Medical Therapy for Diverticular Disease:  
the role of bulking agents.

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Bulking agents in diverticular disease: *fact or fiction*

*Diverticulosis is a dietary deficiency disease of western civilisation, like scurvy, that can be avoided by an adequate diet’*

Burkitt and Painter BMJ, 1971

- Survey 224 gastroenterologists at World Congress
  - 75% prescribe fibre for diverticular disease

- Only 5 RCT in literature: less than 250 patients
Dietary fibre / Bulking agents

- Complex carbohydrate resists digestion
- Classification:
  - Dietary fibre
    - Insoluble
    - Soluble
  - Non starch polysaccharides
Non starch polysaccharides

Cellulose
- 

Non-cellulose polysaccharide
- Gums (sterculia) *Normacol*
- Inulin guar
- Arabinogalactans
- Fungal: chitins
- Glucans
- Pectins
- Mucilages: ispaghula
  - *Mucofalk, Fybogel / Isogel / Regulan*

Insoluble

Variable solubility
Effects of non starch polysaccharides

Nutrient absorption

Reduce bile re-absorption

Increase stool bulk

Colonic fermentation

Recommended UK intake 18g/day
NSPs in diverticular disease

- Insoluble
  - Poorly fermented
    - Maintain form
  - Well fermented
    - Microbial growth

- Soluble
  - Prebiotic
  - Short chain fatty acid release
  - Increased water content
  - Increased stool bulk and faster transit

In UK: average intake of NSP is 12g – stool weight 100g / day
The spectrum of diverticular disease

- 70% asymptomatic
- 30% symptomatic
- 25% severe
Role of fibre in prevention of diverticulosis

Increased incidence in last century
Increased incidence with age
Geographic variability
Ethnic variability

Is this due to changes in the NSP content of diet?

Observational

Mechanistic data from animal models

Interventional data in humans – none!
Observational data...

1200 stool weights in UK and Uganda (Lancet, 1972)
  UK – low fibre diet, stool weight 110g / day, transit 80 hr
  Uganda – high fibre diet, 450g / day, transit 34 hours

1900 Wistar rats fed 9 dietary regimes (Am J Nutr, 1985)
  45% in lowest fibre group cf 9% in highest fibre group developed DD

56 Vegetarians (41.5 g/day) vs 264 non Vegetarians (21.4 g/day)
  All asymptomatic, single contrast enema and age stratified
  Diverticulosis in 12% vs 33% (Lancet, 1979)
Mechanistic data – background...

- Studies of human colon’s at necropsy
  - Collagen content constant irrespective of age
  - Collagen cross linkage (and hence rigidity) increased with age
Mechanistic data - animal models…

- Wistar rats fed different diets for 18 months
  - Low-fibre (17g NSP/kg) vs high fibre (133g/kg)
  - High fibre diet induced 70% increase in colonic contents and caecal SCFA concentrations
  - Diverticulae in 42% low fibre vs 0% high fibre group
  - Total collagen was similar in both groups
  - Collagen cross linking higher in low fibre group
Role of fibre in prevention of symptoms

- 70% asymptomatic
- 30% symptomatic

Data from a prospective cohort of 43,881 male medics 40-75 years of age
All free of diagnosed symptomatic diverticular disease
Dietary analysis from 1986 with bi-annual follow up until 1992
Patients diagnosed with symptomatic diverticular disease in 1990 and 1992 identified
Role of fibre in prevention of symptoms

• During 160,825 years of follow-up - 362 cases

• Inverse relationship between fibre and risk of symptoms
  – RR 0.58 (0.41 - 0.83; P = 0.01) – fruit / vegetable fibre
  – Most significant for ‘insoluble fibre’: RR 0.63 (0.44 - 0.91; p=0.02)
  – Also for cellulose: RR 0.52 (0.36 - 0.75; p=0.002)

Role of fibre in treating symptoms

- 40 patients with symptomatic DD
  - 24g / day bran for 6 months
  - 33 patients had symptomatic response
  - 60% symptoms abolished
  - Increase in transit time and stool weight
  - Decrease in colonic pressure waves 32/39

(Brodribb, BMJ 1976)
Role of fibre in treating symptoms

• Double blind placebo controlled trial 18 patients
  – Wheat crispbread (0.6g fibre) or bran crispbread (6.7g fibre)
  – Standardised scale to assess symptom burden
    • Dyspepsia (nausea, GORD, eructation, distension)
    • Pain
    • Abdominal dysfunction (wind, strain, anal pain, frequency, consistency, blood / mucous, rectal dissatisfaction)
    • 0-6 for both frequency and severity

(Brodribb, Lancet 1977)
Role of fibre in treating symptoms

(Brodribb, Lancet 1977)
Role of fibre in treating symptoms

- 58 patients with symptomatic diverticular disease
- Randomised to ispaghula (9.04g fibre), bran (6.99g), placebo (2.34g)
- Cross over, double blind placebo controlled
- 4 months each arm
  - Subjective assessment – questionnaire
  - Objective assessment – 7 day stool collection
- No benefit of fibre increase on pain, bowel symptom score or total symptom score
- Significant reduction in constipation and increase in stool weight…

(Ornstein, BMJ, 1981)
What are we treating?

Influence of diverticulae in 69 patients with IBS over 6 years

Symptoms and prognosis appeared unrelated to presence of diverticulae

Treatment also independent

(Otte, Am J Gastroenterol, 1986)
Preventing complications....?

- 30% symptomatic
- 25% severe
Role of fibre in preventing complications of diverticular disease

- Retrospective review of 72 patients admitted with symptomatic simple diverticular disease over 10 years (Leahy, Ann R Coll Surg Eng, 1985)

![Diagram]

72

Surgery
16

Conservative
56

Fibre supplementation

31 – High fibre follow up 54/12
6.5% surgery / 19% symptomatic

25 – Low fibre follow up 76/12
32% surgery / 44% symptomatic
NSP for diverticular colitis?

- Redundant mucosa
- Prolapse
- Ischaemia
- Intraluminal antigens
- Stasis
- Altered bacterial flora

Diverticular colitis
Role of NSP in diverticular colitis

• No controlled trials....

• Two largest series report 57 patients!
  – 17 improved spontaneously
  – 9 with bulking agents +/- antibiotics
  – 19 with 5 ASA
  – 5 steroids
  – 7 surgery
Summary – NSP in diverticular disease

- Increase stool bulk - non fermented and fermented
- Decrease intraluminal pressure
- Increase colonic SCFA
- Prebiotic effect

Evidence for a benefit of NSP
Conclusions

• Diet high in NSP prevents diverticulosis  YES
• Diet high in NSP prevents symptoms  YES
• Bulking agents relieve symptoms  Yes - No
• Bulking agents prevent complications  NO
• Bulking agents treat diverticular colitis  NO

Which NSP and how much?
I think you’re eating too much fibre now
Fibre vs lactulose in diverticular disease

- 43 patients over 12 weeks
  - 15ml bd lactulose vs 30g fibre
  - Significant improvement in both groups
    - Pain on defecation and abdominal pain

  *Smits BJ, Br J Clin Pract, 1990*

- Comparison of bran, ispaghula and lactulose
  - Equally effective in controlling symptoms
  - Differential effects on transit and stool weight

  *Eastwood, Gut, 1978*