

# Gastroenterology and Feeding Issues in Fanconi Anemia

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# GI problems in FA

- 5% have gastrointestinal tract abnormalities
- Common gastrointestinal issues
  - Poor oral intake
  - Nausea
  - Abdominal pain
  - Diarrhea
- Liver adenomas associated with androgen treatment
- Complications of stem cell transplant
- Optimal nutrition in FA



# Consider most significant problem

- 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 with diagnosis*



# Some conditions causing GI symptoms

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



# Gastroesophageal reflux

- Commonly associated with esophageal atresia
- 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



# Small bowel overgrowth

- Proliferation of bacteria in the small intestine
- Bacteria in small intestine may be changed by antibiotic therapy
- Risk increased after previous gastrointestinal surgery
- Associated with stasis
  - Impaired peristalsis
  - Abnormal anatomy
  - Blind loop



# Symptoms of SBO

- Excessive bowel gas
- Diarrhea
- Steatorrhea
- Bloating
- Abdominal pain
- Anemia
- B12 deficiency
- Malabsorption
- Weight loss/Failure to gain weight





# Evaluation of gastrointestinal 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
- Family history of inflammatory bowel disease



# Suggested treatment options

- Acid suppression: Proton pump inhibitor
  - Omeprazole, lansoprazole, etc.
- Gastric motility-promoting agents
  - Erythromycin, Augmentin
- Antinausea agents
  - Ondansetron (Zofran)
- Treatment of small bowel overgrowth
  - Metronidazole (Flagyl)
- Supplemental nutrition



# Non-specific management of chronic abdominal pain

- Evaluation completed and no clear etiology found
- Thoughtful planned trials of therapy to reduce pain, nausea or diarrhea can be done
- Pain
  - Acid suppression
  - Visual imaging/self-hypnosis
  - Peppermint oil capsules
  - Trial rifaximin
- Nausea
  - Ondansetron
  - Visual imaging/self-hypnosis
- 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/elevated  $\text{TNF}\alpha$
- Poor oral intake



# Malnutrition

- 22% children underweight for height
- Measure height and weight at each visit
- Failure to thrive
  - Weight for height persistently less than 85%
  - BMI persistently < 3 d percentile for age
  - Persistent decline in either measurement



# 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)
  - Minimal weight gain
  - Well tolerated
  - Initial sleepiness
- Megestrol acetate (Megace)
  - Minimal weight gain
  - Adrenal insufficiency, glucose intolerance





# 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
- Lasting benefits may require long-term therapy.
- Supplementation through GI tract is preferable to supplementation by IV



# Overweight

- 27% FA patients overweight or obese
- Associated with abnormal lipids
- Associated with diabetes
- Although failure to thrive has been a significant problem in FA, over-nutrition and metabolic syndrome are now being seen.

Giri, et al. J Clin Endocrinol Metab 2007



# Managing OW/OB

- 6-day diet diary to initiate dietary intervention
- Explore potential for exercise
- Try to explore the family eating habits



# 5-2-1-0

- “5 a day” fruits and vegetables
- Less than 2 hr/day of screen time
- At least 1 hour of moderate activity each day
- No sweet drinks-0 pop, juice, Kool-ade, sports drinks, ect



# GI evaluation at the time of stem cell transplant

- Previous use of androgens: US/CT/MRI liver
- Chronic abdominal pain: consider endoscopy to detect potential bleeding or infectious risks
- Chronic diarrhea: screen for infections
- Established liver disease
- Nutritional status



# 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 stem cell transplant
- 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





# Hepatic complications of androgens

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



# Screening for androgen-related liver disease

- Liver enzymes every 3 months
- Ultrasound every 6 months
- Consider resection if size increasing



# Secondary iron overload

- May lead to organ damage: liver, heart, pancreas
- Screening
  - Serum iron
  - Transferrin saturation
  - Ferritin
- Must confirm iron overload with liver biopsy or specialized MRI



# Micronutrient supplementation in FA

- Many individuals and families supplement vitamins, flavonoids, and other micronutrients
- Supplements are proposed to alter the oxidative stress and increased inflammatory reaction found in FA
- While we depend on oxygen for life, oxygen is a deadly poison
- All terrestrial life controls oxygen toxicity through reactions called Red-Ox (reduction-oxidation reactions)
- Some evidence suggests that the FA participates in regulating oxidative stress
- Patients with FA also have increased production of inflammatory cytokines



# 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
    - $\beta$ -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

