Nutrition Considerations with Pediatric Inflammatory Bowel Disease

Lindsay Rypkema, RD, CSP, CLEC

CHOC Children's Hospital

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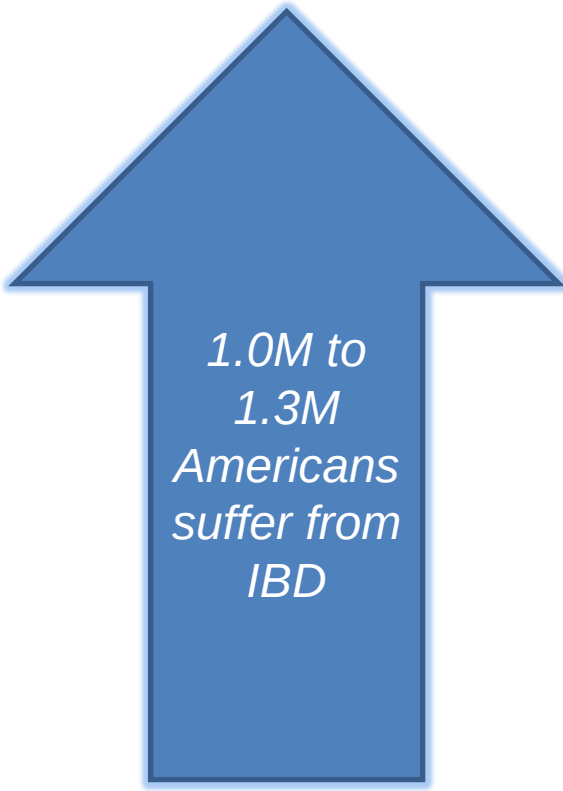
Objectives

- **Define** the basics of Inflammatory Bowel Disease including disease process and treatment
- Review nutrition **assessment,** nutrition concerns, and nutrition therapy in IBD
- **Understand** the past and present research regarding the role of nutrition in IBD
- Gain a strong knowledge base regarding the role of nutrition in IBD to make an **impact** on your patient's care

Define the Basics of IBD

What is inflammatory bowel disease?

- Chronic lifelong disease with times of relapse and remission
- Genetic Predisposition
  - Most common in Caucasian and Ashkenazic Jewish origin
- Environmental factors
  - Most common in Westernized (developed) countries
  - More common in urban areas
- Potential diet factors
  - Saturated fat, Omega-6 PUFA, red meat



1.CDC 2015; http://www.cdc.gov/ibd/ibd-epidemiology.htm

2. Crohn's and Colitis Foundation of America

Differentiating Inflammatory Bowel Disease[1,4]

- Chronic inflammatory disorders that can affect GI tract of children and adults with up to 25% of cases being diagnosed before age 20 [4]
- Crohn's Disease
  - Can occur anywhere in GI tract from mouth to anus and can affect entire thickness of bowel wall
  - Signs & symptoms: cramps, pain, rectal bleeding, diarrhea, constipation, weight loss, malnutrition, fatigue, joint pain
- Ulcerative Colitis
  - Occurs in colon and affects lining of colon
  - Signs & Symptoms: urgent and loose BMs often with blood or mucous, crampy abdominal pain, decreased appetite, joint pain

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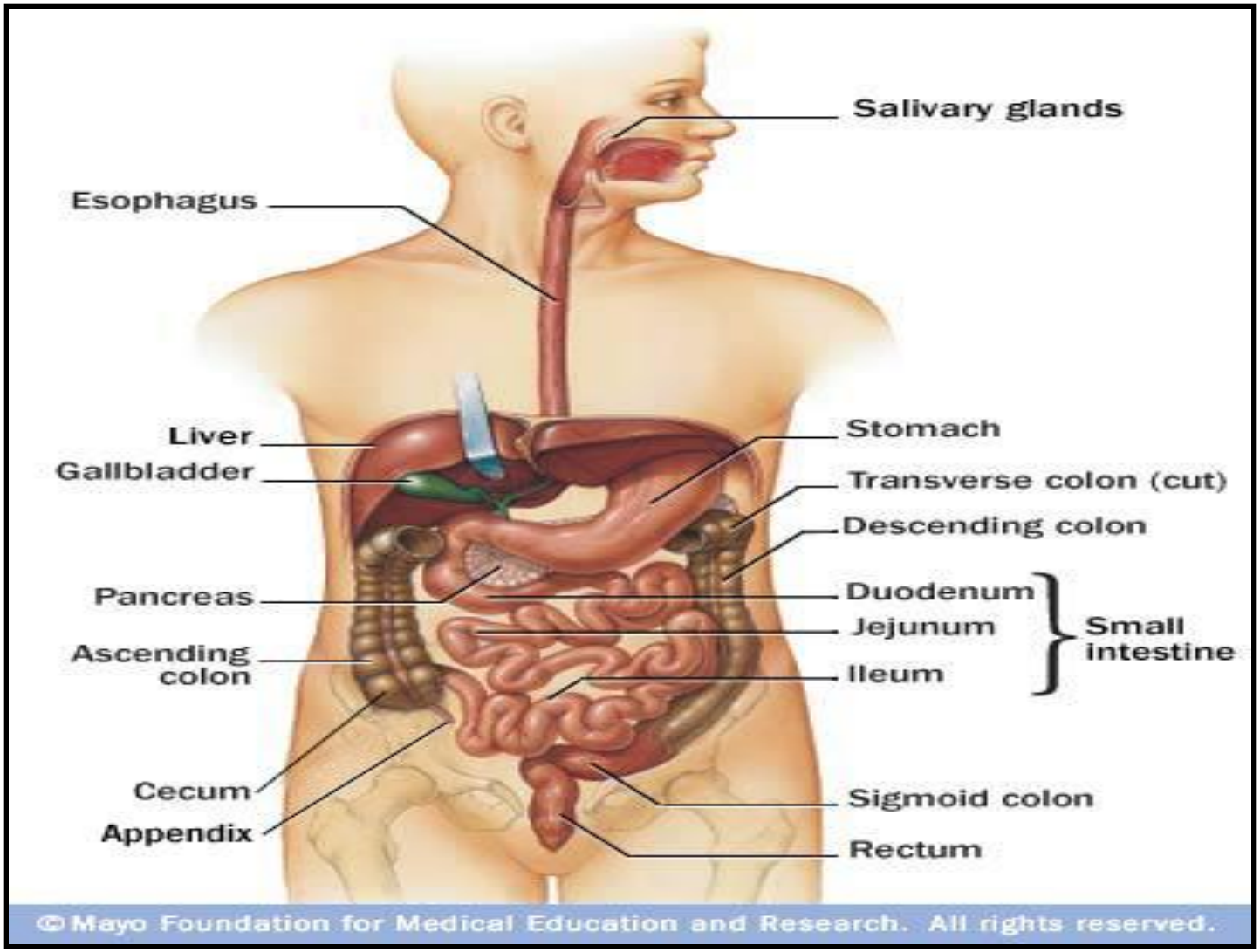
1. http://www.ccfa.org
4.Rufo P,et al. Recommendations.*J Pediatr Gastroenterl Nutr.*2012



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Nutrition Concerns & Assessment

Nutritional Concerns in IBD

- Malnutrition/Poor Growth [5,6]
  - Anorexia or fear of eating due to pain, frequent stooling, social anxiety, exhaustion
  - Risk for malabsorption (high stool output, frequent flare ups, mucosal damage or resections)
  - Growth failure
    - Linear growth failure common in Crohn's Disease
  - Delayed onset of puberty
  - Inflammation – cytokine interaction with IGF-1 leading to suppression of growth factor
  - Steroids may inhibit insulin like growth factor
- Metabolic bone disease
- Micronutrient deficiencies
  - Consider checking Folate, B12, Vitamin D, Iron studies, and Zinc at diagnosis & at least once yearly

5. Wiskin A, et al. *Nutr in Clinical Practice.2007*

*6.*Kleinman R, et al.*.JPGN.2004*

Micronutrient Concerns

Folate

- Studies: Serum Folate, often checked in conjunction with B12
- Possible cause of deficiency: inadequate folate intake, small bowel resection, medications that interfere with metabolism: Sulfasalazine, Methotrexate
- Symptoms of Deficiency: fatigue, glossitis, poor growth, megaloblastic anemia
- Excessive supplementation can mask B12 deficiency
- Primary site of absorption: Jejunum/Ileum

Vitamin B12

- Studies: Vitamin B12, Methylmalonic Acid (MMA) & Homocysteine levels
  - If both increased - early B12 deficiency
  - If Homocysteine increased - Folate deficiency
- Possible cause of deficiency: surgery or resection of terminal ileum, bacterial overgrowth, increased risk with Crohn's disease
- Symptoms of Deficiency: paresthesias, megaloblastic anemia, mood change, fatigue, pale skin, SOB ,smooth tongue
- IM replacement
- Primary site of absorption: Terminal Ileum

7.Hwang C, et al. Zinc.*Inflamm Bowel Dis.*2012

Micronutrient Concerns Continued

Zinc

- Studies: Alk Phos, Serum Zinc, Albumin, inflammatory markers (CRP)
- Possible cause of deficiency: increased GI losses from stool or fistula, malabsorption
- Symptoms of Deficiency: poor growth, anorexia, impaired taste and smell, hypogonadism, decreased immune function, dry, flaky skin, hair loss, diarrhea, impaired wound healing
- Excessive replacement can cause Copper Deficiency
- Supplement short term 2-3 weeks
- Primary absorption site: Duodenum/Jejunum/small amount Ileum

Iron

- Studies: Hgb, Hct, Serum Iron, TIBC, Transferrin, Ferritin
- Possible cause of deficiency: increased losses (blood in stool), malabsorption, decreased intake
- Symptoms of Deficiency: pale, fatigue, SOB, brittle nails, fast heartbeat, poor appetite, PICA
- Mode of supplementation debatable due to risk for GI upset
- Primary absorption site: Duodenum & Jejunum

7.Hwang C, et al. Zinc.*Inflamm Bowel Dis.*2012

Micronutrient Deficiencies – Calcium and Vitamin D

- Recommendations taken from “A Clinical Report of Skeletal Health of Children and Adolescents with Inflammatory Bowel Disease” [8]
- Peak bone mass for males: 18-20 years & 16 for females
- Studies have shown that inflammation has a negative effect on the accrual of bone mass and actual quality of bone
- Studies:
  - Serum Calcium, Ionized Ca, Alk Phos, PTH, Phosphorus
  - 25-OH D – check at the end of winter (goal >30 ng/mL)
- Possible cause of deficiency: lactose intolerance, inadequate intake, steroid use, malabsorption, hypoparathyroid
- Steroids reduce absorption (Ca) and negatively affect bone turnover

8. Papa et al. *JPGN.2011*

Calcium & Vitamin D

- Symptoms of Deficiency:
  - Calcium: muscle spasms, dry,scaly skin, memory loss, abnormal heart rhythm, osteopenia/osteoporosis, tetany
  - Vitamin D: muscle weakness, possible rickets, bone pain
- Primary absorption site: Duodenum/Jejunum
- Replacement:
  - Calcium: Baseline: 1000 – 1300 mg of elemental Calcium daily in children >4 y.o. (500 mg/dose)
  - Recommended to limit bisphosphonates
  - Vitamin D: Cumulative doses over 8-12 weeks of 400,000 IU if level <20 (~ 5700 IU/d) and 250,000 IU over 8-12 weeks if level is 20-32 (~ 3600 IU/d)
    - baseline 800-1000 IU daily

8. Papa H, et al.*JPGN.2011*

Calcium and Vitamin D

- Monitoring:
  - DXA (Dual-energy x-ray absorptiometry) – two dimensional test where bone mineral density = sum of cortical and trabecular bone mass within a projected area
  - Recommended for suboptimal growth velocity or height z-score <-2 or downward trend; weight or BMI Z-score <-2.0 or downward trend; secondary or primary amenorrhea; delayed puberty; severe inflammation (albumin <3); steroid use >/= 6 months
  - Repeat scan every 1-2 years if Z-score </= -1.0 SD
    - lower spine & hip
  - Check 25-OH D at least yearly, more frequently w/ replacement
- Weight bearing exercise

8. Papa H, et al.*JPGN.2011*

Nutrition Assessment

Growth History	• Weight, height, & BMI using Z scores • Weight/length under 2 & FOC if under 3 y.o. • Outside growth records if new to practice
GI symptoms	• N/V, pain, stool output (volume and frequency), floating stools, mouth sores, Onset of symptoms • History of strictures, fistula, or surgery/resection
Intake	• Appetite • 24 hour food recall • Special diets (past or present) • Trigger foods or food groups avoided • Food allergies

Nutrition Assessment

Labs/Tests	• Vitamins, minerals, inflammatory markers, DXA scans
Nutrition Support	• Exclusive enteral nutrition or TPN & bowel rest
Physical exam	• Muscle wasting (MUAC, TSF, MAMC, handgrip strength) • Hair, skin
Physical assessment	• 75 adult patients w/ Crohn's disease assessed for malnutrition[9] • 26.7% considered malnourished with MAC, MAMC = 29.3%, SGA=18.7%, BMI=6.7%, TSF=37.3% , handgrip strength=73.3%

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9.Bin C, et al.*Dig Dis Sci.2010*

Nutritional Requirements

- Calorie needs ultimately based off intake and growth trend
  - Highest need if malnourished, active inflammation, and in need of catch up growth (REE x 1.5-2)
  - If inadequate energy stores and inflammation energy needs are 5-35% above estimated needs [10]
- Kleinman R, et al. summarized refeeding studies in undernourished children w/ Crohn's disease [6]
  - Short term refeeding results in catch up growth (average gain of 8.7 kg in 6 weeks) when receiving 170% REE
  - Long term refeeding results in catch up growth (7 kg/year) when providing 133% estimated needs
- Wiskin A, et al. studied 55 children (37 w/ Crohn's disease and 18 w/ UC) revealing no significant relationship between disease activity and REE [11]
  - Does REE decrease due to severe anorexia and illness similar to prolonged starvation with Anorexia Nervosa?

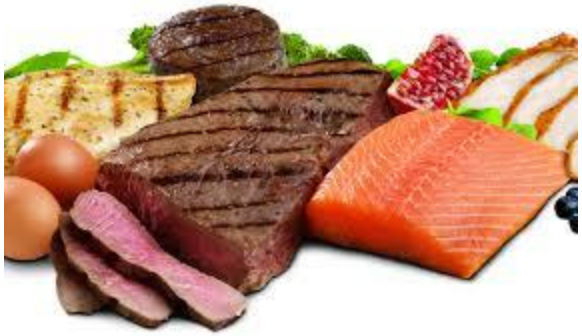
Nutritional Requirements

- Hill R, et al. compared measured REE against Schofield, Oxford, FAO/WHO/UNU, and Harris Benedict [13]
  - 63 children had repeated measurement for total of 243 measurements in study
  - All equations underestimated

Predictive equation	Difference from measured value	
	Ulcerative Colitis	Crohn's Disease
Schofield	-159	-42
Oxford	-202	-95
FAO/WHO/UNU	-162	-54
Harris Benedict	-190	-108

Nutritional Requirements

- Protein
  - No established guidelines but increased need with inflammation and increased losses – recommend increasing by 50%
  - Highest need with fistula losses
  - Protein markers



Treatment & Research of IBD

Treatment of IBD

- Pharmaceutical Therapies
- Nutrition Therapies
  - Diet (SCD, FODMAP, Elimination)
  - Exclusive Enteral Nutrition
  - Parenteral Nutrition
  - Probiotics/prebiotics
  - Omega 3
- Surgery
  - Ulcerative Colitis – total proctocolectomy for cure
    - Ileo pouch-anal anastomosis if possible
  - Crohn's Disease – surgery in not a cure

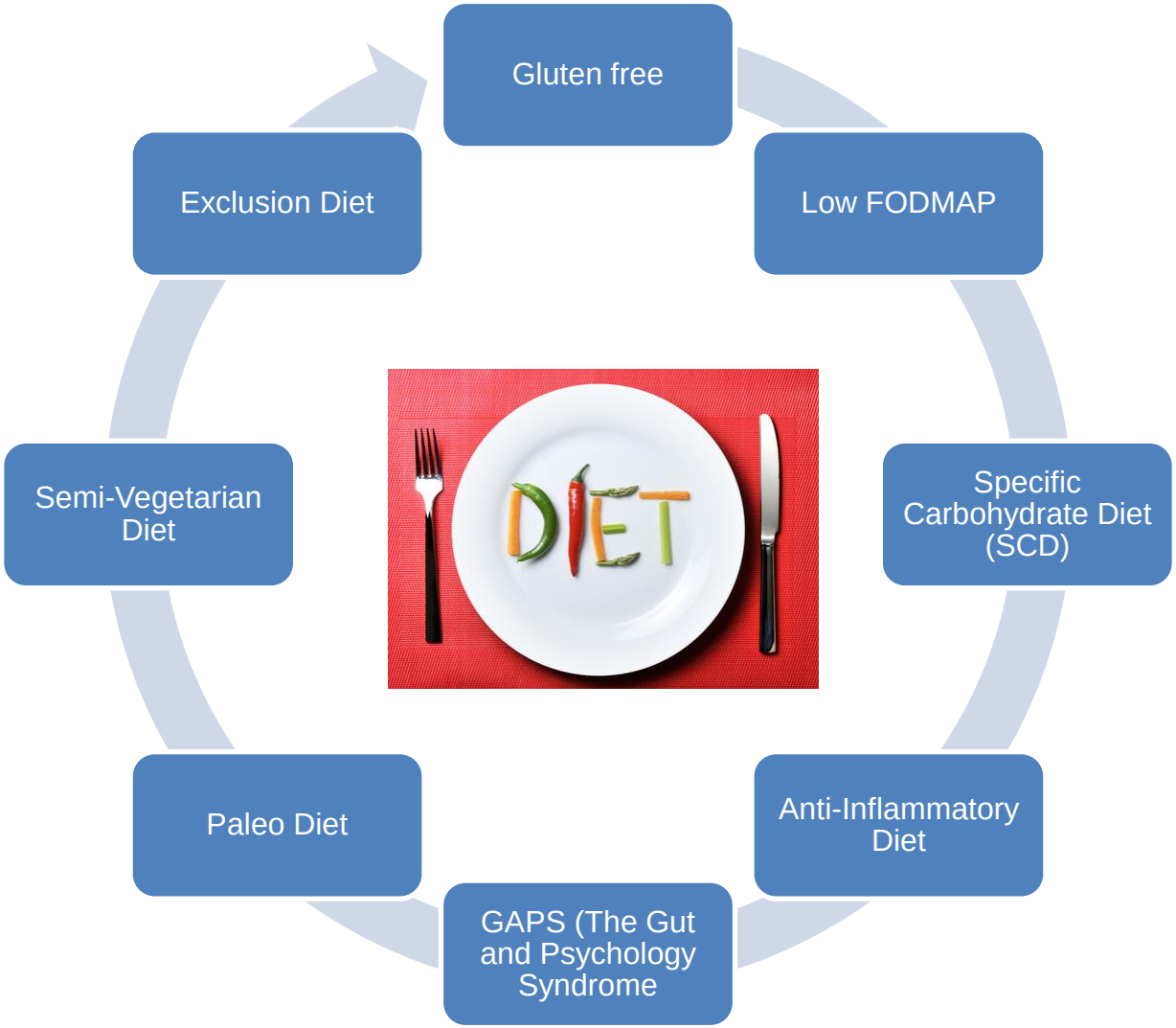
Pharmaceutical Treatment

- Aminosalicylates: Used to achieve and maintain remission in colonic disease
  - 5 –ASA: Mesalamine (Asacol, Lialda, Rowasa), Sulfasalazine
- Corticosteroids: Used for moderate to severe disease not responsive to initial treatment
  - Prednisone
- Immunomodulators – Target the immune system to suppress inflammation
  - Imuran, Methotrexate, Azathioprine,6-MP
- Biologics – Used for moderate to severe disease refractory to other treatments
  - TNF Alpha inhibitors
  - Remicade/Humira
- Antibiotics - Used for Crohn's disease especially in setting of fistulas or abscesses or Ulcerative Colitis with fever
  - Flagyl, Cipro

Side Effects of Pharmaceutical Treatment

Medication	Nutrition Related Side Effects
Prednisone	Hyperglycemia, fluid retention, increased blood pressure, mood swings, growth suppression, osteoporosis
Antibiotics	Abdominal discomfort, diarrhea Long-term use: overgrowth of resistant pathogens, loss of good bacteria
Remicade	N/V, abdominal pain, increased LFTs, lymphoma
Azathioprine	N/V/D, swollen joints, leukopenia, hepatoxicity, lymphoma
6-MP (mercaptopurine)	Anorexia, N/V, mucositis, hepatotoxicity, lymphoma
Methotrexate	Oral ulcers, N/V, hepatotoxicity, renal damage, diarrhea
Aminosalicylic acids	Abdominal discomfort, N/V, headache

Specialized Diets



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Diet Recommendations

- Food/symptom diary
  - Eliminate trigger foods if able to find a pattern
- Common trigger foods: high fat, lactose containing, spicy, insoluble fiber, gas forming foods, caffeine, artificial sweeteners, alcohol
- Consume small, frequent meals
- Sip fluids between meals, don’t use straw and ensure adequate intake
  - monitor urine output and color

Diet Recommendations

- Fiber
  - Soluble fiber
    - slows transit time
    - peeled fruit: apples, bananas, peaches, pears, well cooked vegetables such as carrots, broccoli, barley, oats, and psyllium.
  - Insoluble fiber: more difficult to digest
    - increases bulk
    - whole-wheat flour, wheat bran, brown rice, fruit with seeds and edible peels, cauliflower, celery
  - Consider cooking/steaming fruit & vegetables and removing skins
- Low Residue diet may be effective during Crohn's Disease flare especially if narrowing or strictures
- Avoid nuts, seeds, & popcorn if at risk for strictures – Crohn's disease

Total Parenteral Nutrition

- Indications
  - Refractory disease in acute flare especially if malnourished
  - High output fistulas or obstructions
  - Severe malnutrition with planned surgery
  - Bowel rest required for > 5 days
- Consider additional zinc if high output
- Ensure balanced macronutrient provision with adequate protein
- May need high volume if increased output

Exclusive Enteral Nutrition (EEN)

- Distinct therapy found to be beneficial in Crohn's Disease
- Administration of 100% formula based diet via feeding tube or consumed orally
- Exclusion of normal diet
- Many variations in protocols
  - Duration
  - Formula type
  - Provision of anything else PO
  - Mode of transitioning back to PO

Use of Enteral Nutrition for the Control of Intestinal Inflammation in Pediatric Crohn Disease

- *Journal of Pediatric Gastroenterology and Nutrition (2012)* [15]
  - Authored by Critch J, Day A, Otley A, et al.
  - NASPGHAN developed enteral nutrition workgroup with 5 pediatric gastroenterologists & 1 dietitian with expertise in management of Crohn's Disease to review & summarize current literature

Conclusions

- Up to 85% of newly diagnosed Crohn's Disease achieve remission with EEN
- Limited conclusions regarding use of medications in addition to EEN to induce remission
- Increased mucosal healing with EEN vs. steroids
- Superior improvement in linear growth w/ EEN
- Polymeric formula equivalent success to elemental

Use of Enteral Nutrition for the Control of Intestinal Inflammation in Pediatric Crohn Disease

Conclusions Continued

- More studies needed regarding effectiveness of partial enteral nutrition to obtain remission
- Disease location – more studies need to be completed although current research reveals it may not be as beneficial in colonic disease
- Duration required – highly variably between institutions (3-12 weeks)
  - most commonly 6-8 weeks
- Reintroduction of diet
  - International Survey results revealed varied protocols
    - 52% of centers recommended gradual reintroduction of food with decrease in enteral feeds,
    - 50% recommended initial fiber avoidance
    - allergen free diet or low fat

Polymeric Diet Alone Versus Corticosteroids in the Treatment of Active Pediatric Crohn's Disease: A Randomized Controlled Open-Label Trial

- *Clinical Gastroenterology and Hepatology 2006* [16]
  - Authored by Borrelli O, Cordischi L, Cirulli M, et al.
  - Studied 37 children with newly diagnosed Crohn's disease
  - Randomized, prospective 10 week trial of patients diagnosed with Crohn's disease within 12 weeks of enrollment and disease activity of moderate to severe
    - Oral methylprednisolone vs. EEN
  - Ileocolonoscopy performed before start of study and at 10 weeks
  - PCDAI calculated at 2,4,6,8, &10 weeks
  - Clinical remission: 15/19 EEN & 12/18 steroids
  - 14 /19 EEN patients showed mucosal healing vs. 6 /18 steroid
  - No significant difference in linear growth but greater weight gain in EEN group

Expert Summaries of EEN

- NASPGHAN Recommendations (2012) [4]
  - EEN can be used as primary therapy in children with mild to moderate Crohn's Disease for induction of remission and has shown comparable efficacy to steroids
  - Polymeric formula acceptable
  - Maintenance medication required once in remission
  - Supplemental enteral nutrition is indicated in all IBD children with linear growth failure
- ECCO/ESPGHAN consensus guidelines (2014) [17]
  - EEN is recommended to induce remission in children with active luminal Crohn's Disease
  - Partial Enteral Nutrition should not be used to induce remission

4.Rufo P,et al. Recommendations.*J Pediatr Gastroenterl Nutr.*2012

17.Ruemmele F.M., Veres G, Kolho K.L. et al.*Journal of Crohn's and Colitis.*2014

Exclusive Enteral Nutrition

- Partial enteral nutrition
  - 2 Canadian studies showed benefit with partial enteral nutrition including improved growth, decrease in steroid use, decrease in symptom index & prolonged remission [28,29]
- Efficacy in adults
  - Adult studies have shown less benefit
  - Poor compliance, poor palatability, and poor motivation
    - Better for adults who are treatment naïve
    - Further research needed for newly diagnosed and those with ileal involvement

28.Belli DC, et al.*Gastroenterology.*1998

29.Wilschanski et al. *Gut.1996*

Possible Mechanism of Action – EEN [15,18]

- Improvement in overall nutritional state due to consistent delivery of essential nutrients
- Direct anti-inflammatory effects
  - Increased level of anti-inflammatory protein
  - Exposure to formula decreases response to proinflammatory agents
  - Decrease in inflammatory cytokines
- Alteration of intestinal microflora
- Avoidance of food that may trigger inflammation

15. Critch J, Day A, Otley A, et al. *JPGN.*2012

18. Bannerjee K, et al. *JPGN*. 2004

Barriers to use/possible side effects of EEN

- Physician recommendation
- Nausea, abdominal pain, gas, loose stools, early satiety
  - Fewer side effects than steroids
- Potential for Refeeding Syndrome although not common
- Cost/coverage
  - Cheaper than TPN
  - Often not covered by insurance if consumed orally
- Quality of life
  - Social anxiety, decreased school attendance
  - UK study revealed improved QOL scores in 24 out of 26 children treated w/ Crohn's Disease [19]
    - 90% of these children obtained remission so likely related to improvement in GI symptoms
    - Only 3 of them had NG tube

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19. Afzal NA et al. nutrition.*Aliment Pharmacol Ther.*2004

Probiotics in IBD

- Probiotics and prebiotics influence the intestinal microbiota and can alter metabolic properties of our gut microbiome
  - Increased SCFA may lower pH of colon (prevent growth of pathogenic microorganisms)
  - Some probiotic strains may help to preserve immune regulation
- Probiotics ("good bacteria"): living organisms (bacteria and yeast) which should produce health benefit to host
  - VSL #3 – commonly studied
  - Use cautiously with neonates and immunodeficiency
  - Should technically survive gastric acid and bile in order to reach small intestine and colon
  - Yogurts using term live active cultures must have 10^{8} live lactic acid organisms per gram
- Crohn's Disease – studies have not shown superiority of probiotics to placebo when using as additive to standard care to induce or maintain remission(20)

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20. Ciorba M.A. et al. Probiotics.*Clin Gastroenterol Hepatol.*2012

Probiotics in Ulcerative Colitis

- Probiotics have shown benefit in ulcerative colitis [20]
  - VSL #3 (3.5 trillion cfu/day) has shown increased symptom improvement during flare but not improvement of endoscopic scores
- VSL #3 has also shown to be of benefit in prevention of pouchitis after surgical take down with UC
- 1 year placebo controlled, double blind study with 29 pediatric patients assessing induction and maintenance of remission in active UC [21]
  - VSL #3 (450-1800 billion bacteria/day) or placebo
  - Induction therapy was steroids with Mesalamine maintenance therapy
  - Remission achieved in 92.8% of VSL #3 + induction therapy & 36.4% treated w/ placebo and induction therapy

20. Ciorba M.A. et al. Probiotics.*Clin Gastroenterol Hepatol.*2012

21.Miele E, et al. Colitis.*Am J Gastroenterol.*2009

Expert Summaries

- World Journal of Gastroenterology conclusions 2014 (23)
  - Probiotic as addition to standard therapy for active UC may be beneficial with VSL #3 showing the most promise
  - Probiotics such as VSL #3 may be as efficient as Mesalamine for maintenance therapy in UC
  - Probiotics show no advantage over placebo in maintenance of remission for Crohn's disease
- Consensus guidelines of ECCO/ESPGHAN 2014 (17)
  - Probiotics are not recommended for maintenance of remission in IBD
  - Probiotics may be effective in reducing inflammation in colitis and may be of benefit in some situations such as pouchitis and Ulcerative Colitis

Prebiotics

- Prebiotics: nondigestible but fermentable carbohydrate that may change the composition of gut microbiota
  - Favor beneficial bacteria
- Plantago ovata seeds (fermentable dietary fiber) vs. Mesalamine therapy in Ulcerative Colitis[25]
  - 102 patients randomized into three groups

Treatment	Plantago Ovata seeds	Mesalalamine	Seeds + Mesalamine
Treatment failure rate after 12 months	40%	35.1%	30%

25. Fernandez-Banares F, et al. Colitis. *The American Journal of Gastrolenterology.* 1999

Prebiotics – Germinated Barley Foodstuff [26]

- Treatment of ulcerative colitis patients by long-term administration of germinated barley foodstuff
  - Multi-center open trial
  - GBF: dietary fiber and glutamine rich protein
- 21 patients with mild to moderate UC received 20-30 grams/day of GBF x 24 weeks in conjunction with standard treatment
- Clinical activity index score: # of episodes diarrhea; nocturnal diarrhea; visible blood in stools; fecal incontinence; use of anti-diarrheal drugs; abdominal pain, cramping, and tenderness; general well being
  - Some people had colonoscopies before and after
- Results:
  - After 6 months – blood in stool and nocturnal diarrhea were decreased
  - Further studies needed

26.Kanauchi O, et al. *International Journal of Molecular Medicine.*2003

Omega-3 Supplementation & Research

- Theoretically, Omega 3 intake would reduce inflammation
- EPIC trials [27]
- "Omega-3 Fatty Acids for the maintenance of remission in Crohn Disease"
  - Randomized, double blind, placebo controlled
  - January 2003-February 2007 conducted between 98 Centers around the world
- EPIC-1 : Eligible patients had experienced disease exacerbation within the past year but had been in remission for 3-12 months

27. Feagan B, et al. *JAMA.*2008

EPIC Trials

- EPIC-2: Eligible patients had active disease and were treated with 16 week tapering course of Prednisone or Budesonide
  - Enrolled w/ CDAI score of less than 150 which indicates remission
  - Checked CDAI score at 8 weeks
    - CDAI score: joint pain, anal fissures, fistula, fever, # loose BM, abdominal pain, use of Lomotil for diarrhea, height, weight, Hct
- Exclusions: use of 5-ASA, immunosuppressive medications, TNF antagonist, ostomy, short bowel, severe medical disease outside of Crohn's, substance abuse
  - Medications – no new allowed and current therapies were weaned including Corticosteroids, Budesonide, Prednisone
- Patients were given 4 (1 gram) capsules of Omega-3 fatty acids vs. 4 placebo capsules/day

EPIC Trials- Results

- Relapse was classified as increase of more than 70 points on CDAI score from baseline or score of >150
- Concluded that Omega-3 supplementation was not statistically beneficial

Study	# Patients	1 year relapse rate w/ placebo	1 year relapse rate w/ Omega 3
EPIC-1	363 188 (Omega-3) 186 (Placebo)	35.7%	31.6%
EPIC-2	375 189 (Omega-3) 190 (Placebo)	48.8%	47.8%

- Secondary finding – decrease in Triglyceride level
  - EPIC-1 – decrease of 21.5 mg/dL
  - EPIC-2 – decreased by 27.1 mg/dL

Omega – 3 Supplementation

- Consensus Guidelines of ECCO/ESPGHAN [16]
  - Omega 3 fatty acids are not recommended for maintenance of remission in IBD

- Westernized diet is high in Omega-6 fatty acids and typically low in Omega 3 fatty acids which may increase inflammation

Summary

Patient Resources

- Crohn's and Colitis Foundation of America (CCFA)
  - http://www.ccfa.org/science-and-professionals/programs-materials/patient-brochures/
  - Local Support Groups
- www.gikids.org
- http://www.crohnsandcolitisinfo.com/
- http://www.youandibd.com/
  - (interactive videos)

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Summary of Nutrition Considerations with Pediatric Inflammatory Bowel Disease

- Nutritional needs (calorie, protein, micronutrient) may change with Inflammatory Bowel Disease
- There are multiple ways to provide nutrition to a child with IBD including: nutrition support and multiple specialized diets/supplements
- Nutrition care for the pediatric patient with IBD is constantly evolving and research is ongoing
- Patients and families need professional support when choosing and following a specialized nutrition plan

Thank you!

Questions?

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