Clinical Practice Guideline:	Management of Infants at Risk for Neonatal Refeeding-Like Syndrome
Effective Date:	

Background

Refeeding syndrome (RS), as described in the adult and pediatric literature, is a marked by a combination of fluid and electrolyte disorders that occur when enteral or parenteral nutrition is initiated after a period of starvation. The hallmark sign of RS is hypophosphatemia, which is often accompanied by hypokalemia, hypomagnesemia, hyperglycemia and sodium/fluid imbalance. Untreated RS-associated metabolic disturbances can be fatal, and are preventable with appropriate nutritional management. Emerging evidence in the very low birth weight (VLBW, <1500g) neonatal population demonstrates similar electrolyte abnormalities associated with early, increased provision of parenteral amino acids (AA) with inadequate concurrent electrolyte and mineral provision in the first several days after birth, although death related to these metabolic disturbances have not been reported in the VLBW population. This risk appears to be highest among intrauterine growth restricted (IUGR) preterm infants, specifically those born in the setting of placental insufficiency, likely due to inadequate electrolyte and mineral stores at birth. Refer to DPNM Clinical Practice Guideline "Neonatal Refeeding-like Syndrome" for more detailed background and history.

**Nutrition and Pharmacy services follow all TPN patients. In the event of a late day admission (during regular working hours) of a patient determined to be at risk for developing Neonatal Refeeding-like Syndrome, suggest multidisciplinary huddle/touch base, as able, for contingency planning.*

Prevention and Treatment Flow Chart

Identify at risk patients:
VLBW + ≥1 of the following:
- IUGR
- Maternal preeclampsia
- SGA

Initial Management

First PN: Standard
- 'Neonatal Stock PN with Phosphate' @ 60 mL/kg/day + D5-D10 to meet TF goal

First PN: Custom
- AA 3 g/kg/day
- IL 1 g/kg/day
- If Central: Standard Ca:P (3:1.5)
- If Peripheral: more volume (as appropriate) to deliver more Phos

Monitor @ 24 hours of life
(or before 8 AM on 2nd hospital day to aid in PN writing)
- BMP, Mg, Phos
- Fluid balance

Abnormal

Normal
Repeat in 24-48 hours to establish trend

Abnormal:
per pathway
(or found on routine lab monitoring)

Normal
EXIT

Abnormal Labs

Electrolyte repletion
- See page 2 for repletion thresholds and doses

Continued custom PN
- AA 3 g/kg/day until phosphorus stabilizes then advance by 0.5 g/kg/day to goal with daily lab monitoring
- If central line, adjust Ca:P ratio based on serum levels (refer to page 2 for rec's re: ratios)

Monitor
- Repeat BMP, Mg, Phos within 48-72 hours of life to establish trend of electrolytes of concern
- Consider daily monitoring if down trending Phos

When Enteral Access Available
- Consider early fortification to provide standard/appropriate enteral source of calcium and phos
- Consider enteral repletion of Sodium Phosphate, Potassium Chloride or Potassium Acetate (Cytra-K)

Monitor
- Subsequent monitoring at discretion of team

Clinical Pearls:
- Standard Calcium to Phos ratio (Ca:P) is 3:1.5
- Ideal Phos is >4 mg/dL
- Suggest avoid AA increase with Phos <3.5 mg/dL without ability to increase Phos delivery same day
- Note: If custom PN is discontinued, reorder 'Neonatal Stock PN with Phosphate'.
- If concern for hypercalcemia, turn down PN but try to avoid completely discontinuing as this will also limit Phos delivery
- Avoid altered Ca:P ratios for prolonged amounts of time. Revert to standard ratio as soon as labs stabilized on goal AA and Phos doses

See **Page 2** for Classifications of Electrolyte Abnormalities and Electrolyte Repletion guidelines

Implementation Date: Review Period:

BWH NICU Classifications of Electrolyte Abnormalities

Electrolyte Abnormality	Level/Severity
Hypophosphatemia	Mild: 2.5 – 4 mg/dL
	Moderate: 1.5 – 2.5 mg/dL
	Severe: < 1.5 mg/dL
Hypokalemia	Mild: 2.5 – 3.1 mmol/L
	Moderate/Severe: < 2.5 mmol/L
Hypomagnesemia	< 1.5 mg/dL

Electrolyte Repletion

Electrolyte Abnormality	Level/Severity	Intravenous Intervention	Enteral Intervention
Hypophosphatemia	Mild: 2.5 – 4 mg/dL	Adjustments to PN: -Amino acid (AA) restriction to 3 g/kg/day, check full BMP, Mg, Phos prior to any advance -Adjust Calcium to Phosphorus ratio (Ca: P) If central access: AND <100 mL/kg/day: 4:2 (Avoid with PN volume >100 mL/kg/day) AND elevated serum Calcium: 3:2, AND elevated serum Calcium on 3:2 previously: 2:2 If peripheral access: Low threshold to optimize PN volume to provide more Ca/Phos vs. restrict AA to <3 g/kg/day	Sodium phosphate: 0.5 mmol/kg PO daily; may increase up to 2 mmol/kg/day
	Moderate: 1.5 – 2.5 mg/dL	-Step 1: PN adjustments as above -Step 2: If at risk/clinical suspicion of evolving Neonatal Refeeding-like Syndrome and consecutive phosphorus levels decreasing, may consider IV sodium or potassium phosphate as below	
	Severe: < 1.5 mg/dL	-Sodium phosphate: 0.25 mmol/kg IV x 1 or -Potassium phosphate**: 0.18 mmol/kg IV x 1†	
Hypokalemia	Mild: 2.5 – 3.1 mmol/L	Adjustments to PN as able	Potassium Chloride or Cytra-K: 1 mEq/kg PO Q12H; may increase as tolerated
	Moderate/Severe: < 2.5 mmol/L	Potassium chloride: 0.5–1 mEq/kg IV x 1†	
Hypomagnesemia	< 1.5 mg/dL	Magnesium sulfate: 0.4 mEq/kg IV x 1	n/a

*At risk if VLBW + ≥ 1 of the following: IUGR, maternal preeclampsia, SGA.

** IV potassium phosphate contains aluminum; use only in the setting where sodium phosphate is undesirable based on laboratory results. See BWH NICU DAG page for more details.

† Use discretion with potassium repletion in setting of renal impairment

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