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Parenteral Nutrition for VLBW Infants

Introduction

The development of sophisticated techniques for providing short- and long-term parenteral nutrition (PN) to critically ill infants has been one of the major advances in neonatology of the last several decades. While there is still a wide variation in practice in how parenteral nutrition is used to support VLBW infants, there is a growing body of literature to support evidence-based recommendations for numerous best practices.[1] There are currently a number of excellent reviews of neonatal nutrition, including information on early parenteral nutrition.[1-3]

In recent years, there have been multiple parenteral nutrition component supply issues. It is important to stay up to date with your pharmacy supply and understand the consequences if you do run out of a particular product.[4,5] The sites listed below are resources to check for national shortages, estimated time to replenish, and strategies to minimize detrimental outcomes.

- American Society of Parenteral and Enteral Nutrition
- Federal Drug Administration

POTENTIALLY BETTER PRACTICE #5

Develop and use computerized provider order entry (CPOE) for Parenteral Nutrition (PN).

Background, Rationale, and Goals

- PN is a high-risk medication with ample potential for order input, mixing, and hanging errors. CPOE facilitates clear, timely communication between provider, pharmacy, and bedside nursing.
- Most commercially available CPOE programs can be customized to guide clinical decision support and ensure safeguards to minimize order errors and, in some studies, found to decrease mortality. [6-8]

Recommendations, Guidelines and Algorithms

- Investigate the CPOE program options available to your institution
  - Is it compatible with the TPN compounder?
  - Is it compatible with the EMR?
  - Safety record at other institutions?
  - Program support – local vs. remote?
- Interdisciplinary input on the CPOE program – MD, NNP, PharmD, RD, RN, and technical support
  - Work flow assessment
  - 'Double Check'/Verification of order by clinical pharmacist
  - Who has access to the program? What level of access?
- Clinical Decision Support and Safeguards
  - Different protocols for different populations (neonate vs. pediatric vs. adult)
  - Copying previous order vs. entering new order daily
  - Ability to see past orders and laboratory trends
    - In the same program? (safer)
    - Will the provider have to alternate between different programs? (riskier)
  - Set minimum and maximum ordering limits
  - Override options/potential
    - Who has the authority?
    - Procedure

Quality and Process Improvement

- If CPOE not commonly used, identify obstacles to implementation
- Once CPOE is implemented, identify shortcomings and optimize abilities

Outcome/Process Measures

- Adverse (& 'Near Miss') Drug Events
- Prescription order error
- Product waste
- Time to attain macronutrient goals
- Time to re-gain BW
- Pharmacist verification time &/or intervention frequency

POTENTIALLY BETTER PRACTICE #6

Parenteral nutrition, including dextrose, protein, and lipids should be started as soon as possible after admission, but never greater than 24 hours of life.

Background, Rationale, and Goals

- In order to maximize growth, minimize catabolism, and support neurocognitive development, infusing nutrition with protein as soon as possible after birth has become the standard of care.[1,3,9,10]
- Amino Acids can be started as high as 3 g/kg/day to minimize catabolism.
- Macronutrients should be increased, as tolerated, so that infants receive adequate amino acids (up to 4.0 g/kg/d) and non-protein calories (80-100 kcal/kg/d) within the first five days of life
- Understand your facility's PN availability
  - In-house compounder vs. outsourced production
  - If it is outsourced, establish inventory needs
- Overcome the perception that early amino acid administration is of limited benefit, potentially toxic, or more expensive.
- Amino Acid dose may be limited by fluid restriction.

Recommendations, Guidelines and Algorithms

- Standardized policies and admission order sets
- Including monitoring standards[11]
- Availability of "pre-mixed" amino acid containing parenteral nutrition solutions in hospital pharmacy[9,12,13] OR the ability to obtain individualized parenteral nutrition solutions within the first few hours of life.
- Understand how early infusion of parenteral nutrition may effect electrolytes.[14]

Quality and Process Improvement

- Understand current state and map out ideal process.[3,13,15]
- PDSA Cycles, as necessary
- Measurements before and after process changes

Refer to **TOOL 6** on page 26 and **TOOL 7** on page 27 for guidelines on parenteral nutrition for VLBW infants.

Outcome/Process Measures

- % of VLBW infants started on amino acids at ≤ 2 hrs of age or as part of the first IV maintenance fluids
- TPN hung by ___ hours of life
- % of VLBW infants on amino acids by 24 hours of age
- % of VLBW infants receiving 3-4 g/kg/d parenteral protein by 72 hours of age
- % of VLBW infants receiving 80-100 non-protein kcal/kg/d by 5 days of age
- Total TPN days

POTENTIALLY BETTER PRACTICE #7

Start parenteral lipids within the first 24 hours of life. Lipids can be started at doses as high as 2 g/kg/d. Lipids can be increased to doses as high as 3.0-3.5 g/kg/day over the first few days of life.

Background, Rationale, and Goals

- Early lipids are well tolerated by VLBW infants & are essential components of brain structure.[10,16]
- Delayed introduction of lipids may have adverse consequences.[16]
- Prolonged IV lipids may increase risk for hyperlipidemia and Parenteral Nutrition Associated Cholestasis (PNAC).
- Can monitor triglyceride levels, with goal < 200 mg/dl
- Calls for regular monitoring of direct bilirubin and LFTs.[17,18.]
- Newer, fish oil based IV Lipids may be associated with less PNAC19; however, they may not prevent PNAC.[1-3,20]
- If used, SMOFlipid® dose should be 2.5-3 g/kg/day in order to reduce the risk of essential fatty acid deficiency (EFAD).[21] Refer to **PBP #9** on page 24 for more information.

Quality and Process Improvement

- Standardized policies and admission order sets which include IV Lipid administration starting within the first 24 hours of life

Outcome/Process Measures

- Measure provider consistency in implementation
- Time of order placement to time of lipid infusion start running
- % of VLBW infants receiving lipids by 24 hours of age
- Day of Life 3 g Lipid/kg/day is reached

POTENTIALLY BETTER PRACTICE #8

Discontinue parenteral nutrition, with removal of central catheters, as soon as adequate enteral nutrition is established.

Background, Rationale, and Goals

- Understand that leaving a central line in place caries some risk of catheter-associated infection
- Overcome the perception that the benefit of several more days of lipid administration outweighs the risk of catheter-associated infection
- As enteral feeds advance, advantages of more parenteral nutrition are outweighed by the risks of continued central vascular access and infection[22-24.]
- As feeds advance, optimize the nutrient density of the diminishing volume of PN by giving the maximum amount of Amino Acids to minimize the calorie and protein 'gap' that can occur during this transition from PN to EN [25]

Quality and Process Improvement

- Define the current state and map out ideal processes.[3,13,15]
- Plan Do Study Act (PDSA) Cycle(s), as necessary
- Develop & implement standardized policies and order sets which include discontinuation of parenteral nutrition when adequate enteral calories established. (See Section III)
  - Fortify feeds before PN is discontinued
  - May discontinue IV Lipids prior to stopping parenteral nutrition to maximize Amino Acid content of the remaining volume and as fortified enteral feeding volume and energy is increasing

Outcome/Process Measures

- Number of central line days
- Number of days on PN
- Hospital acquired infection (HAI)/Central line-associated bloodstream infections (CLABSI) Rates

POTENTIALLY BETTER PRACTICE #9

Long term management in those who become PN dependent &/or develop Parenteral Nutrition Associated Cholestasis (PNAC).

Background, Rationale, and Goals

- The development of PNAC is strongly correlated with duration of time on PN and the only evidence for prevention is initiating and advancing enteral feeds.
- Unfortunately, some VLBW infants may remain reliant on parenteral nutrition for over 30 days.
- Lack of enteral feeding, immature organ function, hypoxia, infection, PN components, and hepatotoxic medications are all risk factors that may lead to liver dysfunction.
- Risks of macro- and micronutrient deficiencies can have deleterious effects if they are not corrected.[5,26.]

Recommendations, Guidelines and Algorithms

- If/when the D. Bili becomes >2 mg/dL:
  - Although decreasing the IV Lipid dose to 1 g/kg/day has been done, it is controversial. [27,28]
    - The evidence for this strategy is inconclusive and it is not generally recommended.
    - This strategy may significantly decrease energy provided
    - Fat is essential for brain growth and neurodevelopment
  - If fish oil based IV Lipids are available[27], can transition from Intralipid®
    - Omegaven® is only available in the United States as an investigational drug, therefore access is limited
- Smoflipid® is approved by the FDA for use in adults; however, at the time of this publication, it is not explicitly approved for use in pediatrics and infants though we acknowledge there are some institutions who are using it 'off label'
  - If the Smoflipid® dose is restricted, monitor for EFAD closely[28] and elevated serum Vitamin E.
- Limiting IV Dextrose intake may be more advantageous than IV Lipid dose minimization in decreasing risk of PNAC[18]
- Cycling PN is not currently recommended for VLBW due to the high risk of hypoglycemia and the potential for other metabolic abnormalities
- Ursodiol (ursodeoxycholic acid, common brand: Actigall) promotes bile flow; however data is limited in its use and effectiveness in VLBW infants[27]
- Standardized policies and order sets which on TPN day #30, high risk micronutrients for deficiency are monitored and corrected, if needed
  - Zinc
  - Selenium
  - Copper
  - Possibly Vitamin D, or other fat soluble vitamins if the infant is demonstrating liver dysfunction

Quality and Process Improvement

- Review current policies and procedures for long term TPN management
- Update practice and order-sets, as needed

Outcome/Process Measures

- Annual number of babies on PN for >30 days
- Number of those with altered micronutrient status on PN for 30 days
- Number of diagnoses of cholestatic jaundice due to PN per year

Total Parenteral Nutrition for VLBW Infants

Nutrient	Initiate	Advance	Goal	Other Info
Amino Acids	3 g/kg/day (or maximum allowed if volume restricted)	0.5-1 g/kg/day (dependent on volume and renal function)	4 g/kg/day	
Fat	0.5-2 g/kg/day	0.5-1 g/kg/day (depending on volume and tolerance)	3 g/kg/day	Dose may need to be restricted if PNAC develops
Carbohydrate	4-6 mg CHO/kg/min	1-2 mg CHO/kg/min	<12 mg CHO/kg/min	
Pediatric IV Multivitamin	2 mL/kg/day (Goal)			
Sodium	0-1 mEq/kg/day	0-1 mEq/kg/day	2-4 mEq/kg/day	May need more, adjust dose per labs
Potassium	0-0.5 mEq/kg/day	0-1 mEq/kg/day	2-4 mEq/kg/day	May need more, adjust dose per labs
Calcium	Up to 400 mg/kg/day	50-200 mg/kg/day	400-600 mg/kg/day	Ideal Ca:Phos ratio = 1.3-1.7 mg Ca:1 mg Phos
Phosphorous	Up to 0.5 mM/kg/day	0.5-1 mM/kg/day	1-2 mM/kg/day	
Magnesium	0-0.2mEq/kg/day*		0.2-0.3 mEq/kg/day	*do NOT give if you know mom received Mg prior to delivery
Zinc	400 mcg/kg/day (Goal)			
Copper	20 mcg/kg/day (Goal)			May need to give up to 30 mcg/kg/day, if found to be deficient; OR may need to decrease dose or hold in setting of PNAC26
Selenium	If still on PN @ 30 days, check for deficiency and start at least 2 mcg/kg/day			IF found to be deficient, may need to increase dose to 3-4 mcg/kg/day
Carnitine	3-5 mg/day			Not necessary to routinely add
Heparin	0.5-1 unit/mL			

Adapted from: Moyer-Mileur LJ. Anthropometric and laboratory assessment of very low birth weight infants: the most helpful measurements and why. Semin Perinatol. 2007;31:96-103.

TOOL #7

Monitoring Guidelines for VLBW Infants on Parenteral Nutrition

Measurement	Initial Phase (usually <1 week)	Stable Phase*
Growth		
Weight	Baseline	Daily
Length		Weekly
Head Circumference		Weekly
Intake and Output	Daily	Daily
Glucose		
Serum	Baseline	1-3 x/week, as needed
Meter	Baseline, and as needed	
Urine	As indicated	
Electrolytes (Na, K+)	Baseline	
Calcium, Magnesium, & Phosphorous		
LFTs		
Direct &/or Conjugated Bilirubin		
Alkaline Phosphatase		
Triglycerides	Baseline, and daily with each increase in dose of IV Lipids	1-2 x/week, as needed
BUN and Creatinine	Baseline, 2-3x/week	1-3 x/week, as needed
Serum Proteins	Baseline	
Blood Cell Count		
Vitamin or other Microminerals		As needed

*Clinically and metabolically stable infants on PN for a prolonged period of time may be able to space out their laboratory monitoring outside of the recommended time frames.

Adapted from: Moyer-Mileur LJ. Anthropometric and laboratory assessment of very low birth weight infants: the most helpful measurements and why. Semin Perinatol. 2007;31:96-103.

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