

Nutrition in Inflammatory Bowel Disease

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Disclosure Information

- Abbott Nutrition
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Objectives

- Discuss the frequency and consequences of malnutrition in IBD
- Consider the role of nutrition in the pathogenesis of IBD
- Review when and how nutritional therapy should be used and the clinical impact of these treatments on IBD

Prevalence of Nutritional Deficiencies in IBD


	<i>Crohn's Disease (%)</i>	<i>Ulcerative Colitis (%)</i>
Weight Loss	65-75	18-62
Growth retardation	40	
Hypoalbuminemia	25-80	25-50
Anemia	60-80	66
Iron	25-50	81
Folate	56-62	30-41
Vitamin B12	48	5
Calcium	13	+
Vitamin A	11-50	93
Vitamin D	23-75	35
Vitamin E	0	40
Vitamin K	+	+
Zinc	40-50	
Selenium	+	+

Han PD, et al. Gastro Clin N Amer 1999

- ### Malnutrition in IBD
- CD in remission c/w controls
 - Decreased β -carotene, vitamin C, D, E, Mg, Se, Zn
 - Decreased fat mass and muscle strength
 - Recently diagnosed disease
 - UC: Reduced body wt, β -carotene, Mg, Se, Zn
 - CD: Decrease vitamin B12
- Geerling BJ, et al. Am J Clin Nutr 1998;67:919-26
Geerling BJ, et al. Eur J Clin Nutr 2000;54:514-21

- ### Micronutrient Deficiency
- Plasma levels may not reflect body tissues stores and functional status
 - Deficiency may be asymptomatic

Adverse Consequences of Malnutrition in IBD

Growth retardation		Short stature
Weight loss		Fatigue, weakness
Hypo-albuminemia		Poor wound healing
Anemia		Increased risk CRC
Folate deficiency		Neuropathy
Vitamin B ₁₂ deficiency		Metabolic bone disease
Ca, Mg deficiency		Decreased QoL
Zinc deficiency		

Adverse Consequences

- Postoperative complications
- Prolonged hospitalization
- Increased health care expenditures
- Decrease in the quality of life
- Impaired mucosal healing

Clinical Impact of Malnutrition

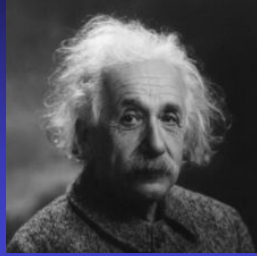
~1% of the Nationwide Inpatient Sample Database

	IBD n=52,142		Non-IBD n=23,548	
	CD	UC		
Malnutrition (%)	6.1%	7.2%	1.8%	<i>p</i> <0.0001
Malnutrition (OR)	5.57			95% CI: 5.29 –5.86
Fistulizing CD (OR)	1.65			95% CI: 1.50 –1.82
s/p surgery (OR)	1.37			95% CI: 1.27–1.48
Mortality (OR)	3.49			95% CI: 2.89–4.23
Length of stay (d)	11.9		5.8	<i>p</i> < 0.00001
Charges (\$)	45,188		29,295	<i>p</i> < 0.00001

Nguyen GC, et al. Inflamm Bowel Dis 2008;14:1105-11

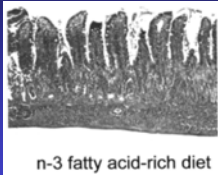
Pathogenesis of IBD: Theory

- Immune dysregulation
- Genetic susceptibility
- Environmental factors

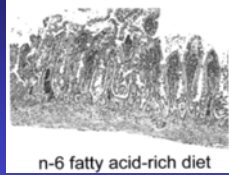


From Wikipedia; Photographed by Oren J. Turner (1947)

N-3 Fatty Acids in TNBS Induced Enteritis



n-3 fatty acid-rich diet



n-6 fatty acid-rich diet

Andoh A, et al. Int J Molec Med 2003;12:721

Nutrients in the Pathogenesis of IBD: Experimental

- Milk (TGF β)
- Glutamine
- Short Chain Fatty Acids
- Soluble fiber (SCFA)
- Fish Oil
- Antioxidants

Why Nutritional Therapy Should Work

- Mucosal healing
 - Oxidative fuel for the mucosa
 - Co-factors for enzymes
- Immune regulation
 - Substrate for inflammatory mediators: cytokines, eicosanoids, adhesion molecules, NO
- Neuroendocrine
 - Growth factors: IGF-1

Diet and Pathogenesis of IBD


- Increased intake of refined sugar in CD
- Reduced risk of CD with breast feeding
- Increased risk of CD with decreased ratio of n-3 to nN-6 PUFA in Japanese

Persson PG, et al. Scand J Gastroenterol 1987;22:385-9
Calkins BM, et al. Epidemiol Rev 1986;8:60-91.
Shoda R, et al. Am J Clin Nutr 1996;63:741-5

Diet and Pathogenesis of IBD

- Despite the theoretic rationale and epidemiologic evidence in favor of dietary therapy, recommending dietary as primary therapy can not be strongly endorsed (except in pediatric patients)

Clinical Practice



A diamond-shaped orange sign with a black border and the text "ROAD WORK AHEAD" in black capital letters.

Causes of Malnutrition in IBD

- Diminished oral intake
- Malabsorption
- Mucosal inflammation
- Increased nutrient requirements
- Drug nutrient interaction

Causes of Malnutrition in IBD

- Extent of TI disease affects absorption of vitamin B12 and fat.
- SBBO may be present (CD, pouchitis)
- REE and protein turnover is increased
- Low levels of IGF-1
- Mucosal loss of protein, blood
- Secretions rich in minerals and TE
- CS affect metabolism of protein, bone, IGF-1
- Folate and MTX interfere with folic acid

Nutrition Assessment

- Diet & weight history
- Anthropometrics
- Physical exam
- CBC
- CMP
- PT INR
- RBC folate
- Iron, TIBC, Ferritin
- Vitamin B12
- Intact PTH
- 25 OH Vit D
- DEXA
- Mg, Zn
- Vitamin A, E

Treatment of Malnutrition

- Dietary modification
- Dietary supplementation
- Oral enteral supplements
- Enteral nutrition
- Parenteral nutrition

Treatment of Inflammation

- In children, Infliximab
 - Decreased proteolysis¹
 - Increased synthesis¹
 - No change in REE.
 - Insulin concentration or resistance²
 - (n=11¹, 15², age 15y)

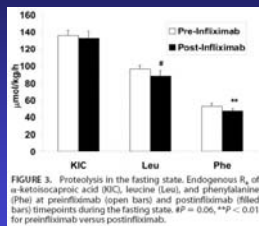


FIGURE 3. Proteolysis in the fasting state. Endogenous R_a of α -ketoglutaric acid (KIC), leucine (Leu), and phenylalanine (Phe) at preinfliximab (open bars) and postinfliximab (filled bars) timepoints during the fasting state. #P = 0.06, **P < 0.01 for preinfliximab versus postinfliximab.

1 Steiner SJ, et al. Inflamm Bowel Dis 2007;13:737-44
 2 Steiner SJ, et al. Pediatr Res 2008;64:673-6

Oral Mineral and Vitamin Supplements

Supplement	Dose
Multiple vitamin	One daily
Ferrous sulfate or gluconate	300 mg TID
Calcium carbonate	1000 to 1500 mg daily
Magnesium gluconate salts	5 to 20 mmol daily
Zinc gluconate	20 to 40 mg daily
Folic acid	1 mg daily
Vitamin D	800 IU daily
Water miscible forms of fat soluble vitamins prn	

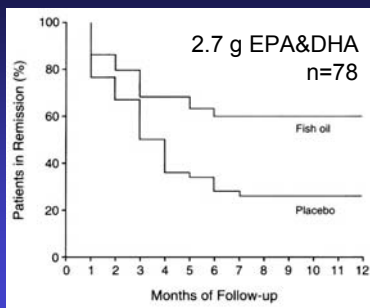
Adapted from: Jeejeebhoy KN. CMAJ 2002;166:913-8

EN for Ulcerative Colitis

- Fish oil
 - Enriches plasma and mucosa with n-3 PUFA at a dose of 10g – 20g of fish oil per day (1/3 is EPA, DHA)
 - Decreases disease activity

Hawthorne AB. Gut 1992;33:922. Lorenz R. J Int Med 1989;225:225.
Aslan A. Am J Gastro 1992;87:432. Stenson WF. Ann Int Med 1992;116:609.
Almallah YZ. Am J Gastro 1998;93:804.

Fish Oil for the Maintenance of CD



Belluzzi A, et al. N Engl J Med. 1996;334:1557-60.

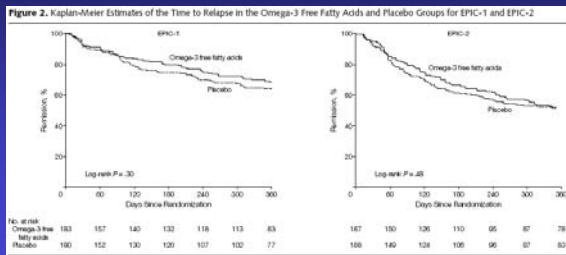
Epinova Study in Crohn's Study

- EPIC-1 n=363, EPIC-2 n=27
- RTC of FO vs. MCT to maintain remission (CDAI <150), ~ 1 yr
- North America, Europe 2003-07
- Epinova 4 gm/d, ~55% EPA, ~ 20% DHA
- Primary endpoint: CDAI >150 or 70 point increase

Feagan BG, et al. JAMA 2008;299:1690

Relapse Rate for Epinova vs. Placebo

EPIC-1: 31.6% vs. 35.7% (hazard ratio, 0.82; 95% CI, 0.51-1.19; P=.30)
 EPIC-2: 47.8% vs. 48.8% (hazard ratio, 0.90; 95% CI, 0.67-1.21; P=.48)



Feagan BG, et al. JAMA 2008;299:1690

Indications for Nutrition Support

- Enteral Nutrition
 - CD refractory to medical therapy
 - PCM and inadequate oral intake
 - Primary therapy for children with active CD¹
 - Adjunctive therapy in UC?
- Parenteral Nutrition
 - Severe PCM, unable to tolerate diet or EN²
 - Intestinal failure

1. Heuschkel R, et al. Inflamm Bowel Dis 2008;14:839-49
 2. Koretz RL, et al. Gastroenterology 2001;121:970-1001

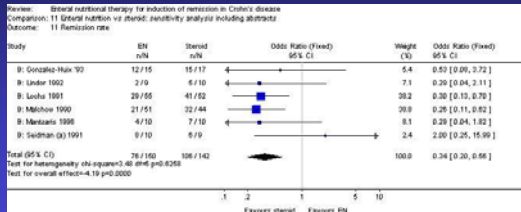
EN: Mechanism of action

- Improved nutritional status
- Reduced antigenic load
- Alteration of gut flora
- Change in mucosal permeability
- Immune modulation by fatty acids
- Provision of trophic polypeptides
- Anti-inflammatory effect on enterocyte

Lochs H. Inflamm Bowel Dis 2007;13:1581-2
de Jong NS, et al. Dig Dis Sci 2007;52:2029-36

EN for Active Crohn's Disease

Cochrane Systematic Review: One of sixteen analyses



Zachos M, et al. The Cochrane Library, 2004, volume 3.

EN for Active Crohn's Disease

- Corticosteroids are more effective than EN
 - 80% vs. 60%¹⁻³
 - OR 0.34 (95% CI: 0.20, 0.56)⁴
- Polymeric and elemental formula are equally efficacious (and semi-elemental)
 - 65% vs. 61%¹⁻³
 - OR 1.15 (95% CI: 0.64, 2.08)⁴

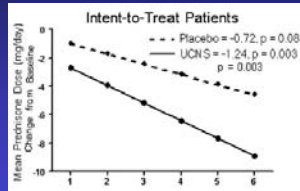
1 Messori A, et al. Scand J Gastroenterol 1996;31:267-72.
2 Fernandez-Banares F, et al. JPEN 1995;19:356-64.
3 Griffiths AM, et al. Gastroenterology 1995;108:1056-67.
4 Zachos M, et al. The Cochrane Library, 2004, volume 3.

Oral Supplementation in UC

Randomized Double Blind Placebo Controlled

- 121 UC w/ DAI 3-9
- UCNS= FO, soluble fiber, antioxidants
- 86 completed study
- UCNS had a greater rate of reduction in the dose of prednisone

(P < 0.001)



Seidner DL, et al. Clinical Gastroenterology and Hepatology, 2005

Bowel Rest in Refractory CD

Group	N	< 3 mo		3-6 mo		6-12 mo	
		Rem	Rel	Rem	Rel	Rem	Rel
TPN+Rest	12	11	1 (1)*	8	3(1)	5	3(1)
DFD	11	9	2(2)	8	1(0)	6	2(0)
PPN+PO	9	8	1(1)	8	0(0)	5	3(2)

Rem = Remission, Rel = Relapse, *Parentheses = Required Surgery

Greenberg GR, et al. Gut 1988;29:1309

Parenteral Nutrition

- Nationwide Inpatient Sample 1998-2003
- ~100,000 medical records reviewed
 - CD:UC 2:1
 - 6% used PN (range 4% in South and Mid-west vs. 9% in North-east)
- Indications ~60% had the dx of....
 - ...malnutrition, fistula, SBO, s/p surgery

Nguyen GC, et al. Aliment Pharmacol Ther 2007;26:1499-507

Parenteral Nutrition

- High rate of use NE, met criteria more often than other regions, did not influence M&M
- PN use associated with longer LOS, charges, mortality
 - LOS 13.7 vs. 5.7 days
 - Charges \$51k vs. \$20k
 - Mortality - OR 2.5 (95% CI: 1.93–3.24)

Nguyen GC, et al. Aliment Pharmacol Ther 2007;26:1499-507

Home PN

- 19%-25 have CD
- Indication: ECF, SBO, ileus, SBS
- By 2 years 75% can d/c HPN
- Life-long HPN if <100 cm SB¹
- Complications may be avoided
 - CRBSI – aseptic technique²
 - PNALD – limit IV lipid to < 1g/kg/d³
 - MBD – formula to maximized Ca retention⁴

1-Messing B, et al. Gastroenterology 1999;117:1043-50
2-Howard L, Ashley C. Gastroenterology 2003;124:1651-61
3-Cavicchi M, et al. Ann Intern Med 2000;132:525-32
4-Seidner DL. JPEN 2002;26:S37-42

Nutritional Therapy in IBD

- Malnutrition is common
- Supplements should be used to treat and prevent deficiencies
- All patients should receive a well balanced diet
- EN should be used in most who require NS
- PN may be necessary to treat intestinal failure
- Just treat it 