Chronic Constipation, IBS-C or Dyssynergia?

Satish S.C. Rao, MD, PhD, FACP
Professor of Medicine
Chief, Division of Gastroenterology/Hepatology
Director, Digestive Health Center
Medical College of Georgia
Georgia Regents University, Augusta, GA

Case Study
38-year-old school nurse

- Increasing constipation –10 years
  - Began during college days following a bout of gastroenteritis
  - Now, B.M. once a week, hard, pellet-like stool, only after enema + suppository + laxatives
  - She describes excessive straining, often spending 20-30 min, & reports incomplete evacuation and intermittent vaginal splinting to complete BM
  - Tried OTC laxatives, MOM, PEG-no relief
  - Over past 3 years, she reports lower abdominal pain and distension sometimes better after B.M.
  - She is also bloated and has excess gas
OBJECTIVES

- What is her problem?
  - Chronic Constipation
  - Dyssynergic Defecation
  - Irritable Bowel Syndrome Constipation Predominant (IBS-C)
- Do these problems overlap
- If so, how to Recognize, Diagnose & Treat

Secondary Causes of Constipation

- Pregnancy
- Medications
- Malignancy
- Mechanical obstruction
- Collagen vascular and muscle disorders
- Metabolic disorders
- Neurological disorders
- Endocrine disorders

Functional Subtypes: Primary Constipation

- Slow Transit Constipation 47%
- Irritable Bowel Syndrome 58%
- Evacuation Disorders 59%
- Slow transit and IBS-C overlap in half of each group


Outlet Obstr:
- Rectocele
- Descending perineum syndrome
- Rectal prolapse

Differentiating Signs and Symptoms of Chronic Constipation (CC) and IBS-C

- Abdominal Pain/Discomfort
- Visceral Hypersensitivity
- <3 BMs/Week
- Normal Stool Frequency

*3 BMs/day to 3 BMs/week is considered range of normal stool frequency
**Differentiating Between Dyssynergic Constipation and IBS With Constipation**

**Dyssynergic constipation**
- Excessive Straining
- Manual Maneuvers
- Feeling of incomplete evacuation

**IBS with constipation**
- (+) Abdominal Pain
- Bloating

**Presence or absence of abdominal pain and bloating is an important differentiating feature**


---

**Pathophysiology-Slow Transit Constipation**

**Methane & STC**
- About 1/3rd of population produces CH$_4$
- Predominant organism is Methanobrevibacter smithii
- Increased prevalence in STC
- A genetic fingerprint

**Altered Intestinal Microbiota**

**Women & Constipation**
- Down-regulation of contractile proteins & Up-regulation of inhibitory G proteins caused by overexpression of progesterone receptors
  - Xiao et al Gastro 2005; 128:667

**Colonic Manometry**
- Absence of HAPC
- Loss of Gastrocolonic/Waking response
- Altered PRMA
- Sensory changes/Reflexes
Pathophysiology of IBS

- Enhanced perception
- Psychosocial factors
- Altered motility
- Visceral hypersensitivity
- SIBO / Post-Infection IBS

Enhanced perception is linked to genetic predisposition. Food intake can alter motility, and SIBO can lead to post-infection IBS.

Adapted from Camilleri & Choi, Aliment Pharmacol Ther 1997; 11: 3

Gut microbiota enterotypes in IBS

The link between IBS severity score and enterotypes distribution is shown in the chart.

Link between IBS severity score and enterotypes distribution

**Pathophysiology-Dyssynergic Defecation**

- Impaired Rectoanal coordination
  - Paradoxical anal/puborectalis contraction
  - Inadequate rectal contraction/pushing force
  - Absent/Inadequate anal/puborectalis relaxation

- Impaired Rectoanal sensation

  *Rao et al, Am J Gastroenterol 1997;92:469-75*

<table>
<thead>
<tr>
<th>Learnt</th>
<th>= 67%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yet to Learn</td>
<td>= 33%</td>
</tr>
</tbody>
</table>

*Rao et al, Gastro Clin N Am 2008*

**Chronic Constipation: ROME III Criteria**

- Chronic constipation must include 2 or more of the following:
  - Straining
  - Lumpy or hard stools
  - Sensation of incomplete evacuation
  - Sensation of anorectal obstruction/blockage
  - Manual maneuvers (e.g., digital evacuation of the pelvic floor)
  - <3 defecations per week

- Loose stools are rarely present without the use of laxatives

- There are insufficient criteria for irritable bowel syndrome (IBS)

*Criteria fulfilled for at least 3 months with symptom onset at least 6 months prior to diagnosis*

*Longstreth GF et al. Gastroenterology. 2006;130:1480.*
**Definition of IBS**

**Clinical Practice**

The American College of Gastroenterology (ACG) defines IBS as Abdominal discomfort associated with altered bowel habits.

**Rome III-Clinical Trials**

At least 12 weeks, which need not be consecutive, in the preceding 12 months of abdominal discomfort or pain that has 2 of the following 3 features:

- Relieved with defecation
- Onset associated with a change in frequency of stool
- Onset associated with a change in form (appearance) of stool

**Diagnostic Criteria-Dyssynergic Defecation**

1. The patient must satisfy diagnostic criteria for functional constipation—Rome III

2. During repeated attempts to defecate must demonstrate Dyssynergic pattern of defecation
   - Manometry
   - EMG

3. Patient must demonstrate one other abnormal test:
   a. Abnormal balloon expulsion Test (> 1 minute)
   b. Prolonged Colonic Transit Time (radioopaque markers or capsule or scintigraphy)
   c. Abnormal Defecography (>50% barium retention)

Bharucha et al, Gastroenterology 2006;130:1514
Constipation, Dyssynergia & IBS

**History**
- Onset
- Diet
- Drugs
- Ignore call to stool
- Abdominal Pain & Discomfort
- Digital maneuvers
- Psychological and effects on QOL
- Sexual abuse / Emotional factors
- Injury = Obstetric / Surgery / Back
- Gastroenteritis

**Stool Form Correlates with Intestinal Transit Time**

**THE BRISTOL STOOL FORM SCALE**

- **Type 1**: Separate hard lumps
- **Type 2**: Sausage-like but lumpy
- **Type 3**: Sausage-like but with cracks in the surface
- **Type 4**: Smooth and soft
- **Type 5**: Soft blobs with clear-cut edges
- **Type 6**: Fluffy pieces with ragged edges, a mushy stool
- **Type 7**: Watery, no solid pieces

3-step DRE-PROTOCOL

1) Inspection

2) Perianal sensation & anocutaneous reflex:
   - normal, impaired, absent

3) Digital maneuvers: mass, tenderness, stool
   - Squeeze x 2: normal, weak, increased
   - Bearing down x 2
     - push effort, sphincter relaxation, perineal descent

Clinically dyssynergia if ... any 2:
- inability to
  - contract abdominal muscles
  - relax anal sphincter
  - paradoxical contraction of anal sphincter
  - absence of perineal descent

Tantiphlachiva K, Rao S et al, CGH 2010

Yield of rectal exam in dyssynergia, n=209

All patients had
DRE
Anorectal manometry
Balloon Expulsion Test

Data Analyzed independently

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dyssynergia from DRE</td>
<td>75%</td>
<td>87%</td>
</tr>
<tr>
<td>Balloon expulsion test</td>
<td>49%</td>
<td>90%</td>
</tr>
</tbody>
</table>

Tantiphlachiva K, Rao S et al, CGH 2010
### Can Symptoms Predict Dyssynergia?

#### 100 Patients With Difficult Defecation

<table>
<thead>
<tr>
<th>Symptom prevalence</th>
<th>Normal pattern (n = 30)</th>
<th>Type I (n = 32)</th>
<th>Type II (n = 24)</th>
<th>Type III (n = 14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Excessive straining</td>
<td>92%</td>
<td>96%</td>
<td>89%</td>
<td>83%</td>
</tr>
<tr>
<td>Abdominal fullness</td>
<td>80%</td>
<td>96%</td>
<td>89%</td>
<td>67%</td>
</tr>
<tr>
<td>Incomplete evacuation</td>
<td>72%</td>
<td>96%</td>
<td>89%</td>
<td>100%</td>
</tr>
<tr>
<td>Abdominal discomfort</td>
<td>88%</td>
<td>81%</td>
<td>74%</td>
<td>75%</td>
</tr>
<tr>
<td>Digital maneuvers to defecate</td>
<td>28%</td>
<td>56%</td>
<td>47%</td>
<td>50%</td>
</tr>
</tbody>
</table>


### Tools for Evaluation

- History
- Stool diary
- Colonoscopy (particularly if aged >50 years)
- Colonic transit study
  - radiopaque markers,
  - Scintigraphy
  - Wireless pH/Motility capsule test
- Balloon expulsion test
- Defecography/MRI
defecography
- Anorectal manometry
- Colonic manometry

38-year-old Nurse, Severe Constipation, pain, gas & bloating, WMC & Radioopaque marker test

New Diagnostic Information with WMC

<table>
<thead>
<tr>
<th></th>
<th>Lower GI n = 50</th>
<th>Upper GI n = 36</th>
<th>Combined Group n = 86</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prolonged Gastric Emptying Time</td>
<td>14/50 (28%)</td>
<td>9/36 (25%)</td>
<td>23/86 (27%)</td>
</tr>
<tr>
<td>Rapid Gastric Emptying Time</td>
<td>2/50 (4%)</td>
<td>3/36 (8%)</td>
<td>5/86 (6%)</td>
</tr>
<tr>
<td>Prolonged Small Bowel Transit</td>
<td>7/50 (14%)</td>
<td>3/36 (8%)</td>
<td>10/86 (12%)</td>
</tr>
<tr>
<td>Prolonged Colonic Transit Time</td>
<td>3/50 (6%)</td>
<td>6/36 (17%)</td>
<td>9/86 (11%)</td>
</tr>
</tbody>
</table>

Rao, Mysore, Attaluri, Valestin J Clin Gastr 2011
Is IBS a diagnosis of exclusion?

- Providers who believe IBS is diagnosis with exclusion order 1.6 more tests and use $364 more than those who do not (p<0.0001)

<table>
<thead>
<tr>
<th></th>
<th>PCPs, nurse practitioners and gastroenterologists (n=281)</th>
<th>IBS experts (n=27)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS is diagnosis of exclusion? (% yes)</td>
<td>72</td>
<td>8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>IBS-D</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive diagnosis (%)</td>
<td>38</td>
<td>67</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diagnostic tests (n)</td>
<td>4.1</td>
<td>2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Cost of testing ($)</td>
<td>658</td>
<td>297</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>IBS-C</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive diagnosis (%)</td>
<td>20</td>
<td>67</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Diagnostic tests (n)</td>
<td>2.2</td>
<td>1.4</td>
<td>0.06</td>
</tr>
<tr>
<td>Cost of testing ($)</td>
<td>550</td>
<td>288</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Positive diagnosis = a diagnosis of IBS made using a patient history without need for further information, lab tests, procedures, etc.

Spiegel et al. Gastroenterology. 2006;130(Suppl. 2):S1134

Types of Dyssynergic Defecation

Dyssynergic patterns:

I

P- Puborectalis
EAS- External anal sphincter
D - Diffuse

II

P- Puborectalis
EAS- External anal sphincter

III

IV


Dyssynergia Type 1- Subtypes

Type I- EAS

Type I- Puborectalis

Type 1-Diffuse

Effect of Body Position on Defecation Patterns

Responders: ≥3 CSBM/wk & Increase of ≥1 CSBM/wk for ≥9/12 wks

- Placebo, n=424
- Linaclotide 145 μg, n=430
- Linaclotide 290 μg, n=418

NNT= ~ 7

*P≤0.01
**P≤0.001

Most common AE diarrhea (14%-16% vs 4.7%); Discontinuation (4% vs 0.5%).

CSBM=complete spontaneous bowel movement.

Courtesy of S. Rao
**Linaclotide: Phase 3 Trial in IBS-C**

**Primary Responder Endpoints**

- **≥3 CSBM/week; and**
- **≥30% reduction in abdominal pain; and**
- **Both for at least 9 of 12 weeks**

- **≥3 CSBM/week; and**
- **Increase of ≥1 CSBM/week**
- **Both for at least 9 of 12 weeks**

- **≥3 CSBM/week; and**
- **Increase of ≥1 CSBM/week**
- **Both for at least 6 of 12 weeks**

- **≥3 CSBM/week; and**
- **Increase of ≥1 CSBM/week**
- **All 3 for at least 9 of 12 weeks**

* % Responder

* = p < 0.05; ** = p ≤ 0.001; *** = p ≤ 0.0001 (vs. placebo)

**Effects of Lubiprostone on Number of Spontaneous Bowel Movements**

- **Onset of action was within 24 hours in the majority of subjects**
- **Most common adverse events were nausea, diarrhea, and headache**
- **9 subjects taking lubiprostone withdrew due to adverse events**

\[ N = 242 \]

**Intent-to-treat population**

- **24 µg BID**
- **Placebo**

P = 0.0001  P = 0.0017  P = 0.0002  P = 0.0002

**Johanssen et al Am J Gastroenterol 2008;103:170-7.**
**Effect of Naloxegol**

Oral peripheral mu opioid receptor antagonist - Dose Response studies x2, n=700/study

**Primary End Point**
**Responder =**

- $>1$ SBM/wk over baseline for $>9/12$ wks
- $>3$ SBM during last 4 wks of treatment

**Naloxegol KODIAC 04-05 Results**

Chey W et al NEJM 2014

---

**Traditional IBS Treatment Options**

- **Address individual symptoms of IBS**
  - Abdominal pain/discomfort
  - Bloating and distension
  - Constipation
  - Altered bowel habits
  - Diarrhea

- **Antispasmodics**
  - TCAs
  - Analgesics
  - CBT

- **Dietary changes**
  - Antispasmodics
  - Antiflatulents
  - Digestive enzymes
  - Antibiotics

- **Fiber**
- **Laxatives**

SATISH S. C. RAO, MD, PHD, FACG

RESULTS

After the diets, FOD-NG and FOD-GF groups showed a significant improvement of bloating, abdominal distension, and pain (p-values equal to 0.000 in the former group and from 0.001 to 0.008 in the latter), and Controls had a slight, but not significant, improvement.

D. PIACENTINO ET AL. SAPIENZA UNIVERSITY. ROME, ITALY.

Effects of Low-FODMAP and Gluten-Free Diets in Irritable Bowel Syndrome Patients: A Double-Blind Randomized Controlled Clinical Study

D. PIACENTINO ET AL. DDW 2014.
Biofeedback-Dyssynergia

**Goals of Therapy:**
- A) Teach Diaphragmatic breathing exercise
- B) Teach anal sphincter & pelvic floor relaxation
- C) Improve Rectal Sensation
- D) Eliminate Sensory Delay
- E) Improve Recto-anal Coordination

Biofeedback Therapy-RCTs

- Biofeedback Vs PEG 14.6 g for Dyssynergia
  - Chiarioni et al, Gastroenterology 2006; 130: 657-64
- Biofeedback vs Diazepam for Dyssynergia
  - Heymen et al, Dis Col Rectum 2007
- Biofeedback vs Sham Therapy vs Standard Therapy
  - Rao et al CGH 2007
- Biofeedback vs Standard Therapy-One Year outcome
  - Rao et al Am J Gastroenterol 2010
- Home vs Office Biofeedback Therapy-Efficacy & Cost Effectiveness
  - Rao et al, Go et al, DDW 2011

Rao s et al. ANMS/ESNM Position paper on BiofeedbackNeuрогastro Motil 2015
Effects of Biofeedback Therapy on CSBM & Dyssynergia- ITT Analysis


Long Term Outcome of Biofeedback- CSBM/week

Rao et al Am J Gastro 2010
How useful is biofeedback in Dyssynergia + IBS

Patcharatrakul T, Gonlachanvit S. J Clin Gastro 2011;45:593-8

Pathophysiological based Treatment

Chronic Constipation

Slow Transit/Functional Constipation
Linaclotide, Lubiprostone
PEG, Laxatives

IBS-C/Normal Transit
Linaclotide, Lubiprostone
SSRI, laxatives

Dyssynergic Defecation
Biofeedback Therapy
Plecanatide, Prucalopride

Home Biofeedback

Take Home Points

- Chronic constipation involves multiple overlapping subtypes
- Detailed History, Physical Exam & DRE important
- DRE is a useful bedside clinical tool
- Dyssynergic defecation is common
- Colonic Transit, ARM, defecography, Colonic manometry are complementary & helpful
- Therapeutic options will depend on a clear understanding of pathophysiology
- Linaclotide, lubiprostone, naloxegol, PEG & Biofeedback therapy are mainstay
- Diet therapy, SSRI, antibiotics help selectively