Parenteral Nutrition Associated Liver Disease

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September 3, 2013

Background

- History
  - 1968 first patient to receive PN
- Reasons for receiving long-term PN
  - Permanent dysfunction of the intestinal tract
    - Severe Crohn's
    - Radiation enteritis
    - Chronic pseudo-obstruction
    - Short-bowel syndrome

Long-Term Complications

- Hepatobiliary Disease
  - Steatosis/Steatohepatitis
  - Cholestasis
  - Fibrosis
  - Cirrhosis
  - Gall stones or biliary sludge
  - Cholecystitis

Steatosis/Steatohepatitis

- Collection of excessive amounts of triglycerides in the liver
  - Risk Factors
    - Alcoholism, protein malnutrition, diabetes mellitus, obesity
  - Parenteral Nutrition Causation
    - Caloric overload and an imbalanced source of energy
- Signs of steatosis
  - Aminotransferases elevated
  - Alkaline phosphatase may be elevated
    - secondary to cholestasis produced by fat infiltration

Cholestasis

- Condition in which the flow of bile from the liver is slowed or blocked
  - Risk Factors
    - Impaired immune response, limited oral intake and bowel stasis, sepsis, presence of jejunostomy, need for GI surgery, duration of PN
  - Parenteral Nutrition Causation(theories)
    - Hemodynamic modifications
    - Fasting state
    - Nutritive composition
- Signs of cholestasis
  - Bilirubin
    - > 2g/dL or more
  - Alkaline Phosphatase
    - > 3x ULN
  - Gamma-glutamyl transpeptidase and aminotransferases may be elevated

Fibrosis/Cirrhosis

- Hepatic fibrosis is a response to chronic liver injury
- Cirrhosis represents a late stage of progressive hepatic fibrosis
  - Risk Factors
    - Prolonged cholestasis or steatosis, proinflammatory state
- Signs of hepatic fibrosis
  - Non-invasive tests include AST to platelet ratio index
- Signs of cirrhosis
  - Aminotransferases, alkaline phosphatase, GGT, bilirubin, PT, and albumin may or may not be elevated

Cholecystitis

- Inflammation of the gallbladder
  - May be acalculous or calculous
    - Serum aminotransferase
    - Amylase
    - Bilirubin
- Biliary sludge or gallstones may present with leukocytosis, elevated liver or pancreas tests
  - Risk Factors
    - Continuous PN, septic episodes, ileal disease, short-bowel syndrome, hematological disease

Toxicity of Parenteral Nutrition

- Excess calorie intake
  - Glucose or lipid overload
  - Impaired hepatic secretion of triglycerides
- Protein content
  - Cholestasis develops earlier in patients receiving higher protein content

Prevention

- Avoid excess calorie intake
  - Maintain PN calories at < 25 kcal/kg/day
  - Lipids = 30% of non-protein calories
    - < 1g/kg/day
  - Amino Acids <2 g/kg/day
  - Dextrose < 5 g/kg/day (<3.5 mg/kg/min)
    - Tight glucose control
- Use a cyclic PN schedule
- Medications
  - Ursodeoxycholic acid (UDCA)
  - Metronidazole 250 mg TID

Management

- Maintain a small amount of lipids in PN
  - 0.5 g/kg/day
- Tight glucose control
  - 15 mg/kg/day
- Cyclic PN
- Combined small bowel and liver transplantation

Long-term plan

- What to watch out for
  - Minor elevations in aminotransferases (< 2x ULN) without an elevation in bilirubin extremely common
- When to react
  - Progressive increase in bilirubin, aminotransferases, alkaline phosphatase or GGT
- What to do
  - Lipids 0.5 g/kg/d
  - Carbohydrates 15 kcal/kg/d
  - Initiate cyclic PN

What's on the horizon for nutrition

- Omegaven evaluation
  - FDA approved trial at Children's in Boston
- Ursodiol evaluation
  - Treatment of PNAC in neonates
- Cyclic TPN evaluation
  - Prevention of PNAC with cyclic PN in infants
- Intestine transplant

Conclusions

- Provide adequate energy needs without overfeeding
- Monitor hepatobiliary enzymes closely
- Understand limitations of parenteral nutrition in the long-term

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