listed below:

Serum Glucose (mg/dL)	Maximum Insulin Dose (units/kg/hr)	Rate (mL/kg/hr)
<220	Off	-
220 - 280	0.1	0.2
280 - 350	0.2	0.4
>350	0.3	0.6

- 3. Blood glucose must be checked no more than one hour before starting the insulin drip (in case the serum glucose has fallen prior to initiation of insulin).
- 4. POC glucoses should be checked each hour during the titration period.
- 5. The charge nurse must be notified before starting infusion. The charge nurse is to assist bedside nurse and both are to independently calculate the infusion rate.
- 6. Fill tubing and wait 20 minutes to saturate binding sites.
- 7. For infants <500g, use 0.5 kg for calculations.
- 8. Insulin drips are run above total fluids unless otherwise specified.
- 9. If glucose measurements are persistently elevated despite the maximum dose of insulin, increase the maximum insulin dose by 25 50%.
- 10. If glucose measurements decrease by a margin >100 mg/dL with the initiation of the insulin drip, decrease insulin dose by 50%.

MONITORING

- 1. Check glucose 1 hour after giving insulin, starting an insulin drip, changing the insulin drip, or changing the GIR.
- 2. Re-check glucose every hour until <220 mg/dl for two consecutive hourly glucose checks with no change made in GIR or insulin dose, and then every 2 3 hours.
- 3. Insulin infusions have been associated with lactic acidosis in neonates, with one review noting a three-fold increase in lactate levels. Serum potassium shifts are also expected to occur.⁴ Obtain arterial or capillary blood gas sample with lactate and potassium level one hour after initiation of insulin infusion. Repeat 4 hours after the start of the infusion. Consider repeating lactate level every 12 hours if elevated or continuing to rise. Monitor potassium levels every 12-24 hours while receiving the infusion.

ADJUVANT THERAPIES

- 1. Optimizing parenteral protein intake has been shown to decrease the need for insulin to treat hyperglycemia in preterm infants.⁷
- Early enteral feedings, including trophic feeds, have been shown to increase pancreatic function leading to increased endogenous insulin secretion. Early enteral feeds should be established whenever possible and should be continued in infants who develop hyperglycemia, particularly those requiring insulin therapy.⁶
- 3. Limiting intralipids may help to lower serum glucose levels.8
- 4. Hypophosphatemia may contribute to glucose intolerance so correction of this electrolyte disturbance may confer some benefit in glycemic control.⁹

References:

- 1. Hays S, O'Brian Smith E, Sunehag A. Hyperglycemia is a risk factor for early death and morbidity in extremely low birth-weight infants. *Pediatrics* 2006;118:1811-8.
- 2. Zamir I, Tornevi A, Abrahamsson T, Ahlsson F, Enstrom E, Hallberg B, Hansen-Pupp I, Sjostrom ES, and Domellof M. Hyperglycemia in extremely preterm infants-insulin treatment, mortality and nutrient intakes. J Pediatrics 2018; Sept 104-110.
- Beardsall K, Vanhaesebrouck S, Ogilvy-Stuart AL, Vanhole C, Palmer CR, van Weissenbruch M, Midgley P, Thompson M, Thio M, Cornette L, Ossuetta I, Iglesias I, Theyskens C, de Jong M, Ahluwalia JS, de Zegher F, Dunger DB. Early insulin therapy in very-low-birth-weight infants. *New England Journal of Medicine*. 2008 Oct 30;359(18):1873-84.
- 4. Alsweiler JM, Harding JE, Bloomfield FH. Tight glycemic control with insulin in hyperglycemic preterm babies: a randomized controlled trial. *Pediatrics*. 2012 Apr;129(4):639-47.
- Tottman AC, Alsweiler JM, Bloomfield FH, Gamble G, Jiang Y, Leung M, Poppe T, Thompson B, Wouldes TA, and Harding JE. Longer-term outcomes of hyperglycemic preterm infants randomized to tight glycemic control. J Pediatr 2018; Feb 193: 68-75.
- 6. Hemachandra AH, Cowett RM. Pediatrics in Review 1999;20;e16.
- Mahaveer A, Grime C, Morgan C. Increasing early protein intake is associated with a reduction in insulin-treated hyperglycemia in very preterm infants. *Nutrition in Clinical Practice*. 2012 Jun;27(3):399-405.
- 8. Arsenault D, Brenn M, Kim S, Gura K, Compher C, Simpser E; American Society for Parenteral and Enteral Nutrition Board of Directors, Puder M. A.S.P.E.N. Clinical Guidelines: hyperglycemia and hypoglycemia in the neonate receiving parenteral nutrition. JPEN *Journal of Parenteral and Enteral Nutrition*. 2012 Jan;36(1):81-95.
- Dreyfus L, Fischer Fumeaux CJ, Remontet L, Essomo Megnier Mbo Owono MC, Laborie S, Maucort-Boulch D, Claris O. Low phosphatemia in extremely low birth weight neonates: a risk factor of hyperglycemia? *Clinical Nutrition.* 2015 Aug 10;