Complementary Medicine and Functional GI Disorders

Eamonn M M Quigley MD FACG
Alimentary Pharmabiotic Center
University College Cork
IRELAND
Complementary and Alternative Medicine (CAM)

“…..those practices not presently considered an integral part of conventional medicine.”

Chesney, NCCAM, NIH, 2005
This Definition is Arbitrary

- Cultural
- Ethnic
- Social
- Religious
- Educational
- Economic
- Medical Professional

... and other factors will influence what is and what is not regarded as CAM!
Herbal Remedy or Drug?

**DIGITALIS**

**DIGOXIN**
CAM Practices

• Manipulative:
  - Massage, chiropractic

• Mind-body:
  - Meditation, hypnosis, prayer

• Biologically based:
  - herbal, dietary, “natural” products

• Energy healing:
  - Qi gong, acupuncture, magnetic fields

• Integrated:
  - Homeopathy, traditional Chinese medicine
<table>
<thead>
<tr>
<th>Type of CAM</th>
<th>% of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phytotherapy</td>
<td>46</td>
</tr>
<tr>
<td>Supplements</td>
<td>36</td>
</tr>
<tr>
<td>Manual therapies</td>
<td>23.7</td>
</tr>
<tr>
<td>Homeopathy</td>
<td>21.9</td>
</tr>
<tr>
<td>Energy medicine</td>
<td>17.3</td>
</tr>
<tr>
<td>TCM</td>
<td>10.8</td>
</tr>
<tr>
<td>Bioelectrical therapies</td>
<td>7.9</td>
</tr>
<tr>
<td>Others</td>
<td>12.6</td>
</tr>
</tbody>
</table>

Patients do not tell doctors about their use of CAM!

- 831 adults, randomly chosen, who saw physician and used CAM
- 63% to 72% did not disclose CAM use to physician
  - “It wasn’t important for the doctor to know” - 61%
  - “The doctor never asked” - 60%
  - “It was not the doctor’s business” - 31%
  - “The doctor would not understand” - 20%

CAM in IBS

- **n = 1,409**
- **GI clinics and supermarkets, UK**
- **CAM use:**
  - IBD 49.5%*
  - IBS 50.9%*
  - General GI 20%
  - Control 27%
  - F>M

Kong et al, 2005

- **n = 207**
- **Community, Australia**
- **CAM use:**
  - IBS/FD 49.8%
  - General GI 20.8%
    - Frequent abdo pain
    - Interference with work
    - Good physician-patient interaction
    - Female
    - Not psychopathology

Koloski et al, 2003
and it is rising!

Placebo Effect in IBS

- Global response: 36±19% (5.2-80.4)
  - More frequent administration*
  - Longer duration
  - More effective active

- Pain reduction: 28±20% (-23.6-69.7)
  - More frequent administration
  - More effective treatment
  - Median age

- $11.2 + 3.97 \times (\text{frequency of admin}) + 0.38 \times (\text{each } \% \text{ of treatment effect}) + 18.7\%$ (parallel design).

- $-13.3 + 8.4 \times (\text{frequency of admin}) + 0.28 \times (\text{each } \% \text{ of treatment effect})$.

Pitz et al, 2005
Placebo Effect in IBS

- Comparing trials on, or before, 1998 to 1999-2004:
  - Larger size (77→306)
  - More telephone contact (3.4%→24%)
  - Lower intervention frequency (2.7→2/dy)
  - Less cross-over design (34→4%)

- No change:
  - Treatment effect (57 vs 49%)
  - Study duration (12 weeks)
  - Placebo response
    - Global (37 vs 34%)
    - Pain reduction (31 vs 21%)

Pitz, et al. 2005
Is CAM the new placebo?

- IBS a suitable target for CAM
  - Placebo effect high
  - Conventional therapy unsatisfactory; can be omitted
  - Conventional therapy risky

Safety not Efficacy the issue!

Vozeh et al, 2003
Issues in CAM trials

- Quality control
- Trial Design
  - Study size
  - Blinding
  - Subjective outcomes
- Publication bias
- Toxicity

Koretz and Rotblatt 2004
Manipulative Reflexology

• 34 Rome II positive IBS

• Reflexology vs non-reflexology foot massage; single-blind

• No difference:
  - Abdo pain
  - Constipation/diarrhea
  - Abdominal distension

Tovey, 2002
Mind-Body Hypnosis

- 250 unselected patients with IBS
- 12 sessions over 3 months
  - Personal practice between sessions
- Poor results:
  - Males with diarrhea

Bowel Symptoms

Extra-colonic Symptoms

Hypnotherapy in IBS: long-term follow up

Cognitive Behavioral Therapy

Biologically-Based Herbal

- 116 Rome I positive IBS
  - Individualized Chinese herbal
  - Standard Chinese herbal
  - Placebo

  - 5 capsules t.i.d. for 16 weeks
    - Improved Bowel Symptom Score: CHM 42%*
      Placebo 22%

No difference individualized vs standard at 16 weeks
At 14 weeks f.u. sustained improvement in individualized only

Bensoussan, et al. 1998
Iberogast (STW5)

A tincture containing:

- German Chamomile flower
- Clown's Mustard plant
- Angelica root and rhizome
- Caraway fruit
- Lemon Balm leaf
- Celandine aerial part
- Licorice root
- Peppermint leaf

Effects

- Motility
  - Accelerates gastric emptying (+/-)
  - Increases proximal gastric volume
  - Promotes antral motility
- Anti-inflammatory
- Decreases sensation
- Anti-oxidant
- Pro-secretory

Iberogast in FD
Change in Most Bothersome Symptom: difference from placebo

Herbal Therapies in IBS

Herbal Laxatives

- Aloe latex
- Cascara Sagrada
- Frangula
- Rhubarb
- Senna
- Prunes
Other Dietary Therapies

- Elimination diets
- Fiber and fiber supplements
- Peppermint oil
- Probiotics, prebiotics and synbiotics

Governed by DSHEA Act, in US
Why does food provoke symptoms in IBS?

• **Physiological effect**
  - Exaggerated gastro-colonic response in IBS
  - Exaggerated response to intra-luminal lipid in IBS
    • Motility
    • Sensation

• **Psychological factors**
  - Interplay with stress
  - Conditioned response
Why does food provoke symptoms in IBS?

- **Dietary components**
  - Tryptophan
    - Depletion/augmentation can influence anxiety and GI symptoms in IBS
- **Food allergy**
- **Food intolerance**
- **Interaction with the gut flora**
Diet and IBS
Not much data!

- Community sample, Olmstead County, Mn
- 218 FGID patients and 119 controls provided diet data
- Calculated weekly intakes:
  - No difference wheat-, lactose-containing food, caffeinated drinks or fructose-sweetened beverages
  - No differences in intake of calories, fiber, protein, micronutrients
  - More fat (33% vs 31%) and less CHO (49% vs 52%) in FGID
  - More epinephrine-containing foods in FGID

Saito et al, 2005
Food Allergy and IBS

• 20% of the population alters their diet for a perceived adverse reaction to food
  - Most not confirmed by testing and challenge
  - Allergy:
    • 6% infants, 3.7% adults in US
    • 1.4-2.1% teenagers in UK
      - Milk, soy, wheat in infants
      - Peanut, tree nuts, sea-food in adults

Mansueto et al, 2006
Food Allergy in IBS

• 128 outpatient IBS patients
  - 62.5% reported adverse reaction to one or more food items
  - 52.3% had positive skin prick test (permeability abnormal in 11%)
    • No correlation with symptoms
    • Not more common in those with ADR’s to food (59% vs 42%)
    • Only 13.7% correlated reaction with test

Dainese et al, 1999
IgG Responses in IBS

- 108 IBS patients and 43 controls
  - IgE and IgG4 titers and skin prick tests to common foods
    - IgE – no differences
    - SPT – positive in 5 of 56 IBS and 1 of 5 controls
    - IgG – higher titers to:
      - Wheat
      - Beef
      - Pork
      - Lamb
      » In IBS, regardless of symptoms
      » Symptoms improved with exclusion diet based on IgG results

Zar et al, 2005¹,²
IgG Responses in IBS

• 150 IBS patients
  - Randomized to exclusion based on IgG titers or to other foods to which they did not have antibodies for 3 mo.
    • Symptom score:
      - $\Delta$ sham 61.5, exclusion 100
      - Therapeutic gain 10% (26% if fully compliant)
    • Global rating improved
    • Trends for other symptoms

Atkinson et al, 2005
Anti-gliadin antibodies not induced
No changes in:
• fecal lactoferrin,
• levels of celiac antibodies
• highly sensitive C-reactive protein
• intestinal permeability
No effect HLA DQ2/DQ8

Biesiekierski et al,
Am J Gastroenterology 2011
What are FODMAPS?

Fermentable Oligo-, Di- and Mono-saccharides and Polyols
<table>
<thead>
<tr>
<th>Food Component</th>
<th>Dietary Form</th>
<th>Sources/Uses</th>
<th>Digestion and/or intestinal absorption</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fructose</strong></td>
<td></td>
<td>Fruits, honey, high fructose corn syrup (sweetener)</td>
<td>Absorptive capacity limited when in excess of glucose - low in 30% (considered to have fructose malabsorption)</td>
</tr>
<tr>
<td><strong>Lactose</strong></td>
<td></td>
<td>Milk, yoghurt, ice cream</td>
<td>No absorption if lactase deficient</td>
</tr>
<tr>
<td><strong>Fructans</strong></td>
<td>Fructooligosaccharide (oligofructose)</td>
<td>Wheat, onions, added for putative health benefit</td>
<td>No suitable small intestinal hydrolases - absorption &lt;5%</td>
</tr>
<tr>
<td><strong>Polyols</strong></td>
<td>Sorbitol, xylitol, mannitol, maltitol</td>
<td>Apples, pears, plums, reduced caloric sweetener</td>
<td>Passive absorption only (&lt;20%)</td>
</tr>
<tr>
<td><strong>Galacto-oligosaccharides</strong></td>
<td>Raffinose, stachyose</td>
<td>Legumes, beans, cabbage, Brussels sprouts, onions</td>
<td>No human -galactosidase - minimal absorption</td>
</tr>
<tr>
<td><strong>Other</strong></td>
<td>Polydextrose, isomaltose</td>
<td></td>
<td>Passive absorption only (&lt;20%)</td>
</tr>
</tbody>
</table>
Peppermint Oil

- **Active ingredient:** menthol
- **7 RCT’s**
  - Substandard study design
    - Cross-over
    - Short duration
    - Small size (<47)
    - Unconventional inclusion criteria
  - Significant global improvement overall (OR=8) but highest quality trials were negative

  Pittler and Ernst, 1998
  Fennerty, 2003
  Koretz and Rotblatt, 2004
Why use probiotics, prebiotics and synbiotics in IBS?

• Alter gut flora
• Anti-inflammatory
• Affect:
  - Stool
  - Gas
  - Bile acids
  - Mucus
Energy Healing

Acupuncture

• Acupuncture
• Homeopathy
• Chinese Traditional Medicine
  - Little data
Summary

• CAM widely employed in FGIDs
• Need to understand implications of placebo effect
• Few high-quality studies:
  - Quality control and blinding problematic
• Good data:
  - Hypnotherapy
  - Chinese herbal medicine, Iberogast
  - Certain dietary interventions, specific probiotics
Conclusions

• While the evidence for most CAM therapies in FGIDs is far from solid, some deserve further study

• Meanwhile, their frequent use among FGID patients must be acknowledged