Parenteral Nutrition Associated Liver Disease: Yes or No?

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Parenteral Nutrition

A truly revolutionary, life saving development in medicine to provide complete nutritional support for patients with acute or chronic intestinal failure.
Parenteral Nutrition

• 1960  first successful PN by Wilmore & Dudrick at CHOP

• 1975  first report of cholestasis by Rager & Finegold
Parenteral Nutrition-Associated Liver Disease

Serum direct bilirubin > 2 mg/dL
↑ Alk P, transaminases, GGT

- Cholestasis
- Steatosis, steatohepatitis
- Fibrosis, cirrhosis
- Liver failure
- Biliary sludge, gallstones
- Cholecystitis
Cholestasis
Parenteral Nutrition-Associated Liver Disease

Children > adults
(40-60% in infants, 15-40% adults)

Risk Factors:
- Prematurity and low birth weight
- Residual bowel length
- Duration of PN
- Duration of enteral fasting
- Lack of ileocecal valve
- Recurrent sepsis
- Multiple abdominal surgeries

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Parenteral Nutrition-Associated Liver Disease

Intestinal failure

- Parenteral nutrition
- Lack of enteral nutrition

Liver disease
Parenteral Nutrition Associated Liver Disease

Intestinal Failure Associated Liver Disease
Pathogenesis

Multifactorial

- Lack of enteral nutrition
- ↓↓ gastrointestinal hormones
  - ↓ gallbladder contractility
  - ↓ gallbladder contractility biliary sludge
  - Intestinal stasis SBBO translocation sepsis
- Sepsis: line infection + SBBO+↓ gut immunity
- Multiple surgeries
- Composition of PN
- Immature neonatal hepatobiliary functions
Components of PN

- Excess non-protein calories
- ↓ taurine and cysteine: essential in neonate
- Choline deficiency
- Manganese toxicity
- Lipid emulsions
  - soybean or soybean/safflower based (omega 6)
  - Soybean oil: phytosterols, inflammatory cytokines
Soybean vs fish oil

Omega-6
- Linoleic acid
  - Arachidonic acid
    - PGE2, PGI2, LTB4
    - LTC4, TXA2, LTE4
  - Pro-inflammatory

Omega-3
- Alpha-linoleic acid
  - EPA
    - DHA
    - PGE3, LTB5, PGI3, LTC5
    - TXA3, LTE5
  - Anti-inflammatory

Lee et al. Hepatology 2007

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Prognosis

• Duration of enteral fasting:
  Better, even reversible with early enteral feeds.

• Duration of PN
  100% mortality rate within a year if unable to be off PN or w/o transplantation
  Wales et al. J Pediatr Surg 2005

• Bilirubin level
  poor prognosis if persistent ↑ bilirubin level (>12 mg/dL)
Prevention and Medical Management

- Enteral Nutrition related
- Parenteral Nutrition related
- Prevention of sepsis
- Avoid multiple resections, surgeries
- Avoid hepatotoxic drugs
- Ursodeoxycholic acid (15-45 mg/kg/d)
Enteral nutrition in IFALD

• Start enteral feeds as soon as possible

  Likelihood of weaning off PN
  – 75% enteral at 12 wk-90% wean off
  – 50% enteral at 12 wk-75% wean off
  – 25% enteral at 12 wk-50% wean off


• Breast milk, amino acid based formulas
• Avoid hyper-osmolar feedings
• Prefer continuous feeds
Parenteral Nutrition

- Prefer cyclic PN
- Avoid excess non-protein calories
  - Min. 2-4% of cal. as linoleic acid
- Amino acids: ↓ methionine, ↑ taurine and cysteine
- Lipid emulsions:
  - MCT, omega 3 not available in US
Soybean vs Fish oil

Omega-6 fatty acid vs Omega-3 fatty acid
Parenteral Fish Oil

Gura et al. Pediatrics 2006

- 2 patients: >50% and 100% PN dependent
- Parenteral fish oil: 1 g/kg/d
- Resolution of cholestasis in 8 weeks
- No evidence for essential fatty acid deficiency
Catheter Related Sepsis: Prevention

Strict antisepsis
   Hand hygiene
   Barrier precautions
   Catheter site antisepsis

Change catheter only if infected or malfunctioning

Remove catheter promptly when no longer necessary

Hadaway LC. Nursing 2006
Bacterial overgrowth

Risk factors:
- absence of ileocecal valve
- dysmotility
- post surgical

Sx: diarrhea, abdominal pain, distention, FTT

Dx: Duodenal fluid analysis, breath test

Rx: cycled oral abx
- probiotics: no data to support routine use.
- glutamine in PN: no effect

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Surgical treatment

Serial Transverse Enteroplasty (STEP)

International STEP Registry (2004-2006)

38 pts, median f/u 12.6 mo

29/38 doubled enteral caloric intake after STEP


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Surgical treatment

- Isolated liver transplantation
  - Bowel adaptation and improved enteral feeding tolerance is reported.

  Botha et al. Liver Transpl 2006

- Liver-small bowel transplantation
Thank you