What is new in functional GI Disorders?

Maria Ines Pinto-Sanchez

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1. FGIDs are the most common diagnoses in gastroenterology

2. Recognized by morphologic and physiological abnormalities that often occur in combination
   - motility disturbance
   - visceral hypersensitivity
   - altered mucosal and immune function
   - altered gut microbiota
   - altered central nervous system processing

FGIDs: Disorders of the gut-brain interaction

Drossman D, Gastroenterology 2016;150:1262–1279
FGIDs

- IBS
- Functional Dyspepsia
Key news out of DDW 2017

Explore the Functional GI and Motility Disorders Track

1. Mechanism
2. Diagnosis
3. Treatment

F. dyspepsia
IBS
# Changes in FD diagnosis

|----------------|-------------------|-----------------------------|--------------|---------------|--------------------------|
| **Main Criteria** | Chronic or recurrent pain or discomfort centered in the upper abdomen. | Chronic or recurrent pain or discomfort centered in the upper abdomen or retrosternal pain, discomfort, heartburn, nausea, vomiting, or other symptom from the GI tract. | Pain or discomfort centered in the upper abdomen with no evidence of organic disease. | *Persistent or recurrent symptoms (pain or discomfort centered in the upper abdomen); AND*  
* No evidence that dyspepsia is exclusively relieved by defecation or associated with the onset of a change in stool frequency or stool form. (exclude IBS and reflux) | One or more symptoms needs to be present  
a. Bothersome postprandial fullness  
b. Early satiation  
c. Epigastric pain  
d. Epigastric burning |
| **Normal Upper endoscopy** | Required | Required | Required | Required | Required |
| **Symptoms** | At least 3 months | At least 4 weeks | - | 12 weeks which need not be consecutive | Criteria fulfilled for the last 3 months |
| **Onset of symptoms** | - | - | - | 12 | 6 |
| **Subtypes** | - | Reflux like dyspepsia | 1. Ulcer-like dyspepsia  
2. Dysmotility(stasis)-like dyspepsia  
3. Reflux-like dyspepsia | 1. Ulcer-like dyspepsia  
2. Dysmotility-like dyspepsia | 1. Postprandial distress syndrome (PPD)  
2. Epigastric pain syndrome |

**Rome IV: PDS postprandial epigastric pain or burning, bloating, belching and nausea.**
Aim: to explore the impact of Rome IV on FD subgroups in a secondary care cohort.

- Ambulatory FD patients (Rome III); 8 secondary care Belgium
- Subgroups: PDS, EPS and overlap PDS-EPS subgroups
- The definition of PDS was adapted to the Rome IV consensus,

<table>
<thead>
<tr>
<th></th>
<th>Rome III</th>
<th>Rome IV</th>
</tr>
</thead>
<tbody>
<tr>
<td>PDS</td>
<td>31%</td>
<td>69%</td>
</tr>
<tr>
<td>EPS</td>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>PDS/EPS</td>
<td>62%</td>
<td>25%</td>
</tr>
</tbody>
</table>

Rome IV considers postprandial epigastric pain as a PDS symptom

Implementation of the Rome IV the PDS-EPS overlap group is dramatically reduced.
F. Dyspepsia: Diagnosis

ANALYSIS OF POSTPRANDIAL SYMPTOM PATTERNS IN ROME III AND ROME IV SUBGROUPS OF FUNCTIONAL DYSPEPSIA PATIENTS (Sa 1611)

AuthorBlock: Tim Vanuytsel, Jan F. Tack

Gastroenterology, University of Leuven, Leuven, Belgium; Gastroenterology, University Hospital Leuven, Leuven, Belgium;

- Gastric emptying breath test: intensity of dyspeptic symptoms (fullness, bloating, belching, nausea, epigastric pain and burning) scored before and after a standardized meal (250 kCal) for 240 min.
- Correlation reported symptoms in the Rome questionnaire and their severity during the breath test

- Rome III
  - PDS 30%
  - Symptoms aggravated after meal 79%
    - Epig pain in 28%
- Rome IV
  - PDS+EPS 61%
  - Symptoms aggravated after meal 72%
    - Epig pain in 71%
  - PDS+EPS 18%
  - Fullness, epig burning and nausea aggravated after meal

Rome IV identifies subgroups with more homogeneous meal-related symptom profiles.
Table 1. Pharmacological Treatment Options for Functional Dyspepsia Based on Double-Blind Randomized Placebo-Controlled Trials

<table>
<thead>
<tr>
<th>Level of evidence</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Helicobacter pylori</em> eradication (level 1)</td>
<td>First line therapy in infected</td>
</tr>
<tr>
<td>Acid suppression (level 1)</td>
<td></td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>First line therapy especially for epigastric pain</td>
</tr>
<tr>
<td><em>H₂</em> receptor antagonists</td>
<td></td>
</tr>
<tr>
<td>Prokinetic (level 1–2)</td>
<td></td>
</tr>
<tr>
<td>Cisapride</td>
<td>Cisapride withdrawn</td>
</tr>
<tr>
<td>Acotiamide</td>
<td>Available in Japan</td>
</tr>
<tr>
<td>Itopride</td>
<td>Mixed data</td>
</tr>
<tr>
<td>Centrally acting drugs (level 1–2)</td>
<td></td>
</tr>
<tr>
<td>Tricyclic low dose (level 1)</td>
<td>Epigastric pain improved</td>
</tr>
<tr>
<td>Mirtazapine (level 2)</td>
<td>Efficacy not established</td>
</tr>
<tr>
<td>Buspirone (level 2)</td>
<td>Postprandial distress syndrome improved</td>
</tr>
<tr>
<td>Miscellaneous therapy</td>
<td></td>
</tr>
<tr>
<td>Iberogast (level 2)</td>
<td>Relaxes the gastric fundus</td>
</tr>
<tr>
<td>Montelukast</td>
<td>One small pediatric trial</td>
</tr>
<tr>
<td>Not efficacious</td>
<td></td>
</tr>
<tr>
<td>Selective serotonin reuptake inhibitors</td>
<td></td>
</tr>
<tr>
<td>Selective norepinephrine reuptake inhibitors</td>
<td></td>
</tr>
<tr>
<td>Antacids</td>
<td></td>
</tr>
<tr>
<td>Sucralfate</td>
<td></td>
</tr>
<tr>
<td>Bismuth</td>
<td></td>
</tr>
<tr>
<td>Mosapride</td>
<td></td>
</tr>
</tbody>
</table>

Dietary advise may help some patients, although RCTs are lacking

Talley NJ, Gut Liver 2017
Are PPIs an option in FD?

✓ 23 RCTs from 22 papers (with 8759 participants)

PPI vs other treatments relieving overall dyspepsia symptoms in FD

1. More effective than placebo (NNT=10)
2. Possibly slightly more effective than H2RAs and prokinetics
3. PPIs plus prokinetics possibly slightly more effective than PPIs alone

✓ No difference subgroup: dose, H pylori status, country of origin, presence of reflux or Rome III subtypes.

#CAREATDDW
F. Dyspepsia: Treatment

ACOTIAMIDE IN COMBINATION WITH A STANDARD DOSE OF RABEPRAZOLE VERSUS DOUBLE-DOSE RABEPRAZOLE FOR SYMPTOM RELIEF IN PATIENTS WITH THE OVERLAP BETWEEN PPI-RESISTANT GERD AND FD: A PROSPECTIVE, MULTICENTER, RANDOMIZED STUDY (Sa 1601)

Author Block: Shinpei Kawaguchi, Yoshiaki Takahashi, Kazuhiro Ota, Satoshi Harada, Yuichi Kojima, Kazunari Tominaga, Kazuhide Higuchi

1 Second Department of Internal Medicine, Osaka Medical Collage, Takatsuki, Japan;

ACh, acetylcholine; AChE, acetylcholinesterase; M1R, muscarinic acetylcholine receptor m1; M2R, muscarinic acetylcholine receptor m2.

Methods: prospective, multicenter, randomized study

- GERD refractory to a standard dose of PPI (>8wks) with overlapped dyspepsia were randomized into two groups: 1) acotiamide 300 mg/day + rabeprazole 10 mg/day or 2) rabeprazole 20 mg/day for 4 weeks.
- Efficacy was assessed by ≥50% reductions in symptom scores using the Izumo scale and modified F-scale questionnaires.

Results:

- 99 patients; acotiamide 300 mg/day + rabeprazole 10 mg/day (n = 49) or rabeprazole 20 mg/day (n = 49).
- Reduction of symptoms: 49 vs 40%; no significant difference between the groups in overall symptoms or three epigastric symptoms (stomach pain, hunger stomach pain, and epigastric burning).

The combination therapy may be an alternative option for long-term treatment of these patients, which may reduce side effects associated to PPIs.
To evaluate the efficacy and safety of once-daily mosapride (UI05MSP015CT) in patients with functional dyspepsia.

Methods:

- Patients with functional dyspepsia were randomly assigned (1:1) to receive either UI05MSP015CT (Mosapride 15 mg once daily before breakfast) vs mosapride (5mg t.i.d before each meal, vs placebo t.i.d. or od. x 4 weeks).

- Endpoint: change of gastrointestinal symptom score (GSS) at 4 weeks.

Results:

- Mean difference GSS was ITT=0.33 (95% CI -1.75, 2.41); PP= 0.24 (95% CI - 1.88, 2.35) demonstrating non-inferiority of UI05MSP015CT (p = 0.755/0.824)
- No difference in overall AEs

Once-daily mosapride (UI05MSP015CT) is not inferior to the conventional mosapride in the efficacy and is safe in patients with functional dyspepsia.
F. Dyspepsia: Other options

RANDOMIZED CONTROLLED TRIAL TO ASSESS THE EFFICACY & SAFETY OF CARAWAY OIL/L-MENTHOL PLUS USUAL CARE POLYPHARMACY VS. PLACEBO PLUS USUAL CARE POLYPHARMACY FOR FD (Sa 1618)

AuthorBlock: Brian E. Lacy, Brooks D. Cash, Michael Epstein, Syed M. Shah

1Division of Gastroenterology, University of South Alabama, Mobile, Alabama, United States; 2Section of Gastroenterology & Hepatology, Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire, United States; 3Digestive Disorders Associates, Annapolis, Maryland, United States; 4IM HealthScience, Boca Raton, Florida, United States;

✓ FD (Rome III) and moderate symptoms (≥ 4 points on Global Overall Symptom [GOS] scale) on ≥ 4 days

✓ Treatment: Two capsules COLM (25 mg of caraway oil and 20.75 mg of L-menthol) vs matching placebo 30 to 60 minutes before a meal b.i.d x28 days

✓ Patient continue existing FD medication regimen (PPIs, H2RAs, anticonvulsants, beta blockers, antihistamines, antidepressants/TCAs, pain modulators, and antacids)

Results:

✓ At end of treatment, 61% of patients given COLM reported improved assessment of CGI compared to 49% in the control group (P=0.23; n=100)

COLM is safe and effective at improving FD symptoms in patients already using commonly available medications for functional dyspepsia.
Food in F. Dyspepsia

1. **FOOD AND FUNCTIONAL DYSPEPSIA: A SYSTEMATIC REVIEW (Sa 1606)**
   - **AuthorBlock:** Kerith Duncanson¹, Tracy Burrows¹, Nicholas J. Talley¹
   - ¹University of Newcastle, Callaghan, New South Wales, Australia;
   - 16 studies of moderate quality; 6 of wheat containing food in FD, and 2 of them involving GFD
   - Wheat ingestion was related to both post prandial distress and epigastric pain symptoms of FD.

2. **INFLUENCE OF GLUTEN INTAKE ON FUNCTIONAL DYSPEPSIA: A CASE-CONTROL STUDY (Sa 1603)**
   - **AuthorBlock:** Jinhua Shen¹, Ning Dai¹
   - ¹Gastroenterology, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou, Zhejiang, China;
   - 101 FD and 30 healthy controls; questionnaires, duodenal biopsy and TJ
   - FD had higher consumption of gluten containing food compared with HC, and gluten consumption was directly correlated with early satiety (p=0.03)
   - FD showed increased IELs and decreased expression of Claudin 1 in duodenum compared to HC

3. **GFD IMPROVES UPPER GI SYMPTOMS AND PROMOTES CHANGES IN GASTRIC EMPTYING IN IBS PATIENTS WITH FUNCTIONAL DYSPEPSIA (Tu 1683)**
   - **AuthorBlock:** MI Pinto Sanchez¹,², N Causada Calo, A Nardelli¹,², R Boroevic¹,², DArmstrong¹,², PMoayyed¹,², SM Collins¹,², EF Verdu¹,², P Bercik¹,²
   - ¹Medicine, McMaster University, Hamilton, Ontario, Canada; ²Farncombe Institute, Hamilton, Ontario, Canada;
   - 22 IBS+FD and 24 healthy controls; questionnaires and gastric emptying (VF)
   - Significant change in gastric emptying in the subset of patients with FD and early satiety (25.4% vs. 7.12%, P=0.03)

#CAREATDDW
Key news out of DDW 2017

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F. dyspepsia

IBS
Mechanisms of IBS

Enk P, Nature reviews 2016 (Adapted)
Dietary triggers in IBS

- Gluten free
- Low FODMAPs

Source: Ford AC, BMJ Clinical Evidence 2015
Low FODMAPs diet in IBS

LFD diet has gained much attention, and information is easily accessible

<table>
<thead>
<tr>
<th>Author</th>
<th>Journal</th>
<th>Clear eligibility criteria</th>
<th>RCTS eligible</th>
<th>Meta-analysis performed</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Moayyedi 2015</td>
<td>Clin Transl Gastroenterol</td>
<td>Yes</td>
<td>1</td>
<td>Not possible</td>
<td>Uncertain benefit</td>
</tr>
<tr>
<td>Rao 2015</td>
<td>Al Phar Ther</td>
<td>Yes</td>
<td>4</td>
<td>Not possible</td>
<td>Uncertain benefit</td>
</tr>
<tr>
<td>Marsh 2015</td>
<td>Eur J Nutr</td>
<td>No</td>
<td>6</td>
<td>Conducted</td>
<td>Effective</td>
</tr>
<tr>
<td>Krogsgaard 2017</td>
<td>Al Phar Ther</td>
<td>Yes</td>
<td>9</td>
<td>Not conducted</td>
<td>Uncertain benefit</td>
</tr>
</tbody>
</table>

- The recommendation of the low FODMAP diet as a first-line treatment for patients with IBS is based on trials with high risk of bias, primarily due to lack of proper blinding and choice of control group.
- All trials in tertiary care; there is a need of studies in other clinical settings
- No RCT intervention more than 6 weeks, and the effect of the reintroduction period are lacking.

More DBPC RCTs are needed
Mechanisms of LFD in IBS

The mechanisms responsible for symptom benefit of LFD in a proportion of IBS patients are not clear.

Serum levels of 7-α-hydroxy-4-cholesten-3-one (7C4) reflect hepatic bile acid synthesis and are elevated in patients with BAM.

Hypothesis: LFD might alter bile acid metabolism - mechanism for symptom benefit in IBS patients.

This is a post-hoc analysis from a prospective, single-blind randomized controlled trial of adult patients with IBS-D (Rome III) who were randomized to 4-weeks of a LFD or a diet based upon modified NICE (mNICE) guidelines.

Results

The LFD but not the mNICE diet led to significant reductions in serum 7C4 levels; LFD may reduce bile acid malabsorption in IBS-D patients.

These results provide a novel mechanism by which the LFD benefits abdominal pain in IBS patients.

Potential biomarker to predict clinical response to the LFD?
Mechanisms of LFD in IBS

TRYPHTOHAN HYDROXYLASE 1 (TPH1) PROMOTER GENOTYPE BUT NOT SERUM SEROTONIN LEVELS IDENTIFY IBS-D PATIENTS MORE LIKELY TO BENEFIT FROM THE LOW FODMAP DIET

AuthorBlock: Juanita L. Merchant¹, Amanda Photenhauer¹, Kenya Jackson¹, Dennis Madriaga², Fabiyola M. Selvaraj², Fred Princen², William D. Chey¹
¹University of Michigan, Ann Arbor, Michigan, United States; ²Prometheus Diagnostic, Inc, San Diego, California, United States;

 ✓ Tryptophan hydroxylase 1 (TPH1) is the rate-limiting enzyme in enterochromaffin cell 5-HT biosynthesis
 ✓ SNP in the proximal promoter of the TPH1 gene is associated with IBS patients with diarrhea-predominant IBS (IBS-D)
 ✓ Post hoc analysis of previous single blind study IBS–D randomized to LFD or mNICE x 4 weeks
 ✓ All patients provided buccal swabs for DNA extraction, PCR amplification of SNP (rs7130929) and Sanger sequencing.
 ✓ Serum serotonin levels were measured before and after the 4-week dietary intervention and the between-group differences from baseline were compared

Results:
 ✓ 92 randomized; 83 completed the study (45 LFD, 38 mNICE)
 ✓ CC or CA genotype randomized to LFD were more likely to have reductions in abdominal pain vs mNICE diet CCC genotype was associated with Improvements in bloating in the LFD vs mNICE diet

The TPH1 proximal promoter SNP correlated with greater relief of pain and bloating after 4 weeks of a low FODMAP diet and could serve as potential marker
Response to LFD in IBS

ORAL α-GALACTOSIDASE IMPROVES GASTROINTESTINAL TOLERANCE TO A DIET HIGH IN GALACTO-OLIGOSACCHARIDES: ADJUNCT THERAPY TO A LOW FODMAP DIET IN IRRITABLE BOWEL SYNDROME

AuthorBlock: Kirstin M. Taylor², Jacqueline Barrett¹, Peter R. Gibson¹, Jane Muir¹
¹Department of Gastroenterology, Monash University, Melbourne, Victoria, Australia; ²Alfred Health, Melbourne, Victoria, Australia;

- Galacto-oligosaccharides (GOS) are indigestible short-chain carbohydrates (FODMAPs) associated with triggering gastrointestinal symptoms in IBS
- DBPC trial to assess whether oral α-galactosidase co-ingestion with foods high in GOS and low in other FODMAPs would reduce symptoms and breath hydrogen production
- 3 arms: full-dose enzyme (300 GALU α-galactosidase), half-dose (150 GALU α-galactosidase) and placebo (glucose).

Results:
- 21/31 patients exhibiting GOS-sensitivity (>10mm increase for overall symptoms)
- Full-dose enzyme reduced overall symptoms (median 24.5 [IQR 17.5-35.8] mm vs 5.5 (1.5-15.0) mm; p=0.006) and bloating (20.5 [9.5-42.0] vs 6.5 [2.0-15.8]; p=0.017).
- Breath hydrogen production was minimal with no differences seen between placebo and full-dose

- Oral α-galactosidase taken with high GOS foods improve significantly symptoms in GOS-sensitive individuals with IBS.
- The mechanism may not be related to reduced hydrogen production.
# Response to GFD in IBS

## Table 2. Clinical Trials on Gluten Challenge or Gluten-free Diet in Patients with Irritable Bowel Syndrome

<table>
<thead>
<tr>
<th>Supportive</th>
<th>Not supportive</th>
</tr>
</thead>
</table>
| Gluten challenge causes symptoms in IBS  
  Biesiekierski et al, 2011<sup>48</sup>  
  Di Sabatino et al, 2015<sup>54a</sup>  
  Zanini et al, 2015<sup>55a</sup>  
  Elli et al, 2016<sup>56</sup>  
  IBS + celiac genes respond to GFD  
  Wahnschaffe et al, 2007<sup>47</sup>  
  Vazquez-Roque et al, 2013<sup>52</sup>  
  Wheat challenge triggers symptoms in IBS  
  Carroccio et al, 2012<sup>50</sup> | No dose response to low/high gluten in IBS  
  Biesiekierski et al, 2013<sup>31</sup> |

- A proportion of IBS patients will benefit from a GFD
- Which patient should try a GFD and how strict should be?
Response to GFD in IBS

ANTIGLIADIN ANTIBODIES PREDICT THE SYMPTOMATIC RESPONSE TO GFD AND IMPROVEMENT IN GASTROINTESTINAL MOTILITY IN IBS PATIENTS

To evaluate the predictors of symptomatic response to the GFD in unselected IBS patients.

- 45 IBS and 24 HV; 53% of IBS patients and 25% of HV had positive AGA either IgA or IgG.
- Overall GI symptoms, constipation (P=0.01), diarrhea (P=0.001) and abdominal pain (P<0.001) improved after GFD in the IBSAGA+ patients while only pain improved in IBSAGA- patients (P=0.01).
- After GFD, IBSAGA+ were more likely to have normal transit compared to IBS AGA- (OR 1.75; 95%CI 1.06-3.06; p=0.04).
- The presence of AGA, but not other factors including changes in motility, GFD adherence or genetic risk, was associated with symptomatic response to the GFD (OR 8.54; 95%CI 1.41-48.21; P=0.01).

- Anti-gliadin antibodies can be used as a biomarker to identify IBS patients that are more likely to respond, symptomatically and functionally, to the gluten-free diet.
- Strict compliance with the GFD does not predict clinical improvement, suggesting that gluten restriction rather than strict gluten avoidance may be sufficient for symptoms management in IBS patients.

AuthorBlock: Maria Ines Pinto Sanchez Andrea Nardelli1,2, Rajka Borojevic1,2, Natalia Causada Calo1,2, Justin McCarville1,2, Kyle Samuels2, Melanie Uhde3, Suzanne Hansen1, Edgardo Smecuol4, David Armstrong1,2, Paul Moayyedi1,2, Armin Alaedin3, Stephen M. Collins1,2, Julio C. Bar4, Elena Francisca Verdu1,2, Premysl Bercik1,2

1Medicine, McMaster University, Hamilton, Ontario, Canada; 2Farncombe Institute, Hamilton, Ontario, Canada; 3Medicine, Columbia University, New York, New York, United States; 4Medicine, Hospital Dr. C.B.Udaondo, Buenos Aires, Buenos Aires, Argentina;
Mechanisms of IBS

- Low-grade inflammation
- Intestinal barrier
- Infection
- Dysbiosis
- Visceral hypersensitivity
- Neuromotor dysfunction

Brain activation and neuroendocrine modulation

Appraisal, emotion, coping and social support

Brain-gut axis

Genetics and epigenetics

External stressors (psychosocial factors)

Internal stressors (food and microorganisms)

Gastrointestinal and extra-gastrointestinal manifestations

Enk P, Nature reviews 2016 (Adapted)
Fecal Microbiota Transplantation (FMT) is suggested as a potential effective treatment in IBS patients. This is the first double-blinded placebo-controlled clinical trial on FMT in IBS patients (clinicaltrials.gov NCT02092402). 16 IBS patients were included; 8 patients received donor feces material (treatment) and 8 received their own feces material (placebo) in the cecum.

Results:
- The GSRS-IBS total score significantly decreased for both the treatment and the placebo group 2 weeks after FMT and 4 weeks after FMT compared to baseline (-0.46 ± 0.32, p<0.01, and -0.71 ± 0.73, p<0.05, respectively).
- The IBS-QoL total score was significantly increased in the treatment but not in the placebo group at 8 weeks (10.0 ± 6.3, p<0.01).
- The bowel cleansing and the processing of the autologous fecal material might have contributed to the placebo effect.
- Further analysis on individual basis, separation into non-responders and responders as well as correlation with additional outcomes such as microbiota composition will provide more insight.
Mechanisms of IBS

- Low-grade inflammation
- Intestinal barrier
- Infection
- Dysbiosis
- Visceral hypersensitivity
- Neuromotor dysfunction
- Gut activation and neuroendocrine modulation
- Brain-gut axis
- Stress response
- Impaired QOL
- Gastrointestinal and extra-gastrointestinal manifestations

Increased abdominal pain perception or visceral hypersensitivity (VHS) is the hallmark of IBS.

Previous studies showed histamine-1-receptor (Hrh1)-mediated sensitization of TRPV1, TRPA1 and TRPV4 in patients with IBS.

To evaluate 1) the prevalence of TRP channel sensitization and its correlation with symptoms in IBS compared to HV; 2) the effect of treatment with the Hrh1 antagonist ebastine on TRP channel sensitization and symptom scores in IBS patients.

Results:

- Sensitization of TRPV1, TRPA1 or TRPV4 was significantly more prevalent in rectal submucosal neurons of IBS patients compared to those of HV.
- Ebastine improved IBS symptoms resulting in 63% pain responders (>30% reduction in pain score).

Sensitization of submucosal neurons could be an interesting biomarker.

Pronociceptive changes in the gut wall involving Hrh1 receptors represent a major pathophysiological mechanism in IBS and thus an interesting target for treatment.
Linaclotide is an oral guanylate cyclase-C receptor antagonist, FDA- and EMA-approved for treatment of moderate to severe IBS-C in adults.

Open-label Phase 3b study of linaclotide in adults diagnosed with moderate to severe IBS-C based on Rome III criteria and an IBS symptom severity (IBSSS) score of >175.

Eligible patients received linaclotide 290 µg once daily for 12 weeks.

Digestive non-intestinal and extra-digestive symptom scores were significantly improved by Weeks 4 and 12. The most common adverse event was diarrhea (n=39; 21%).

Linaclotide relieves intestinal, non-intestinal, and extra-digestive symptoms in patients with clinically relevant IBS-C.

<table>
<thead>
<tr>
<th>Mean score (± SD)</th>
<th>Baseline (Week 0)</th>
<th>Week 4</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Digestive non-intestinal symptomsa</td>
<td>8.65 (3.95)</td>
<td>7.76 (3.55)*</td>
<td>6.81 (3.60)**</td>
</tr>
<tr>
<td>Extra-digestive symptomsb</td>
<td>3.38 (2.47)</td>
<td>2.78 (2.23)*</td>
<td>2.16 (1.97)**</td>
</tr>
</tbody>
</table>
Canadian experience in IBS

IRRITABLE BOWEL SYNDROME PATIENT EXPERIENCE IN CANADA

To learn how IBS affects patients in Canada, the Gastrointestinal Society hosted a survey on its English (www.badgut.org) and French (www.mauxdeventre.org) websites during spring 2016.

Questions on symptom severity, medication use, experience with the health care system, comorbidities, and quality of life.

Results

- 2961 respondents; 53% had IBS for more than 10 years.
- 35% had IBS-D, 18% IBS-C, 41% IBS-M, and 6% unsure. In IBS-C patients, abdominal pain was identified as a distinct predominant symptom; 60% had a colonoscopy and 12% have been hospitalized for IBS.
- 76% indicated that their symptoms interfere with everyday life and 46% missed work or school due to IBS.
- Most IBS patients use ≥2 medications on a regular basis to control their symptoms yet only 21% are confident their symptoms are under control.
- 16% are unable to afford any of their prescribed medications, and 26% can only afford some of them.

We need a different approach to improve symptoms control in our IBS patients
A pilot project REDUCE IBS was designed to study the outcome of a novel management strategy for IBS patients in 13 gastroenterology clinics. Patients received 10 electronic handouts with possible therapies: 1) broad IBS information 2) elimination diet 3) FODMAP-restricted diet 4) probiotics 5) hypnotherapy 6) antibiotics 7) peppermint oil 8) spasmolytics 9) amitriptyline 10) citalopram.

Patients were asked to study the therapies and to choose the 3 most valued options. Two weeks later a gastroenterologist and nurse saw the patient together. The preferred therapy choices were peppermint oil (51%) probiotics (49%) low-FODMAP diet (46%) hypnotherapy (36%) and elimination diet (27%).

Patients greatly appreciated the well-informed choice of 10 therapy options (score 7.7), the personal care of specialist nurses (7.6), the possibility of shared decision-making (7.6) and the improvement as opposed to traditional treatment (6.8).

Time spent by gastroenterologists was reduced from a calculated average patient contact time of 45 minutes per IBS-patient to a standard consultation time in the pilot of 10 minutes.

Individual approach on potential therapies in IBS may improve patient outcomes
Take home messages FGIDs

- The diagnosis criteria has been changing with time
- We are still learning about the pathophysiology
- None of the current therapeutic options are effective for all patients; personalized treatment may be an option
- Diet may have a role, but the quality of evidence is low
- Continue working in research!
Thank you!
Enjoy DDW and Chicago.