Controversies in the stomach

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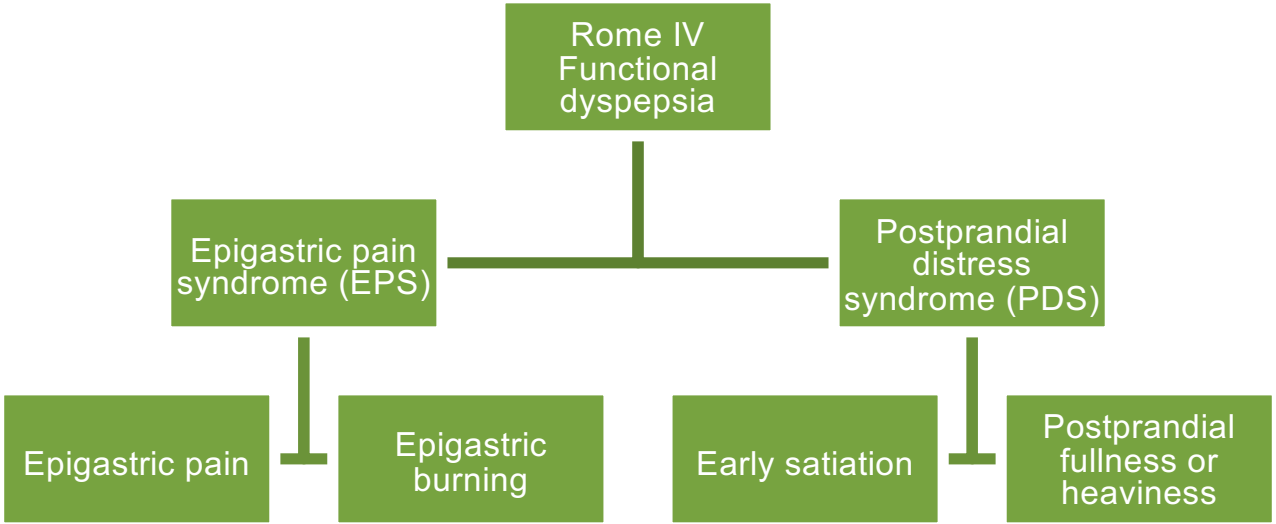
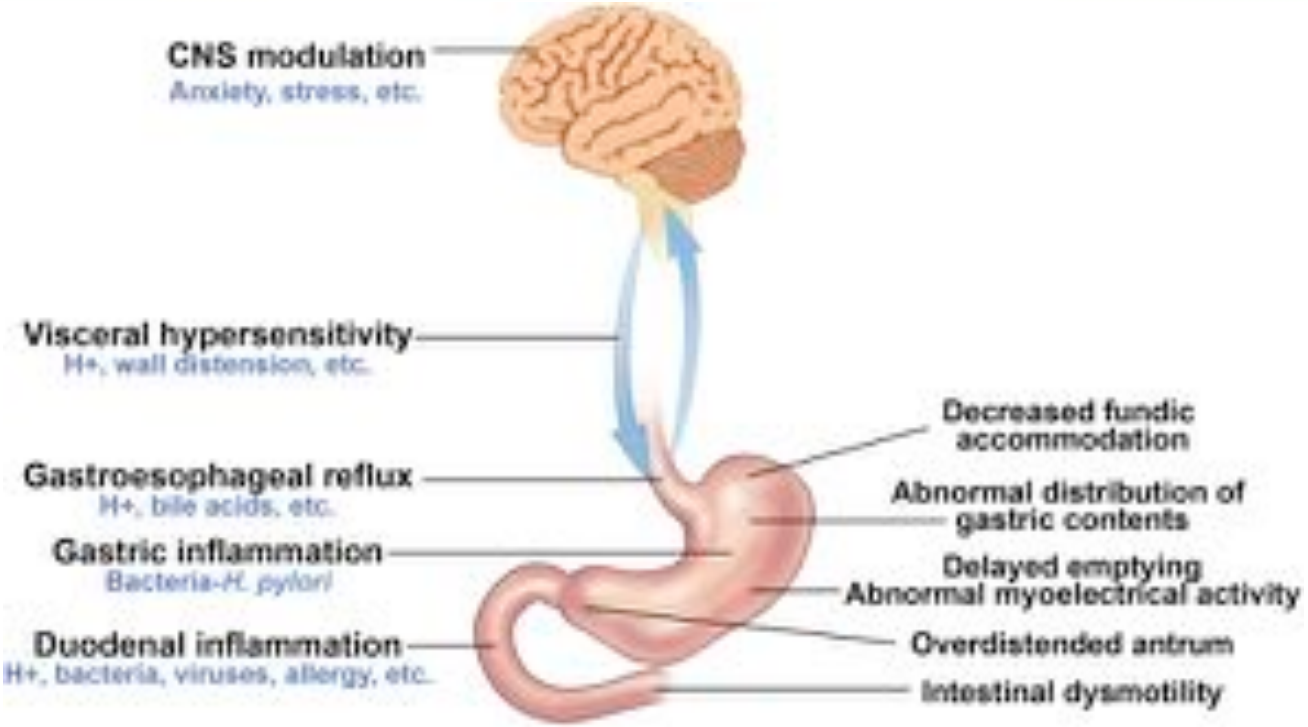
Role of prokinetics in symptom improvement of functional dyspepsia: Cochrane collaboration meta-analysis of randomized controlled trials

- Investigators: Rapat Pittayanon, Yuhong Yuan, Natasha Bollegala, Reena Khanna, Grigorios Leontiadis, Paul Moayyedi
- Subjects: 12285 patients from 39 studies
- Design: Meta-analysis of RCTs
- Not industry funded

Background


Rome IV Functional dyspepsia
Epigastric pain syndrome (EPS)
Postprandial distress syndrome (PDS)
Epigastric pain
Epigastric burning
Early satiation
Postprandial fullness or heaviness

Pathophysiology of functional dyspepsia



Stanghellini. Gastro 2016.

Background

- Prokinetics in FD controversial
- Rome IV recommendations
  - First line in PDS
- ACG and CAG
  - Third line treatment
  - Following PPI and TCAs

Stanghellini. Gastro 2016.
Moayyedi. AJG 2017.

Study aim

- Primary
  - Evaluating the efficacy of prokinetics in improving FD symptoms
- Secondary
  - Evaluating quality of life and adverse events

Study subjects

Inclusion criteria
Age ≥ 18
RCTs with parallel design/cross over
FD by Rome I-IV criteria/compatible
Negative endoscopy, no organic disease
Prokinetic vs placebo/prokinetic

Exclusion criteria
Pts with mainly heartburn/reflux
Assessed prokinetic as anxiolytic
Herbal prokinetics
Treatment <7 days
No binary outcome (yes/no)

Subgroup analyses

- Subtypes of FD
  - PDS, EPS, or mixed
- Risk of bias (RoB)
  - High, low, or unclear
- Type of publication
  - Full paper vs abstract
- Validated dyspepsia questionnaires
- Length of f/u
  - ≥4 wks vs <4 wks)

Results

- Prokinetic vs Placebo
  - 29 studies, 10044 participants
  - RR 0.81 (0.75-0.89)
  - NNT 7
  - I^2 91%
- Removal of cisapride
  - RR 0.87 (0.81-0.94)
  - NNT 12

	Relative Risk
Cisapride	0.71 (0.54-0.93)
Acotiamide	0.94 (0.91-0.98)
Itopride	0.70 (0.47-1.03)
Tegaserod	0.89 (0.82-0.96)
Mosapride	0.91 (0.73-1.13)
ABT-229	1.33 (1.05-1.70)

Results

	Relative Risk (RR)	I^2	Subjects
PDS	0.82 (0.70-0.95)	93%	11 studies, 5822 subjects
EPS	0.67 (0.48-0.93)	6%	2 studies, 124 subjects
Mixed	0.82 (0.73-0.92)	90%	17 studies, 4096 subjects

Secondary aim

- **Very low** change in quality of life scores
  - Heterogeneity, publication bias
- Adverse events
  - Misopride, itopride, acotiamide = placebo
  - Cisapride > placebo
- **Very low** GRADE assessment (subgroup analysis)
  - Heterogeneity, publication bias

Conclusion

- Evidence suggests prokinetics are effective in reducing symptoms for all FD subtypes
- No evidence that prokinetic improves QoL
- Insufficient evidence to support Rome IV recommendation
  - Very low quality of evidence

Chronic cannabis use and gastrointestinal symptomatology, endoscopic, and high resolution manometry findings: a retrospective case-control study

- Investigators: Shelini Sooklal, Meet Parikh, Asyria S. Ahmad
- Design: Retrospective case control study from 2006-2017
- Subjects: 2371 patients GI office
- Intervention: Cannabis use
- Not industry funded

Business Insider. April 2018.

Background

- Endocannabinoid system
  - Endogenous cannabinoid signaling system
  - Involves cannabinoid receptors
  - Ligands located in nerve and immune cells
- Implicated in GI functions
  - Nausea and vomiting, food intake, visceral sensation, motility and inflammation

Subjects and Demographics

	Cannabis users % (n=772)	Controls % (n=1599)	p Value
Male	53 (408)	41 (649)	
Female	47 (364)	59 (649)	
Age (avg)	49.4 (18-84)	59.4 (22-95)	<0.0001
African-American	70 (540)	53 (847)	
Caucasian	22 (167)	32 (516)	
Hispanic	7 (54)	12 (129)	
Asian	1 (11)	3 (57)	
Daily use	64 (249)		
Weekly use	20 (81)		
Monthly use	16 (63)		

Results

	Cannabis users % (n=772)	Controls % (n=1599)	p Value	Odds Ratio (OR)
Abdominal pain	25 (190)	8 (128)	<0.0001	3.7
Heartburn	15 (118)	9 (146)	<0.0001	1.8
Nausea & vomiting	7 (51)	1 (21)	<0.0001	5.2
Diarrhea	4 (31)	6 (91)	0.07	0.7
Constipation	4 (34)	6 (102)	0.04	0.7
Dysphagia	2 (13)	5 (83)	<0.0007	0.3
Weight loss	3 (20)	3 (40)	0.90	1.0
Rectal bleeding	6 (43)	9 (146)	0.002	0.6

Results

Endoscopic Findings	Cannabis users % (n=331)	Controls % (n=1299)	p Value	Odds Ratio (OR)
Esophagitis	8 (26)	3 (41)	0.0003	2.5
Non-erosive gastritis	30 (100)	15 (190)	0.0001	2.4
Erosive gastritis	14 (46)	3 (43)	<0.0001	4.4
Gastric/duodenal Ulcer	1 (3)	0.5 (6)	0.37	1.9
EGJOO	40 (8)	24 (7)	0.24	2.1
Intra-esophageal stasis	65 (13)	17 (5)	0.001	8.9
Hypertensive LES	27 (7)	8 (4)	0.02	4.4
Normal	20 (4)	52 (15)	0.03	0.2

Conclusion

- Largest study evaluating GI complaints of patients with chronic recreational cannabis use
- Most common complaint
  - Abdominal pain
- Hypertensive LES and intra-esophageal stasis may explain increased heartburn and vomiting in cannabis users
- Results suggest that cannabis use may exacerbate, or initiate, a variety of GI symptoms

Per-oral pyloromyotomy (POP) for medically refractory post-surgical gastroparesis

- Investigators: Andrew Strong, Joshua Landreneau, Michael Cline, Matthew Kroh, John Rodriguez, Jeffrey Ponsky, Kevin El-Hayek
- Subjects: 29 pts with post-surgical gastroparesis
- Design: Case series
- Not industry funded

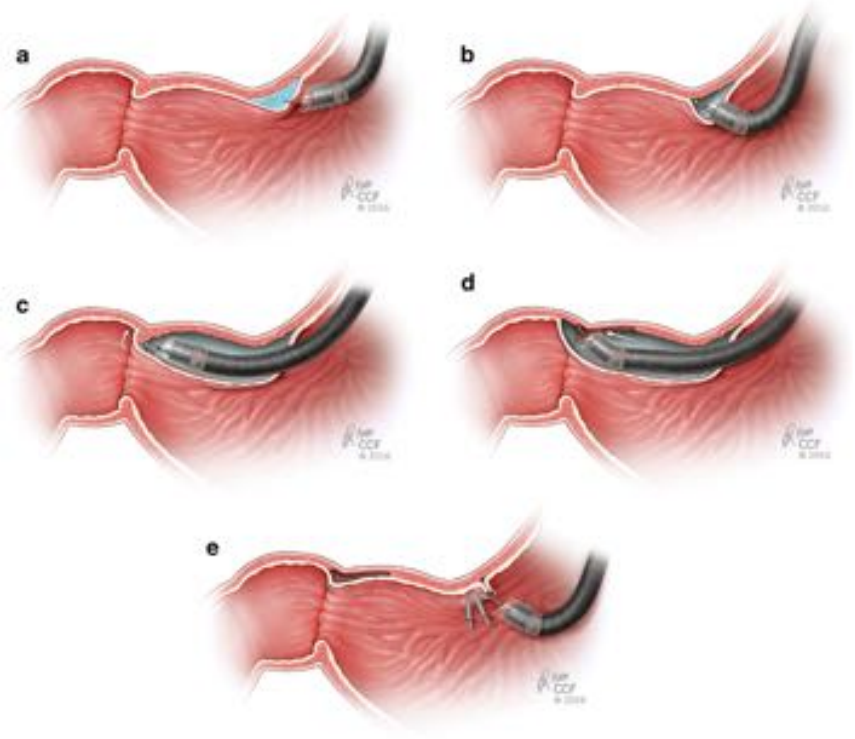
Background

- Gastroparesis is a disease of objective delayed gastric emptying in the absence of mechanical obstruction
- Causes of gastroparesis
  - Diabetic 29%
  - Idiopathic 36%
  - Post-surgical 13%

Current treatment options

	Surgical	Endoscopic
Diet	Gastrojejunostomy	Decompression G tube
Promotility Drugs	Gastrectomy	Jejunal feeds
Antiemetics	Pyloroplasty	Botox injections
Gastric stimulators		Trans-pyloric stents
		G-POEM or POP

G-POEM (gastric-per oral endoscopic myotomy) or POP (per-oral pyloromyotomy)



Allemang. J Gastroint Surg. 2017.

Subjects

Female sex	79.3%
Mean age (±SD)	55.5 ± 14.2
Mean BMI (±SD)	28.0 ± 4.5
HTN	31%
GERD	17.2%
Fibromyalgia	20.7%
Dyslipidemia	17.2%
Diabetes	10.3%
IBS	6.8%
Depression	37.9%
Anxiety	17.2%

Vagotomy	3.4%
Hiatal/paraesophageal hernia repair	41.3%
Fundoplication alone	41.3%
Heller myotomy	3.4%
Other	17.2%
Prior interventions	34.4%
G-tube	6.9%
J-tube	3.4%
Gastric electric stim	3.4%
Botox injection to pylorus	24.1%
GES at 4 hrs	49.7%

Results

	Pre	90d Post-POP	p Value
Mean total GCSI Score (±SD)	3.82 ± 0.67	2.36 ± 1.21	0.0001
Mean Post Prandial Fullness Subscore (±SD)	3.28 ± 0.94	1.68 ± 1.17	0.0002
Mean N/V Subscore (±SD)	3.91 ± 0.98	2.68 ± 1.52	0.0017
Mean bloating Subscore (±SD)	4.27 ± 1.12	2.73 ± 1.73	0.0022

Conclusion

- Largest series of pts who have undergone POP for refractory post-surgical gastroparesis at a single institution
- POP is a safe and effective endoscopic salvage therapy for post-surgical gastroparesis
- This procedure is a reasonable 1st line option for pts with medically refractory gastroparesis

Author	Study design	Subjects	Results
Jacques	Prospective study	20 refractory Gp (10 DB, 10 non) w/ pyloric dysfunction	Improved GCSI, PAGY-QOL, and GES
Yan	Meta-analysis	149 pts	GSCI -1.49, improved GES
Vulcano	Meta-analysis	Total 116 Gp pts	GCSI and GES -1.27 mean change
Avalos	Meta-analysis	130 pts (45% idio, DB 31%, post-vagot 21%, post inf 2%, other 2%	GCSI improved 87%; GES normalized 62.6%
Hustak	Prospective case series	7 pts (4 postsurgical, 2 diabetic, 1 idiopathic) s/p G-POEM	GCSI-decreased GES-normalized in all pts
Parsa	Retrospective comparative study	76 pts s/p Botox injection vs 21 s/p G-POEM (most idiopathic Gp)	Improved in GCSI 35.7% in Botox vs 85% in G-POEM
Sanaei	Prospective study	30 pts with refractory Gp	Improved PAGI-SYM; improved or normalization of GES
Triggs	Case series	8 post-surgical Gp with trans-pyloric stent	7/8 reported symptom improvement, mean increase in DI of pylorus