Irritable Bowel Syndrome

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Case

- **39 yrs old female**
  - **History of 7 years relapsing abdominal discomfort, bloating, pain**
  - **Episodes of diarrhea**
  - **No significant family history of Gastrointestinal diseases or malignancy**
  - ***H. pylori* eradication had been performed**
- **'…Wants to find out what is wrong with her…'**

Differentials

- Peptic ulcer disease
- Gastritis
- Chronic pancreatitis
- Inflammatory bowel disease
- Gluten sensitive enteropathy
- Irritable Bowel Syndrome
- Functional dyspepsia
- Somatization disorder
- Stress related

AIMS

- What are functional GI disorders?
- Diagnostic criteria for IBS?
- How to manage patients with IBS?

Functional Gastrointestinal Disorders:

Symptoms in the absence of structural lesions or biochemical abnormalities

NOT ABSENCE OF ANY ABNORMALITIES

Irritable Bowel Syndrome

Chronic functional disorder of the gastrointestinal tract characterized by chronic abdominal pain & altered bowel habits

- **Most Commonly diagnosed Gastrointestinal Disorder**
- **Symptom Based Diagnosis**
- **Can Substantially reduce quality of Life and Work Productivity**

Diagnostic Criteria of Irritable Bowel Syndrome: ROME III

Recurrent abdominal pain or discomfort At least 3 days per month in the last 3 months associated with two or more of the following:
(1) Improvement with defecation
(2) Onset associated with a change in stool frequency
(3) Onset associated with a change in form of stool

WITHOUT STRUCTURAL OR BIOCHEMICAL CAUSE OF SYMPTOMS

Typical features for IBS

- Loose/frequent stools
- Constipation
- Bloating
- Abdominal cramping, discomfort, or pain
- Symptom brought on by food intake
- Specific food sensitivities

Symptoms are dynamic over time
change in pain location
change in stool pattern

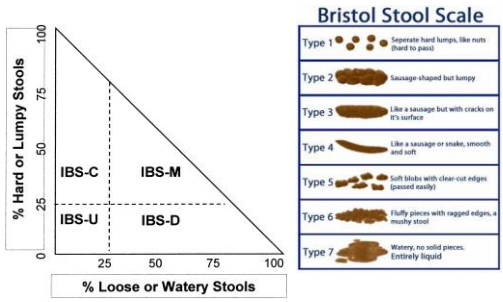
ALARM Gastrointestinal Symptoms

- Symptom onset after age 50 y
- Severe or progressively worsening symptoms
- Unexplained weight loss

REFER URGENTLY TO GASTROENTROLOGY FOR FURTHER EVALUATION

- Rectal bleeding or melena
- Unexplained IDA

Subtyping IBS by Stool Pattern



Longstreth et al, Gastroenterology 2006

Diagnostic Tests for Suspected IBS

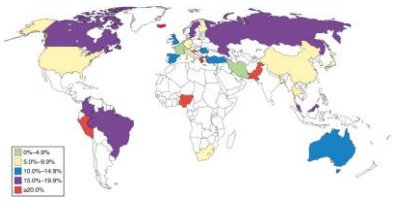
All IBS Subtypes
- FBC
- Age-appropriate CRC Screening

IBS, Mixed
- CRP or Calprotectin
- IgA TtG +/− quantitative IgA
- Stool diary
- AXR

IBS With Diarrhoea
- CRP or calprotectin
- IgA TtG +/− quantitative IgA
- Colonoscopy, random biopsies

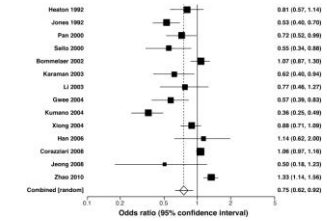
IBS With Constipation
- If severe or medically refractory
- Refer to gastroenterology specialist for physiologic testing

Prevalence and Risk Factors



***Ford et al,* Clinical Gastroenterology and Hepatology 2012**

Prevalence and Risk Factors



Pooled OR for IBS in those aged 50 years or older compared with those aged younger than 50 years.

Prevalence ↑for women (OR, 1.67; 95% CI, 1.53-1.82)

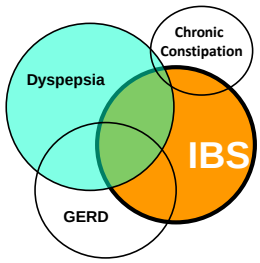
Ford et al, Clinical Gastroenterology and Hepatology 2012

Co-existing GI Conditions

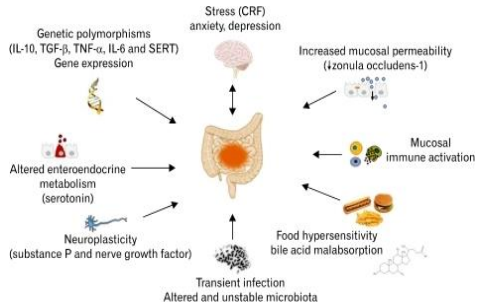
- **IBD**
  - 1/3 of patients with IBD fulfil ROME 3 criteria
- **Coeliac Disease**
  - 4 fold ↑in patients with IBS
- **CRC and benign Neoplasms**
  - Limited prospective literature suggests risk of CRC <1%.
  - Age-appropriate CRC screening
- **Microscopic colitis**
  - Age>50 years
  - Nocturnal stools
  - Weight loss
  - Shorter duration of diarrhoea
  - Introduction of new drug
  - Autoimmune diseases
- **Dys-synergic defecation**
  - Sense of incomplete evacuation or
  - Need for digital evacuation
  - Overlap is common.

Comorbidities

- **Somatic pain syndromes**
  - Fibromyalgia
  - Chronic fatigue syndrome
  - Chronic pelvic pain
- **Gastrointestinal disorders**
  - GERD
  - Dyspepsia
- **Psychiatric disorders**
  - Major depression
  - Anxiety
  - Somatization



Pathophysiology : IBS

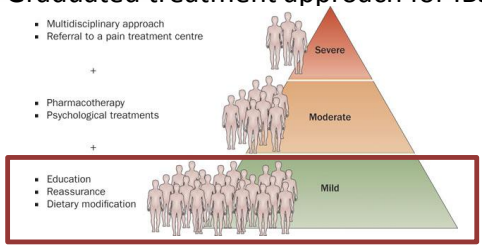


Barbara G et Al, **J Neurogastroentro Motil 2011**

The most effective drug in functional gastrointestinal disorders

PLACEBO

Graduated treatment approach for IBS



Khan, S. & Chang, L. (2010) ***Nat. Rev. Gastroenterol. Hepatol.***

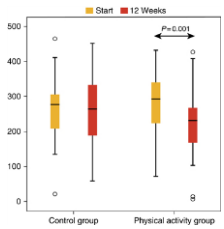
Treatment

TRUSTING patient-physician relationship is the ***CORNORSTONE*** of managing IBS

Commonly Used Treatments That Can Exacerbate IBS

- **Over-the-Counter**
  - Antihistamines
  - Calcium
  - Iron
  - Magnesium
  - Nonsteroidal anti-inflammatory drugs
  - Wheat bran
- **Prescription**
  - Antibiotics
  - Antidepressants
  - Antiparkinsonian drugs
  - Antipsychotics
  - Calcium-channel blockers
  - Diuretics
  - Metformin
  - Opioids
  - Sympathomimetics

Physical activity



- 20-minute walk each day.
- Distance and pace can be gradually increased as tolerated.

Johannesson et al, AJG 2011

Dietary Factors

- IBS symptoms often associated with meals.
- Up to 90% of IBS patients restrict their diet to prevent or improve their symptoms.
- True food allergies are uncommon in IBS.
- Conversely, food intolerances or sensitivities are common

Dietary Factors

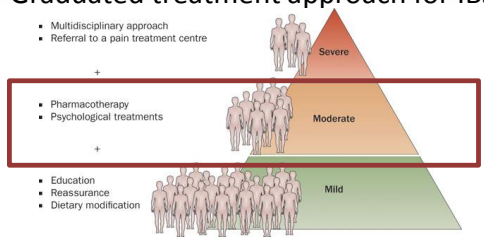
- Lactose-Avoidance
- Food allergy Testing
- Low FODMAPs Diet
- Gluten Avoidance

FODMAPs

- Short-chain, poorly absorbed, highly fermentable carbohydrates
  - Lead to increased small bowel & colonic water secretion and fermentation
  - Causing increased production of SCFA
- Important trigger of meal-related symptoms in IBS patients
- RCT in 30 IBS patients found lower overall symptom scores on the low-FODMAP diet vs a typical Australian diet ($P < .001$)

Gibson et al, Gastroenterology 2014

Graduated treatment approach for IBS



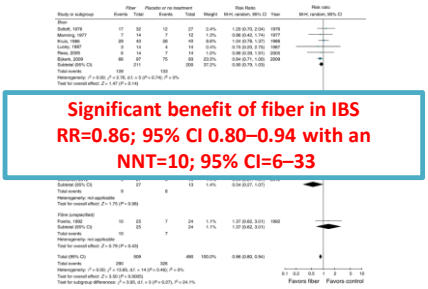
Khan, S. & Chang, L. (2010) *Nat. Rev. Gastroenterol. Hepatol.*

Medical Management for IBS

- IBS-D
  - **Antidiarrheals**
  - **Serotonin Agents: 5-HT_3 Receptor Antagonists**
  - **Antispasmodics**
- IBS-C
  - **Fibre Supplements**
  - **Laxative Agents**
  - **Prosecretory Agents**

- Centrally Acting Interventions
- Modification of Microbiota: Probiotics and Antibiotics
- Complementary and Alternative medicine
- Psychological therapies

The Effect of Fiber Supplementation on IBS: A Systematic Review &Meta-analysis



Significant benefit of fiber in IBS RR=0.86; 95% CI 0.80–0.94 with an NNT=10; 95% CI=6–33

Moyaadi et al, AJG 2014

Laxatives

- Osmotic Laxatives:
  - PEG are frequently recommended as first-line therapy for IBS-C patients.
  - Improves
    - stool frequency and consistency
  - Does not reliably improve abdominal pain or bloating.
- Stimulant laxatives
  - ***No randomized, controlled trials in IBS-C patients***. Adverse effects are abdominal pain and cramping.

Prosecretory Agents

Expert Opinion on Pharmacotherapy

2 phase 3 trials (1711 IBS-C patients), pts treated with lubiprostone 8 µg twice daily responded compared with those treated with placebo
17.9% vs 10.1%; *P* = .001

Brian E Lacy PhD MD & William D Chey MD

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2013;11:1084–1092

SYSTEMATIC REVIEWS AND META-ANALYSES

3 RCT IBS-C patients reported RR response of linaclotide (290 µg once daily) vs placebo of **1.95 (95% CI, 1.3-2.9) NNT 7 (95% CI, 5-11)**

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Anti-diarrhoeals

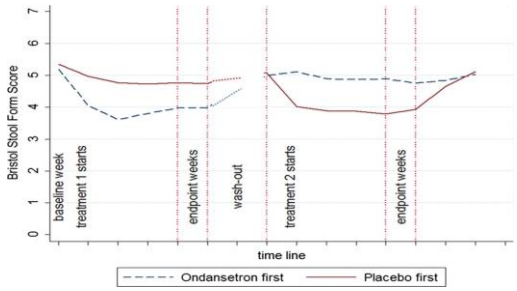
- Loperamide
  - No evidence to support the use for relief of global symptoms in IBS
- Bile acid Sequestrants
  - Cholestyramine / Colesevelam to treat diarrhoea.
  - Not evaluated in RCT in IBS patients

***Ford et al,* AJG 2014**

Serotonin Agents: 5-HT_3 Receptor Antagonists

- Serotonin influences gastrointestinal motility and visceral sensation
- Two Agents
  - Alosetron -0.5-1 mg once to twice per day
  - Ondansetron-4-8 mg 1-3 times per day

Ondansetron for IBS-D:A RCT



***Klara Garsed et al.* Gut 2014**

Anti-Spasmodics

- Drugs with anticholinergic or calcium-channel blocking properties may improve IBS symptoms
  - by relaxing gut smooth muscle.
- The ACG Functional Bowel Disorders Task Force recently concluded that
  - Certain antispasmodics, provide symptomatic short-term relief in IBS."
    - Otilonium, hyoscine, cimetropium, pinaverium, and dicyclomine

***Ford et al,* AJG 2014**

Anticholinergics should be avoided in the elderly

Medical Management for IBS

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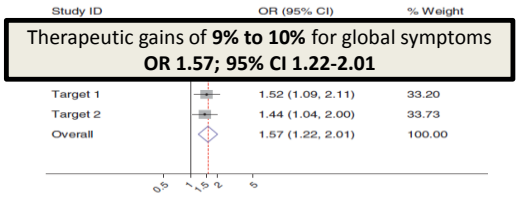
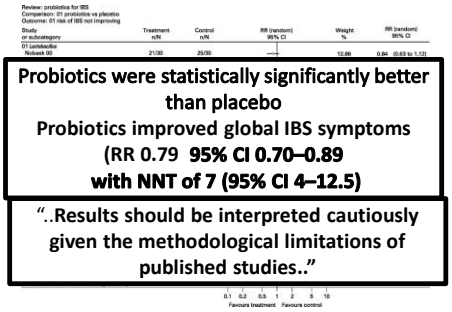
Modification of Microbiota: Role of Antibiotics

Efficacy and Safety of Rifaximin for the IBS: A Systematic Review & Meta-Analysis



Menees et al, AJG 2012

Modification of Microbiota :Probiotics in IBS Meta-analysis

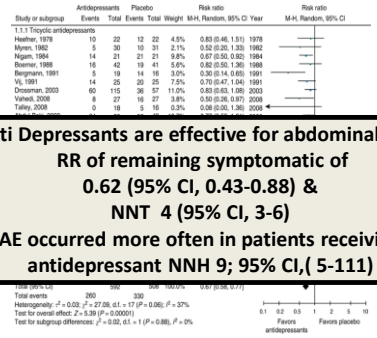


Probiotics were statistically significantly better than placebo
Probiotics improved global IBS symptoms (RR 0.79 95% CI 0.70–0.89 with NNT of 7 (95% CI 4–12.5)

"..Results should be interpreted cautiously given the methodological limitations of published studies.."

***P Moayyedi et al*. Gut 2010**

Effect of Antidepressants in IBS: Systematic Review &Meta-Analysis



Anti Depressants are effective for abdominal pain
RR of remaining symptomatic of 0.62 (95% CI, 0.43-0.88) & NNT 4 (95% CI, 3-6)
AE occurred more often in patients receiving antidepressant NNH 9; 95% CI,(5-111)

Ford et al, AJG 2014

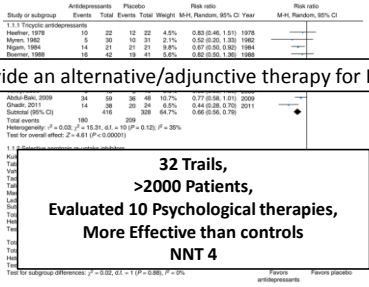
Anti-Depressants: Moderate to Severe IBS

- TCA
  - Act via anticholinergic properties
  - Slow intestinal transit time
    - Beneficial in IBS-D
    - Cautious use in patients with IBS-C.
  - Better choice for patients with insomnia, anorexia, or weight loss
  - Dose-dependent SE constipation, dry mouth & eyes, drowsiness, weight gain, QT-interval prolongation
- SSRI
  - Due to prokinetic effects Better choice for IBS-C patients
  - Better in patients with significant anxiety
  - Adverse effects
    - Sexual dysfunction
    - Agitation
    - Nausea
    - Drowsiness
    - Diarrhoea

Anti-Depressants

- Start low and titrate slowly
- Initial dose should be adjusted based upon tolerance &response.
- Due to the delayed onset of action of antidepressants,
  - 3-4Weeks of therapy should be attempted before increasing the dose.

PSYCHOLOGICAL THERAPIES



Provide an alternative/adjunctive therapy for IBS Pts

32 Trails,
>2000 Patients,
Evaluated 10 Psychological therapies,
More Effective than controls
NNT 4

Ford et al, AJG 2014

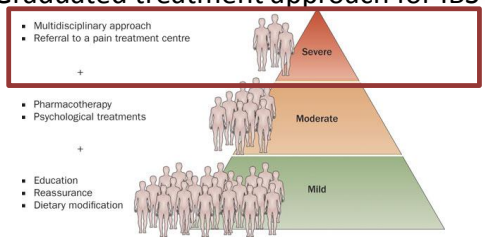
Systematic review: CAM in IBS

Hypnotherapy, forms of herbal therapy, specific diets & probiotics, may well have efficacy in IBS

Difficulties include:
- Need more controlled studies
- No randomized placebo-controlled trials
- Lack of clear understanding of the active ingredients
- Lack of standardization

Hussain et al, APT 2006

Graduated treatment approach for IBS



Khan, S. & Chang, L.* (2010) *Nat. Rev. Gastroenterol. Hepatol.

Take Home Messages

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- IBS is a symptom-based illness
  - Presence of abdominal pain or cramping in association with constipation, diarrhoea, or both.
- Confidently establish diagnosis
  - by symptom-based criteria
- Recognize & Investigate alarm GI symptoms
  - refer appropriately.
- Successful management
  - Involves a trusting, positive, patient-physician relationship.
- Holistic approach including
  - lifestyle changes, dietary interventions, medications, or behavioural strategies

THANK YOU

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