Management of Irritable Bowel Syndrome

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University of Manchester
Perception of IBS

Nuisance rather than serious

Not life threatening

Largely psychological
IBS

Severity underestimated
Severity of illness

Pain (severity)

Miller et al. 2004
Severity of illness

Pain (severity)

IBS-D (urgency, incontinence)
Severity of illness

Pain (severity)
IBS-D (urgency, incontinence)
IBS-C (BO x 1/week or more)
Severity of illness

Pain (severity)

IBS-D (urgency, incontinence)

IBS-C (BO x 1/week or more)

Exaggerated gastro-colonic reflex
Severity of illness

Pain (severity)

IBS-D (urgency, incontinence)

IBS-C (BO x 1/week or more)

Exaggerated gastro-colonic reflex

Afraid to eat: diarrhoea worse (IBS-D)
Severity of illness

Pain (severity)
IBS-D (urgency, incontinence)
IBS-C (BO x 1/week or more)
Exaggerated gastro-colonic reflex
Afraid to eat: diarrhoea worse (IBS-D)
Afraid to eat: pain worse (IBS-C)
Severity of illness

Pain (severity)

IBS-D (urgency, incontinence)

IBS-C (BO x 1/week or more)

Exaggerated gastro-colonic reflex

Afraid to eat: diarrhoea worse (IBS-D)

Afraid to eat: pain worse (IBS-C)

Bloating and distension (particularly IBS-C)
Severity of illness

Sexual function

Guthrie et al 1987
Severity of illness

Sexual function

Non colonic symptoms
Non colonic symptoms

Nausea
Chest pain
Backache
Lethargy
Urinary symptoms
Gynaecological symptoms

→ burden of illness
→ diagnostically useful
→ inappropriate referral

*Whorwell et al, 1986
Maxton et al, 1991*
Inappropriate referral
(gynaecological, urological, orthopaedic, geriatric)

Poor outcome

Unnecessary investigation

Unnecessary treatment

Prior et al, 1989
Francis et al, 1997
Agrawal et al, 2009
Severity of illness

Sexual function

Extra-intestinal features

Absenteism from work

Schuster 1991
Severity of illness

Sexual function
Extra-intestinal features
Absenteemism from work
Quality of life
Mean SF-36 scores for subjects with IBS compared with other medical conditions

Score

SF-36 scales

Physical functioning | Role physical | Body pain | General health | Vitality | Social functioning | Role emotional | Mental health

- IBS
- Heart disease
- Diabetes
- Renal disease

Lea et al 2004
Faecal incontinence

500 consecutive IBS patients
IBS-D 65%
IBS-A 63%
IBS-C 38% (laxatives 35%)
23% not told anyone
Only 50% had told their doctor
66% carried a change of clothes
30% regularly used incontinence pads

Suicidal ideation in IBS

Comparison of severe IBS with active ulcerative colitis and Crohn’s disease

“Have you ever seriously contemplated or attempted suicide solely on account of your gastrointestinal disorder as opposed any other issues”
Suicidal ideation in IBS and IBD

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Miller et al 2004
## Suicidal ideation in IBS and IBD

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Indicator of hopelessness and despair

Miller et al 2004
Management
Pathophysiology

Multifactorial

Motility
Visceral sensitivity
Central processing
Inheritance
Inflammation
Bacterial imbalance
Dietary factors
Psychological factors
Treatment approach

There is no single ‘stand alone’ treatment

Education
Dietary manipulation
Medication
Behavioural approaches
Other medications
Follow up
Education

Positive diagnosis

Understanding the disorder (multifactorial)

Explanation of symptoms (IBS / non colonic)

Role of investigation (avoid disappointment)

Tailor treatment to the patient

What can and cannot be achieved (no cure, but control)

Follow up until under control
The IBS patient

Eating makes symptoms worse

Patient: blames food

dietary allergy

wants discussion of food

diet sheet

Ragnarsson et al, 1998
Dietary management
Cereal fibre
# Overall symptomatic response to fibre

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*Francis et al, 1994*
Diet sheet

Cereal fibre exclusion

Refined wheat allowed (eg white bread)

1 month trial
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Carbohydrate intolerance
(fermentable oligo- di- mono- saccharides and polyols FODMAPS)

Examples:

Fructose
Lactose
Fructans
Galactans
Sorbitol

Widely used in the food industry
Occur in fruit and vegetables
FODMAP restriction improves IBS
Foods with high fructose content
(in ascending order)

- Pineapple
- Orange
- Melon
- Honey
- Mandarin
- Peach
- Mango
- Apple
- Pear
- Fruit juice
# Foods containing polyols

<table>
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<tr>
<th>Fruits</th>
<th>Artificial sweeteners</th>
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<tr>
<td>Apples</td>
<td>Sorbitol</td>
</tr>
<tr>
<td>Pears</td>
<td>Mannitol</td>
</tr>
<tr>
<td>Apricots</td>
<td>Isomalt</td>
</tr>
<tr>
<td>Peaches</td>
<td>Xylitol</td>
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<td>Plums</td>
<td></td>
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Vegetables

Fibre and FODMAPS!
Is 5 a day good advice for IBS?
Drugs
Antispasmodics
Anticholinergics

Dicycloverine *(Merbentyl)*

Hyoscine *(Buscopan)*

Propantheline *(Probanthine)*
Anti-smooth muscle

Mebeverine (*Colofac*)

Alverine (*Spasmonal*)

Peppermint (*Colpermin*)
Antispasmodics

Beneficial:  n=16 trials  
n=23 trials  

Pain and distension improved

10 - 30% greater than placebo

NNT 3 - 7

Dependent on drug

Jailwala et al, 2000
Poynard et al, 2001
Antispasmodics

Best approach:

try them all

combinations

not necessarily before meals

as necessary usage
Anti-diarrhoeals
Anti-diarrhoeals

Loperamide (mu opioid agonist)
Diphenoxylate
Codeine phosphate - central effects
Anti-diarrhoeals

Loperamide (first pass metabolism)

Improves anal tone (incontinence)

Regular use

Low dose

No effect on pain

Combination with antispasmodics
Laxatives
Laxatives

**Osmotic**
- Polyethylene Glycol
- Lactulose
- Magnesium salts

**Stimulant**
- Sodium Picosulphate
- Bisacodyl
- Senna

**Softeners**
- Docusate
Laxatives

Polyethylene Glycol

Regular dosing

Patient: no evidence for “gut damage”
guilt
re-assurance

Avoid lactulose
Antidepressants
Antidepressants in IBS

Meta analysis 9 placebo controlled TCA trials
Jackson et al, 2002
NNT = 3

Meta analysis of 12 placebo controlled TCA or SSRI trials
Ford et al, 2002
NNT = 4
Antidepressants

Extremely useful

Patient resistance

Have to “sell” them - not depressed
- low dose

Diarrhoea - tricyclic

Constipation - tricyclic (laxative)
- SSRI
New drugs
Serootonin
(5HT)
Serotonin

- motility
- secretion
- visceral sensitivity

Receptors

- $5HT_1$
- $5HT_3$
- $5HT_4$
5-HT concentrations in IBS

Data points represent average values

Atkinson et al, 2006
5HT drugs

$5HT_3$ antagonists - diarrhoea

$5HT_4$ agonists - constipation
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<td>Tegaserod</td>
<td>$5HT_4$ agonist</td>
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<td>Cilansetron</td>
<td>$5HT_3$ antagonist</td>
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<tr>
<td>Ramosetron</td>
<td>$5HT_3$ antagonist</td>
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<td>Renzapride</td>
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<td>Prucalopride</td>
<td>$5HT_4$ agonist (CC)</td>
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<tr>
<td>Ondansetron</td>
<td>$5HT_3$ antagonist (IBS-D)</td>
<td>(not licensed)</td>
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Other drugs for constipation

**Chloride channel activators**
- Lubiprostone
- NICE approved for CC

**Guanylate cyclase receptor agonists**
- Linaclotide
- NICE approved for IBS-C
Other drugs for diarrhoea

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| Mixed opioid receptor        | eluxadoline      |
| agonist & antagonist         | mu & kappa agonist, delta antagonist |
Other approaches

Acupuncture - equivocal

Probiotics

Behavioural approaches
Rationale for probiotics in IBS
Inflammation and bacteria in IBS

Post infectious IBS

Chaudhary & Truelove 1962

Persistent inflammation

Gwee et al 1999

Previous antibiotic use

Mendall & Kumar 1998

Bacterial imbalance

Kassinen et al 2007

Small bowel bacterial overgrowth

Pimental et al 2003
Inflammation and bacteria in IBS

Something going on around inflammation

Something going on with bacteria
Probiotics

Preparations containing live organisms that exert a potential health benefit on the host
Properties of probiotic bacteria (1)

Enhance hosts anti-inflammatory and immune response

Stimulate anti-inflammatory cytokines

Pathogenic bacteria stimulate pro-inflammatory cytokines

Restore balance between pro and anti-inflammatory cytokines
Properties of probiotic bacteria (2)

- Improve epithelial cell barrier
- Epithelial adhesion - exclusion of pathogens
- Inhibit bacterial translocation
- Inhibit growth of pathogens (eg salmonella)
- Inhibit adhesion of viruses (eg rotavirus)
Properties of probiotic bacteria (3)

Elaborate active proteins and metabolites:
  immune modulation
  proteolytic/bacteriocidal properties
  toxin binding

Reduce hypermotility (animal model)

Reduce visceral hypersensitivity (animal model)

Reduce anxiety behaviour (animal model)
Properties of probiotic bacteria (4)

Different organisms - different properties
Pathophysiology
(multifactorial)

Motility
Visceral sensitivity
Central processing
Inheritance
Inflammation
Bacterial imbalance
Dietary factors
Psychological factors
Pathophysiology (multifactorial)

- Motility
- Visceral sensitivity
- Central processing
- Inheritance
- Inflammation
- Bacterial imbalance
- Dietary factors
- Psychological factors
Probiotics

Lactobacillus

Bifidobacterium

Non pathogenic:
  e-coli (eg *E. Nissle*)
  streptococcae (eg *S. Salivarius*)
  yeasts (eg *S. Boulardii*)
Probiotics in IBS
Conclusions

75% of trials positive (>30 trials)
Different symptoms improved
Formulation is also critical
Not all organism effective
Single organisms or mixtures
No apparent safety issues
High patient acceptability
Designer probiotics in the future
Conclusions

NICE recommendation:

Probiotics do not appear to be harmful (unless they come from an unreliable source) and they might benefit people with IBS. They should be advised to take the product for at least four weeks while monitoring the effect.
Behavioural treatments

Psychotherapy
Cognitive behavioural therapy
Hypnotherapy
Hypnotherapy for GI disorders
Hypnotherapy package

Gut focused

Tutorial on IBS

Normalisation of function:
  tactile
  visualisation

Twelve sessions

Weekly intervals

Daily practice with CD
IBS symptom score

Data as median plus interquartile range

Am J Gastroenterology 2002;97:954-961
Extra-colonic features

Data as median plus interquartile range

* p<0.001
Quality of life measures

- Psychic well-being
- Physical well-being
- Mood
- Social/relationships
- Locus of control
- Work

* indicates significant difference between pre-HT and post-HT.
### Anxiety and depression

#### HAD Scores

<table>
<thead>
<tr>
<th></th>
<th>pre-HT</th>
<th>post-HT</th>
<th>‘p’ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAD ‘A’ Score</td>
<td>11.1 ± 0.3</td>
<td>7.3 ± 0.3</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>% anxious (score ≥9)</td>
<td>68.3%</td>
<td>34.6%</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>HAD ‘D’ Score</td>
<td>7.2 ± 0.3</td>
<td>4.1 ± 0.3</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>% depressed (score ≥9)</td>
<td>36.1%</td>
<td>14.6%</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

*HAD Scores expressed as mean ± S.E.M.
*post-HT v pre-HT, paired ‘t’ test

Am J Gastroenterology 2002;97:954-961
Hypnotherapy for irritable bowel syndrome: an audit of 1000 patients

Response: 80% in females, 62% in males

Miller et al. Aliment Pharm Ther 2015;41:844-55
Long term benefits of hypnotherapy
Long term benefits in IBS
Total symptom scores

pre-HT
post-HT

years

Am J Gastroenterology 2002;97:954-961
Long term benefits in IBS

Total symptom scores

years

pre-HT
post-HT
follow-up

Am J Gastroenterology 2002;97:954-961
Long term benefits in IBS
Total symptom scores

years

pre-HT
post-HT
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Am J Gastroenterology 2002;97:954-961
Long term benefits in IBS
Total symptom scores

Am J Gastroenterology 2002;97:954-961
Functional dyspepsia
Non cardiac chest pain
Hypnotherapy in inflammatory bowel disease

IJCEH 2008;56:306-17
Mechanism of action
Physiological
Motility (stomach)
gastric emptying

Healthy controls

Functional dyspepsia

* p<0.005
** p<0.001

Alimentary Pharmacology and Therapeutics 2006;23:1241-49
Change in rectal hyper-sensitivity

Tracking pain threshold (mmHg)
Change in rectal hyper-sensitivity

Tracking pain threshold (mmHg)

* p<0.05

Alimentary Pharmacology and Therapeutics 2003;17:635-42
ACC - important pain processing area

Painful rectal stimulus activates ACC activation in IBS > controls

Gastroenterology 2000;118:842
Hypnotic suggestion reduces suffering from but not perception of a painfully hot stimulus.
IBS symptoms worse with food

Exaggerated gastrocolonic response
Duodenal lipid infusion
Colonic sensory and motor responses
Hypnotherapy results in reduced reactivity

*Psychosomatic Medicine* 2004 66 233-8
Mechanism of action

Pathophysiology

Motility
Visceral sensitivity
Central processing
Inheritance
Inflammation
Bacterial imbalance
Dietary factors
Psychological factors
Mechanism of action

Pathophysiology

- Motility
- Visceral sensitivity
- Central processing
- Inheritance
- Inflammation
- Bacterial imbalance
- Dietary factors
- Psychological factors
Summary

60-70% response rate
Sustained relief of all symptoms
Modifies motility
Modifies visceral sensitivity
Improves quality of life
Less time off work
Back to work
Less GP consultations
Reduced medication needs
Refractory patients

Consider intramuscular buscopan
Intramuscular buscopan

Spastic type pain
20mg prn up to 3 times daily
Test dose under medical supervision
86% gained pain relief
72% complete or substantial
32% reduced or stopped opiates
No major side effects
Only 48% GP’s agreed to this approach

Conclusion

IBS can be managed effectively but individually

- Patient education essential
- Manipulate diet
- Target drugs to symptoms
- Provide continuing support
- Consider probiotics
- Consider hypnotherapy / CBT / psychotherapy
  - Operator dependent
- Consider non standard medication
- Avoid inappropriate referral and treatment