Practical Approaches in Gastroenterology

Irritable Bowel Syndrome

Diarrhea

Constipation

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## Disclosures

<table>
<thead>
<tr>
<th>Recipient: Self or Spouse/Partner</th>
<th>Company</th>
<th>Type of Relationship**</th>
<th>Content Area (if applicable)</th>
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Agenda

- Review of Irritable Bowel Syndrome
  - Diagnosis and Management
- Clinical Approach to Diarrhea
- Clinical Approach to Constipation
Case 1

- 26 year old female assistant district attorney comes to the office complaining of 1 year of intermittent crampy lower abdominal pain along with watery diarrhea with increased frequency at times. No blood in stool or weight loss. She does have nighttime symptoms. Her family history is unremarkable except for her aunt and grandmother who have said they had problems with diarrhea is past. She has been told that she has fibromyalgia. She does have a history in the past of physical abuse as a child. Physical exam unremarkable.
Does this patient have IBS?

- A yes
- B no
What would be your plan?

- A. reassurance and PRN antidiarrheal agents
- B. referral to psychiatrist
- C. CBC, Chemistries, TFTs, LFTs, ESR, stool studies, flex sig
- D. all of the above plus CT scan, SBFT, EGD, colonoscopy, additional lab testing
Case 2

- 45 year old male television producer presents with a 20 year history of frequent bouts of diarrhea and constipation along with lower abdominal pain since he has been working for a large network. Pain is relieved with defecation and changes in bowel pattern corresponding to pain. Work is stressful and college tuition is expensive. ROS is otherwise negative. Physical exam unremarkable. He has not had a workup of this in the past.
Does this patient have IBS?

- A Yes
- B No
What would be your workup?

- A. reassurance and PRN antidiarrheal agents
- B. referral to psychiatrist
- C. CBC, Chemistries, TFTs, LFTs, ESR, stool studies, flex sig
- D. all of the above plus CT scan, SBFT, EGD, colonoscopy, additional lab testing
Irritable Bowel Syndrome (IBS)

- Definition
- Epidemiology and Pathogenesis
- Evaluation
  - diarrhea, constipation
- Management
IBS Definition- Rome IV Criteria

- In the absence of structural or metabolic abnormalities to explain symptoms:

  - recurrent abdominal pain or discomfort for at least 3 days per month – 1 day per week during the previous 3 months with symptom onset at least 6 months prior to diagnosis
IBS Definition- Rome IV Criteria

- ≥ 2 of the following:
  » Improvement with Related to defecation and/or
  » Onset associated with change in frequency of stool and/or
  » Onset associated with change in form or appearance of stool
IBS Definition - Supportive Symptoms

- Altered Stool frequency
  - >3 bm/day or <3 bm/wk
- Altered Stool form
  - Lumpy/hard or loose/watery
- Altered Stool passage (straining and/or urgency or feeling of incomplete bowel movement)
- Passage of Mucus
- Abdominal Bloating or Distention
Stool Form Correlates to Intestinal Transit Time

<table>
<thead>
<tr>
<th>SLOW TRANSIT</th>
<th>Type 1</th>
<th>Separate hard lumps, like nuts</th>
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<tbody>
<tr>
<td></td>
<td>Type 2</td>
<td>Sausage-like but lumpy</td>
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<tr>
<td></td>
<td>Type 3</td>
<td>Like a sausage but with cracks in the surface</td>
</tr>
<tr>
<td></td>
<td>Type 4</td>
<td>Like a sausage or snake, smooth and soft</td>
</tr>
<tr>
<td></td>
<td>Type 5</td>
<td>Soft blobs with clear-cut edges</td>
</tr>
<tr>
<td></td>
<td>Type 6</td>
<td>Fluffy pieces with ragged edges, a mushy stool</td>
</tr>
<tr>
<td></td>
<td>Type 7</td>
<td>Watery, no solid pieces</td>
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FAST TRANSIT

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IBS Definition - Rome IV Criteria

- Subcategories according to predominant symptom
  - of limited pathophysiological value but necessary for clinical trials
- Diarrhea Predominant: IBS-D
- Constipation Predominant: IBS-C
- Alternating Diarrhea and Constipation: IBS-A
- Mixed Diarrhea and Constipation: IBS-M
- Within 1 yr, 75% pts change subtypes and 29% switch between IBS-C and IBS-D
Irritable Bowel Syndrome

◆ Biopsychosocial Disorder
  – Psychosocial
  – Motility
  – Sensory
  – ? Infectious

◆ Disturbs QOL, Social Function, Healthcare Utilization
IBS-Epidemiology

- most common diagnosis made by gastroenterologists
- accounts for 12% of visit to primary care providers
- estimated $8 billion direct medical costs, $25 billion indirect costs annually in US
- 9 to 22% of US population afflicted but only 25% seek medical attention
IBS-Epidemiology

- those that seek care are more likely to have behavioral or psychiatric problems
  - have an increased risk for other functional disorders - non-cardiac chest pain, fibromyalgia, interstitial cystitis
  - higher prevalence of physical, emotional, sexual abuse in IBS patient population
    » not causal, felt to be an association

- female to male: 3 to 1 ratio
Make a positive diagnosis\textsuperscript{1,2}

- Abdominal pain/discomfort as dominant symptom with altered bowel function
- Look for “red flags”
- Perform diagnostic tests/physical exam to rule out organic disease
- Make/confirm diagnosis
- Initiate treatment program as part of diagnostic approach
- Follow up in 3 to 6 weeks

“Red flags” may suggest an alternative or coexisting diagnosis

Additional diagnostic screening needed for atypical presentations such as

- Evidence of GI Bleeding
- Fever
- Persistent diarrhea
- Rectal bleeding
- Severe constipation
- Weight loss

- Nocturnal symptoms of pain and abnormal bowel function
- Family history of GI cancer, inflammatory bowel disease, or celiac disease
- New onset of symptoms in patients 50+ years of age

If patient has typical features of IBS:

- If <50 years of age, order CBC, electrolytes, LFTs, TFTs, ESR, screen stool for occult blood, and consider sigmoidoscopy.\(^1\)

- If ≥50 years of age, order CBC, electrolytes, LFTs, TFTs, ESR, and perform a colonoscopy.\(^1,2\)

REFERRAL TO GASTROENTEROLOGISTS

- Alarm symptoms: weight loss, rectal bleeding
- Symptoms not responding to initial therapeutic trial e.g. failure of constipation to respond to fiber may suggest presence of an evacuation disorder or slow transit constipation
- Patient's usual symptoms "change" e.g. marked worsening of diarrhea, constipation or pain, especially if associated with alarm symptoms, or abnormal screening blood tests or colon has not been imaged for >2 years
Diarrhea

- Excess water in fecal contents, daily stool weight > 250 grams
- Secretory-excessive secretion of electrolytes by intestinal villi
- Osmotic-decreased absorption of an ingested solute
  - disappears with fasting
- Stool Osmotic Gap: 290-2(Na + K) > 50 mmol
- most cases have component of both secretory and osmotic
Diarrhea: Acute- < 1 month

- should be evaluated for evidence of inflammation
  - fever, increased leukocyte count, bandemia, RBC/WBCs in stool

- Inflammatory-invasive, usually colonic, may require hospitalization, and antibiotic therapy

- Non-inflammatory- usually small bowel, usually milder and of shorter duration, managed by fluids alone

- acquired in hospital is usually iatrogenic
Diarrhea: Chronic- > 1 month

- rarely due to infection.
- Is there evidence of malabsorption?
  - weight loss, muscle wasting, anemia, excessive flatus, low albumin, calcium, iron, folate, carotene, cholesterol
- Is there evidence of inflammation?
  - fevers, pain, weight loss, leukocytosis, increased ESR, bloody diarrhea, anemia, low albumin
- Are there risk factors?
  - travel, drugs, dietetic foods and chewing gum (sorbitol), AIDS, vascular disease, radiation, dairy products, surgery, endocrinopathies
Diarrhea: Evaluation

- history, physical exam, screening labs
- stool studies: occult blood, fecal leukocytes, culture, ova and parasites, C difficile culture and toxin
  - 20 to 40% of acute diarrhea still remains undiagnosed
- trial of lactose free diet
- empiric trial of metronidazole for Giardia
- flexible sigmoidoscopy with biopsies
Diarrhea: Evaluation

- quantitative (48 to 72 hour) stool collection
  - weight, fat, electrolytes, osmolality
  - weight <200 mg/dl, non-liquid is normal
  - if steatorrhea present (Sudan stain), fat malabsorption workup
    » pancreatic versus small bowel disease
  - secretory vs osmotic diarrhea
Diarrhea Evaluation

◆ Gastrointestinal Imaging
  – small bowel series
  – Abdominal CT scan for extra-luminal causes-pancreas

◆ Breath testing-Lactulose
  – Bacterial Overgrowth
  – Empiric treatment
    » Flagyl, tetracycline
    » Rifaximin- 200mg TID for 3 days for traveler’s diarrhea
## Exclude Only If Suspect

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Test</th>
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<tbody>
<tr>
<td>Lactose intolerance</td>
<td>Restriction trial, breath test</td>
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<tr>
<td>Giardiasis</td>
<td>Stool study</td>
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<tr>
<td><strong>Celiac sprue</strong></td>
<td>Anti-endomysial antibody</td>
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<td>History</td>
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<td>Bowel malignancy</td>
<td>Colonoscopy/BAE</td>
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<tr>
<td>IBD/microscopic colitis</td>
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<tr>
<td>Thyroid disorder</td>
<td>TSH</td>
</tr>
<tr>
<td>Carcinoid tumor</td>
<td>Urine 5-HIAA</td>
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</tbody>
</table>
Constipation

- according to population surveys, frequency of defecation of 2x week or less

- Slow Transit Constipation- prolonged transit of stool from ceacum to rectum
  - “does not get the urge to defecate for prolonged period of time”

- Functional Outlet Obstruction- difficulty with defecation
  - “gets the urge to defecate normally, but has difficulty expelling the stool”
Constipation- Etiologies

◆ Mechanical Colonic Obstruction
  – colorectal cancer, benign causes: strictures, ischemia, inflammatory bowel disease

◆ Metabolic and Endocrine Disorders
  – diabetes, pregnancy, hypothyroidism

◆ Neuropathic Disorders
  – spinal lesions, Hirshprung’s Disease

◆ Myopathics Disorders
  – myotonic dystrophy, amyloidosis, scleroderma, systemic lupus erythematosis
Constipation - Etiologies

◆ Medications
  - Anticholinergicis
    » antispasmodics, tricyclic antidepressants, antipsychotics, anti-parkinsonian medications
  - Cation containing agents
    » iron, aluminum, antacids, calcium, barium, heavy metals
  - Agents which inhibit neural function
    » opiates, certain antihypertensives, ganglionic blockers, vinca alkaloids, anticonvulsants, calcium channel blockers
Classification of Primary Constipation

Slow Transit

Outlet Obstruction

IBS-C

Current management of IBS

◆ Establish a positive diagnosis\(^1\)

◆ Reassure patient that there is no serious organic disease or alarming symptoms\(^1\)

◆ Success of current treatment options in addressing multiple symptoms of IBS has been limited\(^2\)

Current management components of IBS

- Education
- Reassurance
- Dietary modification
- Fiber
- Symptomatic treatment
- Psychological/behavioral options
- Realistic goals

IBS Tx: Comprehensive Multicomponent Approach

Treatment program is based on dominant symptoms and their severity and on psychosocial factors

◆ Medical management

◆ Diet: Food Allergies and FOD Map Diets
  -- increasing evidence of food intolerance
  -- avoiding gluten and fructose

◆ Psychological or behavioral options
  – psychotherapy
  – stress management

Symptomatic Medical Therapy - IBS

- Anticholinergic/Antispasmodics
  - TCAs
  - SSRIs
  - serotonin agents

- Promotility

- Pain
- Bloating

- Antispasmodics
  - Antiflatulents
  - Promotility

CONSTIPATION
- Misoprostol
- Osmotic agents
  - Lactulose
  - 70% sorbitol
  - PEG solution
  - serotonin agonists
  - lubiprostone

DIARRHEA
- Loperamide
- Cholestyramine
- Opioids
- serotonin antagonists
- anticholinergics
Multiple medications needed to treat multiple symptoms

<table>
<thead>
<tr>
<th></th>
<th>Lower abdominal pain</th>
<th>Bloating</th>
<th>Altered stool form</th>
<th>Altered stool passage</th>
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Medical Treatment

- Effective patient/physician relationship, patient education/reassurance paramount
- Most drugs can help with associated diarrhea or constipation related symptoms but pain as an endpoint has been more difficult to treat
- Concerns about trial evidence: placebo effect, duration of trial, properly measured endpoints
- Psychotherapy, hypnosis, biofeedback, mind-body programs starting to show benefits but requires further evaluation
Medical Treatment

◆ Bulking Agents - psyllium and bran
  - majority of trials show no significant benefit for IBS specific symptoms
  - helps with constipation
  - Significant amounts can cause worsening of bloating

◆ Prokinetic Agents - cisapride, domperidome
  - evidence not support cisapride in constipation predominant IBS
  - inconclusive with domperidome
Medical Treatment

- Smooth Muscle Relaxants
  - agents tested in high quality trials are not based available in US
  - majority showed a significant improvement in abdominal pain but not the ones available in US
    » hyoscomine, belladona, dicyclomine, and combinations have not studied in well designed controlled studies
  - anticholinergic side effects were similar in drug and placebo in most trials
  - Constipation as a side effect
Medical Treatment

- Loperamide - antidiarrheal
  - helpful for diarrhea
  - inconclusive for abdominal pain and distention

- Psychotropic Agents - tricyclics, SSRIs
  - shows some benefit in overall symptoms and impact of psychiatric disturbance is unclear
  - TCAs: constipating  SSRIs: diarrhea
  - amitryptilline high quality study showed only a trend towards global improvement, not individual symptoms
Medical Treatments

- Probiotics, Bacterial Overgrowth, Gut Microbiome
  - Concept that there is a imbalance in gut milieu
  - Need to restore balance
- Not a single probiotic agent but a cocktail
  - Lactobacillus acidophilus
  - Bifidobacteria infantis
  - VSL#3
- Variation in results but may have benefit in cases
- Fecal Transplant indicated for C Diff multiple cases
  - not IBD or IBS as yet
Bacterial Overgrowth

- Testing - Imperfect
  - Breath Testing - Hydrogen, Lactulose
  - Small bowel Aspirate
  - Empirical treatment

- Rifaxmin - Non-absorbable Antibiotic
  - 550 mg TID for 2 weeks
  - Adequate relief after 4 weeks 40% vs 30%
  - NNT 1 to 10

- metronidazole, tetracycline, ciprofloxin
  - alternating, short duration - 1 week, 3 weeks off
Medical Treatment

- Serotonin Agents—promise but now restricted access
  - 5HT₃ Antagonists: Alosetron for diarrhea predominant IBS
    » trials to suggest benefit in decreased stool frequency, prolonged transit, and decreased pain in women
    » Alosetron available under tight restrictions due to concerns about constipation and ischemic colitis
  - 5HT₄ Partial Agonists: Tegaserod
    » Benefit in constipation and constipation predominant IBS
    » Restricted due to cardiac events in aggregate clinical trials
  - Has potential but not available clinically now until further notice, risk/benefit profile being evaluated with other compounds in development
Medical Treatment - Lubiprostone

- Chloride Channel Modulator in Gut (ClC2)
  - Bicyclic fatty acid
- Not absorbed, local luminal effects causing secretion of fluid into lumen
- Chronic Constipation 24 mcg BID
- IBS-C 8mcg BID in women
- SE: Nausea ameliorated when taken with food
- Helps with bloating
Medical Treatment - Linaclotide

- Guanylate cyclase peptide agonist
  - Chloride channel activator increasing intestinal fluid secretion

- Chronic Constipation - 72 mcg qD
- Chronic Constipation - 145 mcg qD on empty stomach
  - 20% drug vs 6% placebo, increased BMs

- IBS-C - 290 mcg qD
  - Decrease of pain and global symptoms

- SE: diarrhea
Medical Treatment-Plecanetide

- Guanylate cyclase peptide agonist
  - Chloride channel activator increasing intestinal fluid secretion
- Chronic Constipation- 3 mg qD
- Complete Spontaneous Bowel Movements (CSBM)
  - 21% vs 10.2% placebo, p<0.001
- SE: diarrhea
IBS: CURRENT MANAGEMENT

- Positive Diagnosis by Symptoms
- Limited Investigations Exclude ORGANIC Disease + Evacuation Disorders
- Current Therapy for Predominant Symptom: Important Role for the *Therapeutic Trial* (with Effective Rx) in Reducing Costs