SickKids
THE HOSPITAL FOR SICK CHILDREN

UNIVERSITY of TORONTO

Nutritional Issues in Cholestatic Disease

NASPGHAN-CPNP Joint Session

Binita M. Kamath, MBBChir MRCP MTR
Associate Professor
Division of Gastroenterology, Hepatology and Nutrition
The Hospital for Sick Children
University of Toronto

October 2015

Disclosure: Speaker for Retrophin

OUTLINE

- Overview of cholestatic diseases
- Mechanisms of nutritional impairment in cholestasis
- Impact of poor nutrition in cholestasis
- Optimizing nutrition in cholestasis

Cholestatic Diseases

Cholestatic Diseases

- Cholestasis = interruption in bile flow
- Bile: bile salts, bilirubin, cholesterol, phospholipids, drugs
- Hallmark disease: biliary atresia (BA)
- Other diseases
  - Alagille syndrome
  - Progressive familial intrahepatic cholestasis
  - Alpha-1-antitrypsin deficiency

Mechanisms of Nutritional Impairment in Cholestasis

Mechanisms of Malnutrition in Cholestasis

1. **Severe depletion of intraluminal bile acids and secondary fat malabsorption**
2. Poor intake due to
   a. organomegaly and/or ascites (reduced gastric capacity)
   b. anorexia (toxins?)
3. Portal hypertension exacerbates malabsorption
4. Pruritus

Mechanisms of Malnutrition in Cholestasis

5. **Increased energy expenditure**
   - Measured REE almost 30% higher than expected in BA
   - Normal infants retain 50% energy intake for growth, but only 35% in BA
6. Hepatic IGF-1
7. Recurrent infections

Assessment of Malnutrition in Cholestasis

1. Weight – affected by ascites
2. Anthropometrics
   a. Mid-arm circumference *(body protein)*
   b. Triceps and subcapsular skinfold thickness *(body fat)*
   c. Head circumference

Impact of Poor Nutrition in Cholestasis

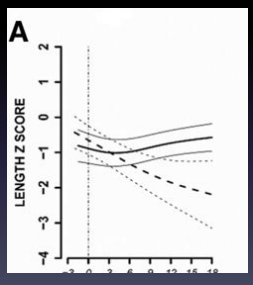
Malnourished Cholestastic Children have Poor Outcomes

- Growth failure is an important factor associated with death or moving to ICU in a multi-center cohort (mostly BA)
  - height or weight <2 s.d., associated with increased morbidity and mortality ➡ PELD
- Growth failure was an independent risk factor for pre-transplant mortality, post-transplant mortality, and even graft failure in 755 listed BA patients (SPLIT)

McDiarmid et al, Transplantation 2002 & Utterson et al, J Ped 2005

Malnourished Cholestastic Children have Poor Outcomes

- BA Research Consortium
- N=100
- Infants with BA who ultimately required LT or died had poorer growth after HPE compared to those who survived with their native liver at 24 months of age



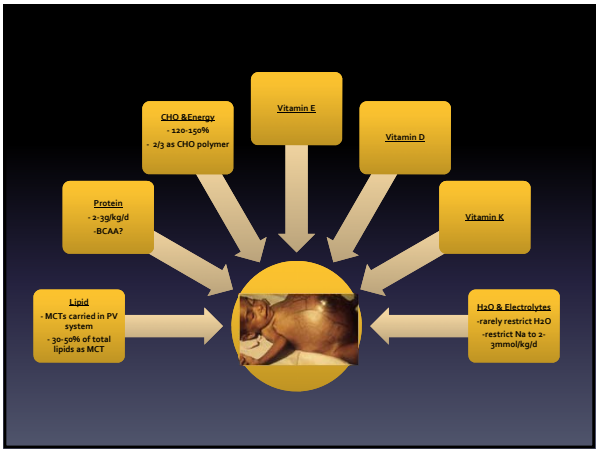
DeRusso et al, Hepatology 2007

Outcomes of Malnutrition in Cholestasis

- Severity of malnutrition and poor growth in children with BA before LT is predictive of cognitive performance years after transplantation
  - 40 children, underwent LTx <2 years and Bayleys pre-Tx and at 3 and 12 months
  - At 1 year post-LTx., 35% diagnosed with developmental delay – associated with **decreased weight, low albumin**, length of stay and age at tx.

Wayman KI et al, J Ped 1997

Optimizing Nutrition in Cholestasis



MCTs: The Data?

- Difficult to specify the ideal dietary fat content and ratio of MCT to LCT
  - Limited data point to better fat solubilization and growth of cholestatic infants fed with 30% or 70% MCT against a 50/50% mixture of MCT/LCT
  - Very high (>80%) MCT to total lipid risks of essential fatty acid deficiency
  - Recent study shows effectiveness of enteral MCT formula (140% DRI) as compared to ad lib oral intake of same formula

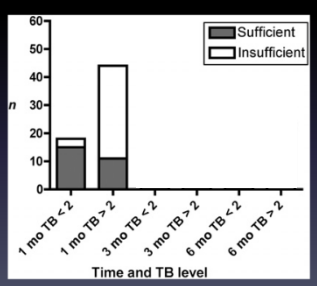
Macias-Rosales, JPGN 2015

Branch chain amino acids (BCAA)

- Low levels of BCAAs documented in liver disease
  - reflect increased BCAA utilization in muscle
- Randomized study in children with ESLD demonstrated improved nutritional status and body composition in those with BCAA-enriched formula
- MCT-containing complete BCAA formulas are expensive and not readily available

Chin SE et al, 1992

TB>2mg/dl: Severe Fat Soluble Vitamins Deficiency



Shneider, Pediatrics 2012

Parenteral Nutrition

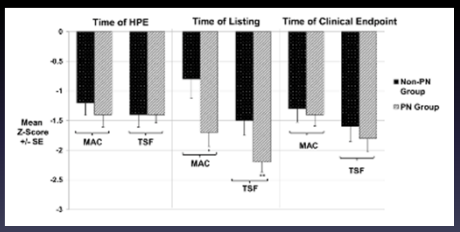
- Indications:
  - diarrhea, vomiting*
  - repeated episodes of gastrointestinal hemorrhage
- Risk of worsening decompensated liver disease with PN is low
  - mild biochemical deterioration
- Can typically achieve mixed enteral and PN

Parenteral Nutrition

- 20 year retrospective review, single center:
  - BA listed for LTx, <36 months
  - PN=25, Non-PN=22
  - Mean TSF z-score increased from -2.5 ± 0.2 to -1.8 ± 0.2 (p=0.003), and mean MAC z-score increased from -2.2 ± 0.2 to -1.4 ± 0.2 (p<0.0001)
- Of the 22 patients in the non-PN group, 6 (27%) received NG feeds

Sullivan J, Liver Transp 2012

Parenteral Nutrition



Gaps in Knowledge

- What is the right nutritional regime for BA – Should all babies have an NGT placed post-Kasai or even TPN (Top-down therapy)?
- Are MCTs the correct fuel in cholestasis? What is the ideal %?
- How much Vit K is enough? May be enough for INR to be normal – but what about bones?
- Is all cholestasis the same?
- ETC.

Summary

- Nutrition is crucial in cholestatic liver disease to optimize medical and functional outcomes
- Be aggressive, early – top down therapy
- **Measure vitamins, especially D in cholestatic infants and supplement properly**
- Substantial gaps remain in determining optimal nutritional regimens
  - Please think about to how to address these!

PUFA / EFA

- Intraluminal bile salt depletion results in long chain triglyceride malabsorption and EFA deficiency
- Levels difficult to measure and interpret
- Most centres lack access to clinical measurement
- Levels adequate in most MCT containing formula but can consider supplementation with corn oil or safflower

Water and Electrolytes

- Typically normal fluid – rarely restricted
- Sodium restricted to 1-2 mmol/kg/day
  - Do not correct the hyponatraemia of ESLD
  - Severe hyponatraemia may require fluid restriction
- Potassium 2mmol/kg/day

Nutritional Requirements in Cholestasis

Nutritional element	Daily Requirement	Source
Lipid	30-50% of total energy 30-70% MCT	
PUFA/LCP	>10% of total energy	rapeseed, walnut, fish, sunflower, soybean oils
Protein	2-3g/kg	Whey protein
BCAA	10% total AAs	
Energy	120-150% requirement for age	2/3 as CHO, 1/3 as lipid
CHO		CHO polymer
Na	Minimum	
K	2-3 mmol/kg	