Therapeutic options for the management of chronic constipation

Vincenzo Stanghellini
Dept of Digestive Diseases & Internal Medicine
University of Bologna
St. Orsola-Malpighi Hospital, Bologna, Italy
Leading Gastrointestinal Symptoms Prompting an Outpatient Clinic Visit in US (2009)

<table>
<thead>
<tr>
<th>Rank</th>
<th>Symptom</th>
<th>Estimated visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abdominal pain</td>
<td>15,863,956</td>
</tr>
<tr>
<td>2</td>
<td>Diarrhea</td>
<td>4,236,051</td>
</tr>
<tr>
<td>3</td>
<td>Constipation</td>
<td>3,175,842</td>
</tr>
<tr>
<td>4</td>
<td>Vomiting</td>
<td>2,861,790</td>
</tr>
<tr>
<td>5</td>
<td>Nausea</td>
<td>2,814,364</td>
</tr>
<tr>
<td>6</td>
<td>Heartburn and indigestion</td>
<td>1,982,517</td>
</tr>
<tr>
<td>7</td>
<td>Rectal bleeding</td>
<td>1,702,331</td>
</tr>
<tr>
<td>8</td>
<td>Other GI symptoms, unspecified</td>
<td>1,357,602</td>
</tr>
<tr>
<td>9</td>
<td>Dysphagia</td>
<td>1,148,041</td>
</tr>
<tr>
<td>10</td>
<td>Gastrointestinal bleeding</td>
<td>1,073,771</td>
</tr>
<tr>
<td>11</td>
<td>Appetite decrease</td>
<td>725,705</td>
</tr>
<tr>
<td>12</td>
<td>Bloating and distention</td>
<td>699,928</td>
</tr>
<tr>
<td>13</td>
<td>Anorectal symptoms (including incontinence)</td>
<td>520,772</td>
</tr>
<tr>
<td>14</td>
<td>Symptoms related to the liver and biliary system</td>
<td>454,355</td>
</tr>
</tbody>
</table>

Data are from 2009 National Ambulatory Medical Care Survey ([http://www.cdc.gov/nchs/ahcd.htm](http://www.cdc.gov/nchs/ahcd.htm)).

Peery et al, Gastroenterology 2012;143:1179–1187
Normal defecatory functions

Propulsive intestinal contractions
Colonic mass movements
Pt with infrequent or hard stools or difficult to pass stools

History and physical examination

Alarm features?

No

Yes

Technical examinations as indicated

Abnormality identified?

No

Yes

Organic disease with constipation, treat accordingly

No

Yes

Chronic functional constipation (Rome III criteria)

Adequate relief?

No

Stop drugs if possible

Adequate relief?

No

Drug-induced constipation

Yes

Stop laxative and commence with enterokinetic drug

Adequate relief?

No

Add/switch laxative

Adequate relief?

No

Stop laxative and commence with enterokinetic drug

Adequate relief?

Yes

Addition of laxatives

Yes

Long-term management

Refactory constipation

testing following Rome guidelines

Long-term management

No

No

No

No

Yes

Yes

Yes

Yes

Long-term management

Tack, Muller-Lissner, Stanghellini, et al. NGM 2011;23:697-710
Pt with infrequent or hard stools or difficult to pass stools

History and physical examination

Alarm features?

No

Technical examinations as indicated

No

Abnormality identified?

Yes

Organic disease with constipation, treat accordingly

No

Yes

Constipating drugs?

No

Stop drugs if possible

No

Adequate relief?

Yes

Drug-induced constipation

No

Adequate relief?

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Stop laxative and commence with enterokinetic drug

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Adequate relief?

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Long-term management

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Stop laxative and commence with enterokinetic drug

Adequate relief?

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Long-term management

No

Refactory constipation

Yes

testing following Rome guidelines

No

Long-term management

Education; lifestyle and dietary measures

Addition of laxatives

Adequate relief?
Pt with infrequent or hard stools or difficult to pass stools

History and physical examination

Alarm features?

Yes

Technical examinations as indicated

No

Constipating drugs?

Yes

Stop drugs if possible

No

Adequate relief?

Yes

Drug-induced constipation

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chronic functional constipation (Rome III criteria)

Education; lifestyle and dietary measures

Addition of laxatives

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No

Add/switch laxative

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Yes

Long-term management

No

Stop laxative and commence with enterokinetic drug

Adequate relief?

Yes

Long-term management

No

Refractory constipation

Refactory constipation testing following Rome guidelines

No

Organic disease with constipation, treat accordingly
**THE “FIBER HYPOTHESIS”**

Stool weight and intestinal transit in healthy subjects according dietary fiber intake

![Denis Burkitt 1911-1963](image)

<table>
<thead>
<tr>
<th></th>
<th>Fiber Intake</th>
<th>Stool weight (g/day)</th>
<th>Transit Time (hours)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Africa</td>
<td>High</td>
<td>275-470</td>
<td>33-35</td>
</tr>
<tr>
<td>UK</td>
<td>Low</td>
<td>107</td>
<td>69</td>
</tr>
</tbody>
</table>

Burkitt & Painter, Burkit & Trowel (eds) 1975; pp:69-84
DIET AND LIFE HABITS IN FUNCTIONAL CONSTIPATION

- Slow transit related to: ↓ water intake, ↓ caloric intake, ↑ % protein, (but no dietary fibre)
  

- 25 g/day dietary fibre: ↑ frequency bowel movements in 173 pts; 1.5-2.0 L water/day ↑ efficacy of fibre
  
  Anti et al, Hepatogastroenterology 1998

- Defecation suppression ↑ total and segmentary transit
  
  Klauser et al, DDS 1990
## SIMILAR FIBER INTAKE IN CHRONIC CONSTIPATION AND CONTROLS

<table>
<thead>
<tr>
<th>Author</th>
<th>Subjects</th>
<th>N° (F)</th>
<th>Fiber Intake (g/day)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preston, 1986</td>
<td>Slow-transit Constipation Controls</td>
<td>64 (64)</td>
<td>14.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>64 (64)</td>
<td>15.0</td>
</tr>
<tr>
<td>Anderson, 1986</td>
<td>Constipation (III*-trim pregnancy) Controls</td>
<td>9</td>
<td>18.2</td>
</tr>
<tr>
<td></td>
<td>(III*-trim pregnancy)</td>
<td>9</td>
<td>18.3</td>
</tr>
<tr>
<td>Klauser, 1992</td>
<td>Self-defined Constipation Controls</td>
<td>62 (51)</td>
<td>18.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>100 (72)</td>
<td>18.8</td>
</tr>
<tr>
<td>Klauser, 1992</td>
<td>Slow-transit constipation Normal-transit constipation</td>
<td>19 (15)</td>
<td>17.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>21 (20)</td>
<td>19.8</td>
</tr>
<tr>
<td>Towers, 1994</td>
<td>Self-defined constipation Controls</td>
<td>18 (10)</td>
<td>17.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>18 (8)</td>
<td>14.7</td>
</tr>
</tbody>
</table>
Effect of bran, fruit and vegetables on IBS symptoms

Effect of fibre on global symptom improvement

**SOLUBLE FIBRE**
- Arthurs and Fielding, 1983
- Jalihal and Kurian, 1999
- Longstreth et al., 1981
- Nigam et al., 1984
- Prior and Whorwell, 1987
- Toskes et al., 1993
- Ritchie and Truelove, 1979
- Ritchie and Truelove, 1980

Subtotal (95%CI) (41% pla vs 64% treatment)
Test for heterogeneity chi square=13.44; \( P = 0.062 \)
Test for overall effect \( z = 6.31; P < 0.0001 \)

**INSOLUBLE FIBRE**
- Cook et al., 1990
- Fowlie et al., 1992
- Snook and Shepherd, 1994
- Soltoft et al., 1976

Subtotal (95%CI) (56% pla vs 50% treatment)
Test for heterogeneity chi square=0.68; \( P = 0.88 \)
Test for overall effect \( z = -1.01; P = 0.3 \)

Total (95%CI) (45% pla vs 60% treatment)
Test for heterogeneity chi square=27.97; \( P = 0.0033 \)
Test for overall effect \( z = 4.93; P < 0.00001 \)
Treatment algorithm for chronic constipation

AGA Medical Position Statement on Constipation
Gastroenterology 2013;144:211-7
Pt with infrequent or hard stools or difficult to pass stools

- History and physical examination
  - Alarm features?
    - No
    - Yes: Technical examinations as indicated
  - Yes: Constipating drugs?
    - No
    - Yes: Stop drugs if possible
      - Adequate relief?
        - No
        - Yes: Drug-induced constipation
          - Abnormality identified?
            - No
            - Yes: Organic disease with constipation, treat accordingly
    - Yes: Abnormality identified?
      - No
      - Yes: Organic disease with constipation, treat accordingly

- Chronic functional constipation (Rome III criteria)
  - Education; lifestyle and dietary measures
  - Addition of laxatives
    - Adequate relief?
      - No
      - Yes: Long-term management
  - Add/switch laxative
    - Adequate relief?
      - No
      - Yes: Long-term management
    - Stop laxative and commence with enterokinetic drug
      - Adequate relief?
        - No
        - Yes: Long-term management
      - Refractory constipation
        - testing following Rome guidelines

Tack, Muller-Lissner, Stanghellini, et al. NGM 2011;23:697-710
Main Laxative Classes

• BULK FORMERS
• CONTACT LAXATIVES
• OSMOTICS
• LUBRICANTS / STOOL SOFTNERS
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Dietary fiber/bulking agent</td>
<td>1C</td>
<td>B (psyllium)</td>
<td>B (fiber/psyllium)</td>
</tr>
<tr>
<td>Osmotic laxatives</td>
<td>1B</td>
<td>A (PEG and lactulose)</td>
<td>A (PEG) B (lactulose)</td>
</tr>
<tr>
<td>Diphenyl methanes, anthraquinones</td>
<td>2B</td>
<td>Insufficient evidence (Grade B)</td>
<td>C</td>
</tr>
<tr>
<td>Stool softeners</td>
<td>-</td>
<td>Insufficient evidence (Grade B)</td>
<td>C</td>
</tr>
<tr>
<td>Biofeedback therapy (selected cases)</td>
<td>1B</td>
<td>Insufficient evidence (Grade C)</td>
<td>B</td>
</tr>
<tr>
<td>Surgery (severe colonic inertia)</td>
<td>2B</td>
<td>-</td>
<td>B</td>
</tr>
</tbody>
</table>

Tack, Muller-Lissner, Stanghellini, et al. NGM 2011;23:697-710
Long-term efficacy of PEG (17.5 gr. bid) in the treatment of idiopathic chronic constipation in 70 patients

Corazziari et al, Gut 2000;46:522-6
Long-term efficacy of PEG (17.5 gr. bid) in the treatment of idiopathic chronic constipation in 70 patients

Corazziari et al, Gut 2000;46:522-6
Low dose PEG 3350 vs lactulose for the treatment of chronic constipation in 99 patients

Attar et al, Gut 1999; 44:226-30
Low dose PEG 3350 vs lactulose for the treatment of chronic constipation and accompanying symptoms in 99 patients

Attar et al, Gut 1999; 44:226-30

- *p<0.05

10 randomized trials comparing PEG and lactulose
PEG superior to lactulose in improving stool frequency / consistency, abdominal pain

Lee-Robichaud et al, Cochrane Database Syst Rev 2010;7:CD007570
Effect of macogol on bowel movements and abdominal symptoms in IBS-C patients


<table>
<thead>
<tr>
<th>Treatment period</th>
<th>Macrogol 3350</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean abdominal discomfort/pain</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Run-in</td>
<td>Week 1</td>
<td>Week 2</td>
</tr>
<tr>
<td>0</td>
<td>1</td>
<td>2</td>
</tr>
</tbody>
</table>

Mean number of SCBMs

<table>
<thead>
<tr>
<th>Treatment period</th>
<th>Macrogol 3350</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>P&lt;0.0001</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Statistically significant difference
Types of laxatives used by 1355 respondents with CC to an internet survey

- Diphenolic laxatives > Macrogol > Anthraquinones > Sugars (preferences vary between language subsets)

68% used laxatives

Chronic constipation survey in referral centers in Italy

39 centres = 878 interviews collected, an average of 23 patients per centre distributed as follows:

- North West: 24%
- North East: 20%
- Centre: 20%
- South & islands: 36%
A multi-symptom condition with straining/hard stools, bloating and incomplete evacuation most troublesome...

<table>
<thead>
<tr>
<th>Symptom</th>
<th>0 Absent</th>
<th>1 Mild</th>
<th>2 Moderate</th>
<th>3 Strong</th>
<th>4 Very strong</th>
</tr>
</thead>
<tbody>
<tr>
<td>Straining or pushing to expel faeces</td>
<td>7</td>
<td>13</td>
<td>27</td>
<td>30</td>
<td>20</td>
</tr>
<tr>
<td>Bloated abdomen</td>
<td>7</td>
<td>18</td>
<td>30</td>
<td>27</td>
<td>14</td>
</tr>
<tr>
<td>Excessively hard faeces</td>
<td>11</td>
<td>14</td>
<td>31</td>
<td>28</td>
<td>13</td>
</tr>
<tr>
<td>Feeling one hasn't evacuated everything</td>
<td>11</td>
<td>18</td>
<td>32</td>
<td>24</td>
<td>12</td>
</tr>
<tr>
<td>Inability to defecate despite urge to do so</td>
<td>24</td>
<td>19</td>
<td>23</td>
<td>21</td>
<td>11</td>
</tr>
<tr>
<td>Small faeces</td>
<td>18</td>
<td>18</td>
<td>27</td>
<td>22</td>
<td>9</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>15</td>
<td>21</td>
<td>35</td>
<td>19</td>
<td>5</td>
</tr>
<tr>
<td>Anal burning</td>
<td>36</td>
<td>23</td>
<td>21</td>
<td>11</td>
<td>5</td>
</tr>
<tr>
<td>Stomach pains</td>
<td>24</td>
<td>25</td>
<td>29</td>
<td>14</td>
<td>4</td>
</tr>
<tr>
<td>Pain when defecating</td>
<td>36</td>
<td>22</td>
<td>20</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Blood loss or anal tears</td>
<td>59</td>
<td>17</td>
<td>11</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Stomach cramps</td>
<td>48</td>
<td>20</td>
<td>17</td>
<td>8</td>
<td>2</td>
</tr>
</tbody>
</table>

N=878 patients

Neri et al., Submitted for publication
Only one patient in five was satisfied with their chronic constipation therapy in Italy.

N=878 patients

Neri et al., Submitted for publication
... and one out of two patients with severe chronic constipation was dissatisfied...

Base: 706 patients in therapy (110 with fibre/bulk-forming laxatives; 81 with stimulating laxatives; 172 with osmotic laxatives; 134 with a combination of two or more laxatives)

Neri et al., Submitted for publication
... and changing the laxative did not improve satisfaction with therapy

Base: 706 patients in therapy (110 with fibre/bulk-forming laxatives; 81 with stimulating laxatives; 172 with osmotic laxatives; 134 with a combination of two or more laxatives)

Neri et al., Submitted for publication
Pt with infrequent or hard stools or difficult to pass stools

History and physical examination

Alarm features?

Yes

No

Technical examinations as indicated

Constipating drugs?

No

Yes

Stop drugs if possible

Adequate relief?

Yes

Drug-induced constipation

Abnormality identified?

No

Yes

Organic disease with constipation, treat accordingly

Education; lifestyle and dietary measures

Addition of laxatives

Adequate relief?

No

Yes

Long-term management

Chronic functional constipation (Rome III criteria)

Add/switch laxative

Adequate relief?

No

Yes

Long-term management

Stop laxative and commence with enterokinetic drug

Adequate relief?

No

Yes

Long-term management

Refractory constipation

testing following Rome guidelines

Tack, Muller-Lissner, Stanghellini, et al. NGM 2011;23:697-710
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History and physical examination

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No

No

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Constipating drugs?

Yes

Stop drugs if possible

No

Adequate relief?

Yes

Drug-induced constipation

No

Chronic functional constipation (Rome III criteria)

Adequate relief?

Yes

Addition of laxatives

No

Adequate relief?

Yes

Stop laxative and commence with enterokinetic drug

No

Add on PRU to current laxative

Adequate relief?

Yes

Long-term management

No

Long-term management start step-down laxatives

Refractory constipation

testing following Rome guidelines

Long-term management

Education; lifestyle and dietary measures

No

Adequate relief?
Peristalsis & related neuronal circuitries

Serotonergic 5-HT$_4$ receptor distribution

- **Ascending reflex contraction**
  - s. muscle enterocytes
  - 5-HT$_4$ -
  - 5-HT$_4$ +

- **Descending reflex relaxation**
  - 5-HT$_4$ +


Diagram showing the interaction of excitatory (ACh/TK) and inhibitory (ACh/TK) motor neurons with sensory neurons, releasing 5-HT and NO/VIP/ACh, and the effect on the intraluminal content.
Cumulative Best Response – Graphically

Total Clinical Benefit

% responders

- ≥ 3 SCBM
- Δ ≥ 1 SCBM
- Δ ≥ 1 Satisf
- Δ ≥ 1 SBM

Stanghellini, et al. submitted
Prucalopride’s effect size on symptoms associated with chronic constipation, evaluated by PAGI-SYM

Placebo (n = 531)  Prucalopride 2 mg (n= 511)

Effect size (mean change from baseline divided by baseline standard deviation)
Pooled safety and tolerability: Adverse events

Most common drug-related adverse events

- **Placebo (n=661)**
- **Prucalopride 2 mg (n=659)**
- **Prucalopride 4 mg (n=657)**

**Events during treatment period**

- Headache
- Nausea
- Diarrhoea
- Abdominal pain

**Events excluding Day 1**

- Headache
- Nausea
- Diarrhoea
- Abdominal pain

Tack et al. Gastroenterology 2008;134:A530
… what if prucalopride fails ?

1. Different drug classes
2. Refer for functional testing (transit times, ano-rectal manometry, balloon expulsion test, defecography, pelvic floor functional-MRI, other?)
3. Biofeedback
4. Combination therapies ?
5. Surgery
Effects of linaclotide and other ligands through the GC-C receptor on enteroocytes

- **GC-C**: guanylate cyclase c
- **EE**: entero endocrine
- **CFTR**: cystic fibrosis transmembrane conductance regulator
- **CCI2**: chloride channel type 2
- **GTP**: guanosine triphosphate
- **cGMP**: cyclic guanosine monophosphate
- **PKG**: cGMP-dependent protein kinase

Corsetti and Tack, UEGJ 2013;1:7-20
Two Randomized Trials of Linaclotide for Chronic Constipation

1276 patients;
Linaclotide od for 12 wks
Primary endpoint: \( \geq 3 \text{CSBM} \)
Secondary endpoint: ↓ pain

# IBS-C Phase III adverse events: 12 weeks

**TEAEs occurring in ≥3% in either 266 μg linaclotide group**

<table>
<thead>
<tr>
<th></th>
<th>MCP-103-302 (12 weeks)</th>
<th>LIN-MD-31 (12 weeks)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Placebo N=403</td>
<td>Placebo N=396</td>
</tr>
<tr>
<td><strong>Any TEAE</strong></td>
<td>187 (46%)</td>
<td>212 (53%)</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>7 (2%)</td>
<td>71 (18%)</td>
</tr>
<tr>
<td>Nausea</td>
<td>17 (4%)</td>
<td>17 (4%)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>14 (3%)</td>
<td>15 (4%)</td>
</tr>
<tr>
<td>URTI</td>
<td>13 (3%)</td>
<td>14 (3%)</td>
</tr>
<tr>
<td>Flatulence</td>
<td>7 (2%)</td>
<td>13 (3%)</td>
</tr>
<tr>
<td>Headache</td>
<td>8 (2%)</td>
<td>14 (4%)</td>
</tr>
</tbody>
</table>

Note: TEAEs where the rate was higher in the placebo group in both trials are not presented, safety populations; n (%) represent number and % of patients
Increased guanylate cyclase C (GC-C) signaling disturbs normal bowel function and appears to have a proinflammatory effect, either through increased chloride secretion or additional effects of elevated cellular cGMP.
autosomal-recessive phenotype of meconium ileus not associated with cystic fibrosis (CF) caused by different homozygous mutations in \textit{GUCY2C} \xrightarrow{↓} enzymatic activity of the encoded guanylate cyclase 2C in two unrelated consanguineous Bedouin kindreds

Romi et al, Am J Hum Gen 2012;90:893-9
Lubiprostone

- Non-absorbable fatty acid derived from PgE$_1$\textsuperscript{1}
- Selectively activates apical CIC-2 chloride channels, Pg receptors and CFTR, thus enhancing intestinal fluid secretion
- FDA-approved in January 2006 in US for treatment of chronic idiopathic constipation and IBS-C in women\textsuperscript{2}

2. FDA Consum 2006;40:8
Effect of Lubiprostone on bowel function in IBS-C

Weekly bowel movements

(a)

Mean (95% CI) change from baseline

Month 1

Month 2

Month 3

Placebo
16 µg (8 µg b.d.)
32 µg (16 µg b.d.)
48 µg (24 µg b.d.)

P = 0.0004
P = 0.0204
P = 0.0296

Johanson et al., APT 2008;27:685-96
Effect of Lubiprostone on abdominal discomfort/pain in IBS-C

Johanson et al., APT 2008;27:685-96
Pt with infrequent or hard stools or difficult to pass stools

History and physical examination

Alarm features?

No

Constipating drugs?

No

Chronic functional constipation (Rome III criteria)

Adequate relief?

No

Stop drugs if possible

No

Abnormality identified?

Yes

Organic disease with constipation, treat accordingly

No

Stop laxative and commence with enterokinetic drug

Adequate relief?

No

Long-term management

Yes

Add/switch laxative

Adequate relief?

No

Stop laxative and commence with enterokinetic drug

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No

Refactory constipation

No

Testing following Rome guidelines

Yes

Long-term management

Adequate relief?

No

Addition of laxatives

Adequate relief?

Yes

Long-term management

Tack, Muller-Lissner, Stanghellini, et al. NGM 2011;23:697-710
Prevalence of subtypes in 1009 Mayo Clinic tertiary referrals with chronic constipation

General Ano-Rectal Examination

- Observation: a) perineum descent during simulated evacuation; b) elevation during squeeze; c) anal reflex; d) soiling; e) prolapse; f) patulous opening; g) hemorrhoids / fissures

- Digital examination: a) sphincter / puboprectalis tone during resting / squeezing; b) rectolece; c) internal prolapse; d) dyssinergic defecation
Digital rectal examination (DRE) for the diagnosis of pelvic dyssynergia

- 209 Rome III CC pts (191 F)
- 183/209 (87%) dyssynergia at ARM
- 134/187 (73%) dyssynergia at DRE
- Sensitivity 75%
- Specificity 87%
- +ve predictive value 97%

Pelvic dyssynergia by DRE based ≥ 2 of
- a) impaired perineal descent;
- b) paradoxic anal contraction;
- c) impaired push effort
EFFECT OF BIOFEEDBACK
IN FUNCTIONAL OUTLET OBSTRUCTION

Before

20 mmHg
Rectum

Anal canal
1.5 cm

courtesy of Satish S.C. Rao, MD
Systematic review of randomized trials of the effectiveness of biofeedback for pelvic floor dysfunction

Studies retrieved by applying search terms

\[ n = 5028 \]

Excluded
\[ n = 4981 \]

Trials relevant to PFD
\[ n = 47 \]

Excluded \[ n = 40 \]
Retrospective, uncontrolled or not randomized

Included studies
\[ n = 7 \]

Systematic review of randomized trials of the effectiveness of biofeedback for pelvic floor dysfunction

<table>
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<td>Chiarioni et al.</td>
<td>14.008 (5.577, 35.180)</td>
<td>5.618</td>
<td>&lt; 0.001</td>
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<td>Heymen et al.</td>
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<td>3.442</td>
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<td>Rao et al.</td>
<td>2.444 (0.878, 6.806)</td>
<td>1.711</td>
<td>0.087</td>
<td></td>
</tr>
<tr>
<td>Overall</td>
<td>5.861 (2.175, 15.794)</td>
<td>3.497</td>
<td>&lt; 0.001</td>
<td></td>
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Biofeedback vs non-biofeedback

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<tr>
<td>Glia et al.</td>
<td>1.867 (0.392, 8.894)</td>
<td>0.784</td>
<td>0.433</td>
<td></td>
</tr>
<tr>
<td>Bleijenberg et al.</td>
<td>10.667 (1.387, 82.033)</td>
<td>2.274</td>
<td>0.023</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6.738 (2.914, 15.580)</td>
<td>4.461</td>
<td>&lt; 0.001</td>
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</table>

BIOFEEDBACK IN CHRONIC CONSTIPATION
COMPLIANCE AND SUCCESS RATES

Compliance
62% pts Complete therapy
Lau et al, DCR 2000

Number of sessions
6 (2-10) Rao et al, DDS 1997
4-5 Chiotakakou-Faliakou et al, Gut 1998
1.5 (1-2), (83% efficacia, 11 mesi FU) Frazzoni et al, SIMI 2003

Success in obstructed defecation
70% (10 pts) Bleljenberg & Kuipers, DCR 1987
87% (15 pts) Kawimbe et al, Gut 1991
78% (9 pts) Dahl et al, DCR 1991
89% (18 pts) Wexener et al, DCR 1992
100% (9 pts) Fleshman et al, DCR 1992
85% (25 pts) Koutsomanis et al, EurJGE&Hepat 1994
73% (11 pts) Bleljenberg & Kuipers, Am J Ge 1994
60% (25 pts) > 75% satisfaction; Rao et al, DDS 1997
57% (100 pts) 23 mesi, range 12-44 Chiotakakou-Faliakou et al, Gut 1998
55% (108 pts) Lau et al, DCR 2000
Long term maintenance of biofeedback training in pts with different types of chronic idiopathic constipation


entry→24 mos follow up
open bars: STC n= 12→9
grey bars: MIX n= 6→4
black bars: PFD n= 34→32
Long term maintenance of biofeedback training in pts with different types of chronic idiopathic constipation

entry→24 mos follow up

- **STC n= 12→9**
- **MIX n= 6→4**
- **PFD n= 34→32**

*BFB normalizes TT in 2/3 of mixed constipation*
Conclusions

• Chronic constipation is a frequent chronic functional syndrome bearing major social and personal burdens

• It is often underestimated by doctors and traditional laxatives are associated with a high degree of dissatisfaction

• Better understanding of underlying mechanisms and development of new therapies is leading to more coherent and successful management and treatment of affected individuals