Gastrointestinal, Hepatic, and Nutritional Challenges in FA

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GI problems in FA

- 5% have gastrointestinal tract abnormalities
- Common gastrointestinal concerns
  - Poor oral intake
  - Nausea
  - Abdominal pain
  - Diarrhea
- GI and liver complications of treatment
- Complications of stem cell transplant

Routine GI/Nutrition care

- Evaluate height and weight at each clinical visit
- Screen for gastrointestinal problems
  - Abdominal pain
  - Nausea and vomiting
  - Constipation or diarrhea
  - Excessive bowel gas
- Consider seeing a gastroenterologist if these problems do not respond to initial management

Preparing for a clinical visit

- Abdominal pain?
  - Location
  - Inciting agents
- Nausea and vomiting?
  - Time of day
  - Association with drugs or food
- Excessive gas?

A simple symptom diary for 1-3 months may help pinpoint the problem

Some conditions causing GI symptoms

- Complications of anatomic gastrointestinal abnormalities
  - Strictures
  - Obstructions
- Chronic inflammation/infection
  - Diarrheal disease
  - Small bowel overgrowth
  - Urinary tract infections
- Medication side effects
- Neurologic/behavioral problems

Gastroesophageal reflux

- Commonly associated with esophageal atresia (TEF)
- Commonly seen in children without TEF
- Reflux may become more common with age
- Medical management is essential to reduce complications
- Many require anti-reflux surgery

Symptoms of GER

- Heartburn
- Abdominal pain
- Excessive burping, hiccuping
- Poor appetite, vomiting
- Poor sleep, nightmares

Treatment for GER

- Acid suppression: Proton pump inhibitor
  - Omeprazole, lansoprazole, etc.
  - Avoid H2-antagonists because of bone marrow suppression
- Head of bed up on blocks
- Reduce food intake 2 hours before bedtime
- Antacids (Tums, Mylanta) may give temporary relief

Small bowel overgrowth

- Growth of bacteria in the small intestine beyond what is normal
- Type of bacteria in small intestine may be changed by antibiotic therapy
- Risk increased after previous gastrointestinal surgery

Symptoms of SBO

- Excessive bowel gas
- Diarrhea
- Greasy, orange stools
- Bloating
- Abdominal pain
- Anemia
- B12 deficiency
- Weight loss/Failure to gain weight

Treatment of SBO

- Metronidazole (Flagyl)
- Rifaximin (Xifaxin)
- Probiotics will not treat SBO; unclear if they may help prevent SBO
- If recurrent, consider evaluation for bowel motility

Evaluation of GI symptoms

- Good history and physical exam
- Diagnostic testing possibilities based on history and physical exam
  - Blood for CRP, ESR
  - Stool for ova and parasites, giardia, cryptosporidium, other pathogens
  - Urine culture
  - Hydrogen breath tests
  - Endoscopy with biopsy
  - Avoid radiographic imaging, if possible
    - Ultrasound and MRI are safe

Alarm symptoms and signs

- Involuntary weight loss
- Deceleration of linear growth
- Gastrointestinal blood loss
- Significant vomiting
- Chronic severe diarrhea
- Unexplained fever
- Persistent right upper or right lower quadrant pain

Non-specific management of chronic abdominal pain

- Evaluation completed and no clear etiology found (50% of time)
- Thoughtful planned trials of therapy to reduce pain can be done
  - Acid suppression
  - Visual imaging/self-hypnosis
  - Peppermint oil capsules
  - Trial rifaximin

Non-specific management of chronic abdominal symptoms

- Nausea
  - Ondansetron (Zofran)
  - Visual imaging/self-hypnosis
  - Trial of motility agent
- Diarrhea
  - Trial rifaximin, nitazoxanide

Poor growth in FA

- Short stature associated with genetic defect: >50% have shorter than average height
- ~80% have endocrine abnormalities
- Inflammatory disease
- Important to look at BMI or weight for height, not just weight

Malnutrition

- 20-30% children underweight for height
- May be related to
  - Poor intake, particularly with increased nutrient needs
  - Diarrhea
- If persistently underweight or weight is declining, consider
  - Consult with a dietician for intake analysis
  - Evaluation by gastroenterologist

Appetite stimulants

- None tested directly in FA patients
- Must evaluate first for treatable causes of poor intake
- Weight gained is usually lost when drug is stopped

Appetite Stimulants

- Cyproheptadine (Periactin)
  - Improves gastric accommodation
  - Minimal weight gain
  - Well tolerated
  - Initial sleepiness
- Megestrol acetate (Megace)
  - Minimal weight gain
  - Adrenal insufficiency, glucose intolerance

Behavioral/Nutritional therapy

- Not directly studied in FA
- Often valuable in children <5 years
- Involves teaching parents behavioral techniques and goal setting to improve oral intake and reduce stress associated with feeding

Plan for supplemental feeds

- Nutritional goals
  - Normal growth for genetic potential
  - Energy to meet demands of daily living
  - Adequate reserve to face short-term malnourishment during acute illness
  - Reduction in family/mealtime stress
- Lasting benefits may require long-term therapy.
- Supplementation through GI tract is preferable to supplementation by IV

GI evaluation prior to HCT

- Goal to insure good nutrition and healthy GI tract before procedure
- Review current and past gastrointestinal problems
- Chronic abdominal pain
  - consider endoscopy to detect potential bleeding or infectious risks
- Chronic diarrhea
  - screen for infections
- Nutritional status

Liver evaluation prior to HCT

- Evaluate for the presence of known liver disease
- Previous use of androgens
  - Risk of adenomas that may bleed after cytoreduction
  - US/CT/MRI liver
- Complete immunization
- Avoid alcohol

Hepatic complications of androgens

- Hepatic adenoma 6-7%
- Peliosis
- Potential complications
  - Intrahepatic bleeding
  - Hepatoma

Screening for androgen-related liver disease

- Evaluate pain in RUQ, liver enlargement
- Liver enzymes every 3 months
- Ultrasound every 6 months
- Consider resection if size increasing

GI concerns after stem cell transplant

- Liver
  - Chronic graft versus host disease
  - Chronic viral hepatitis
  - Iron overload
- Intestine
  - Chronic graft versus host disease with diarrhea and weight loss

Gastrointestinal graft-versus-host disease

- Complication of HCT
- Mild to very severe damage to lining of GI tract
- Severe, watery diarrhea and/or nausea and vomiting
- Liver may also be involved with jaundice and reduced function

Gastrointestinal GVHD in FA patients

- Incidence
  - Early data suggested increased incidence of GVHD in FA patients
  - Risk and severity have decreased as HCT has improved
- May increase risk of squamous cell carcinoma

Secondary iron overload

- Iron derived from repeated red cell transfusions
- May lead to organ damage: liver, heart, pancreas
- Screening
  - Serum iron
  - Transferrin saturation
  - Ferritin
- Must confirm iron overload with liver biopsy or specialized MRI

Supplements in FA

- Biology of FA suggests reducing oxidative stress might reduce cancer
- Unclear if supplements can be safely delivered at level to make a difference
- Randomized clinical trials are difficult in a highly variable, rare disease
- Information from other diseases may be of value.

Micronutrient supplementation and cancer prevention

- Trials targeting populations with nutrient deficiency may prevent cancer
- Supplementation in populations with higher nutritional status or to achieve pharmacological exposures may promote cancer

Effects of anti-oxidant supplements

- 78 trials, 296,707 participants in randomized trials of anti-oxidants versus placebo
- Anti-oxidants do not decrease mortality
- Some anti-oxidants appear to increase mortality
  - **Vitamin A**, vitamin E
  - β-carotene
- No evidence of problems with Vitamin C and selenium

Fruits and Vegetables vs. Supplements

- Fruits, vegetables, tea and cocoa are rich natural sources of flavonoids
- High intake of these foods decrease risk of cardiovascular disease; supplements lack the same evidence
- Micronutrients from fruits and vegetables are not reproduced in supplements

Suggested guidelines

- Diet should be high in highly colorful fruits and vegetables (5 or more servings each day)
- Flavonoid supplements or individual vitamins should be viewed as drugs
  - Have side-effects
  - Interact with other medications and nutrients
  - May alter absorption of other nutrients