Optimizing Parenteral Nutrition for Short Bowel Syndrome
East Bay Newborn Specialists Guideline
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Neonates receiving long-term parenteral nutrition (PN) are at significant risk for development of parenteral nutrition associated liver disease (PNALD). A multifactorial etiology may be related to decreased bile acid secretion, chronic endotoxemia, or toxic constituents of the PN such as excessive protein, hepatotoxic amino acids (methionine), excessive glucose infusion rates, deficient choline, or deficient sulfated amino acids. Risk factors include prematurity, low birth weight, duration of PN, and sepsis. The most effective treatment for PNALD is increasing feedings and decreasing PN, but this may be a prolonged process. Approaches to delay and possibly prevent PNALD are cycling PN, minimizing intralipid (IL), reducing trace elements, use of fish oil-based parenteral lipid instead of soy based Intralipid, and use of enteral fish oil.

PN Cycling
Cycling of PN provides the total daily PN volume in less than 24 hours. Advantages include disconnection from the intravenous line, improvement in protein stores, and reduction of the incidence of hyperinsulinemia. Cycling PN is recommended for patients who are expected to be on prolonged courses of PN (i.e., 30 days) and whose cardiac, renal, and endocrine function can tolerate shifts in fluid and dextrose infusion rates. Patients should be metabolically stable on their goal solutions for several days before attempting to cycle PN. It can be attempted when patients can be removed from PN without development of hypoglycemia (generally 44-48 weeks postmenstrual age). In an attempt to avoid hyper- or hypoglycemia, the PN infusion rate is gradually decreased and increased prior to the 2-4 hour cycle off period. The PN rate is tapered off over 1 hour prior to discontinuing PN. When the infusion is restarted, it is gradually increased over 1 hour to the baseline rate. In neonates, cycling should be limited to no more than 6 hours off PN to avoid diminishing of glycemic reserves. A chemstrip should be obtained during the middle of the cycle off and one hour after the cycle ends. In the event of persistent hypoglycemia while cycling off PN, a two hour tapering schedule should be attempted.

Minimizing Intralipid®
Soybean lipid emulsions (e.g., Intralipid®) are the most common form of lipids used for PN and have been implicated in the pathogenesis of PNALD. While Intralipid is rich in omega-6 fatty acids and supplies essential fatty acids, it may be an important contributor to the pathogenesis of PNALD. Excessive omega-6 fatty acids have proinflammatory effects that impair triglyceride transport and contain phytosterols that reduce bile secretion and may contribute to liver injury. Animal models showed that a soy-based lipid emulsion is associated with liver injury as compared with a fish-oil based emulsion, which is rich in omega-3 fatty acids. Preliminary studies in infants who are changed from soy-based to fish-oil-based fat emulsions (e.g., Omegaven®) demonstrate a reversal of PNALD. Other studies in children show a decrease in cholestasis with lipid lowering techniques.
In order to provide essential fatty acids and limit potential hepatitis toxicity related to Intralipid, the following schedule is recommended for infants with short bowel syndrome:

- For the first month of life, provide 3 gm/kg/day every day
- When the patient is $\geq$ 1month old, provide 2 gm/kg/day for 3 times/week
    - if the patient is not growing and the patient does not have significant cholestasis, then increase lipids to 3 gm/kg/day either 3 times/week or daily to achieve appropriate weight gain for age
    - if the patient is not growing and the patient has cholestasis with direct bili $\geq$ 3mg/dL, then use of Omegaven should be investigated
- If the patient is growing, but the direct bili is $\geq$ 3, then decrease Intralipid to 1.5 gm/kg/day for 3 times/week

Sodium Balance

Na depletion via stool losses may be extremely high in the patient with short bowel syndrome and must be replaced to maintain proper electrolyte balance and growth. With inadequate Na replacement, serum Na levels may be kept within the normal range by physiologic hyperaldosteronism, reduced urine excretion of Na, and increased kaliuresis. Urine electrolytes should be monitored similarly to serum electrolytes. Na replacement in PN and enteral feeds should be provided to maintain a urine Na > 30 mEq/L and urine Na to K ratios of 1:1.

Trace Elements

Because copper and manganese are primarily excreted through the biliary tract, these trace elements may accumulate in patients with cholestasis and contribute to hepatic injury and/or cause neurotoxicity. When the direct bilirubin is >3mg/dL, the dose of the trace elements in the PN is reduced to 0.25 mL/kg/day. Maintain the usual level of zinc supplementation in the PN. Because the reduced dose of trace elements may cause mineral deficiency, monitor ceruloplasmin, copper, zinc, and selenium every 3-4 months.

Monitoring

Patients should be monitored for signs of cholestatic injury characterized by progressive/persistent elevation in bilirubin, transaminases, and gamma-glutamyl transpeptidase, prothrombin time, and interval surveillance for fat-soluble vitamin deficiency. Monitor for evidence of portal hypertension (splenomegaly, ascites, and hypersplenism with thrombocytopenia).