Inside Out: Gastroenterology & Hepatology Workshop

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Clinical Skills Development Service |
RBWH







GORD/PPI use

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GORD and PPIs:

But Doc...are these bad for me?

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Disclosures

- Research funding and grant support from Crohn's and Colitis Australia (CCA) and the Gastroenterology Network of Intestinal Ultrasound (GENIUS)
- Speaker, consultant or advisory board honoraria for AbbVie, Ferring, Janssen and Takeda
- Conference and educational support from Ferring, Pfizer, AbbVie, Falk, Janssen, Celltrion, BMS and Sandoz

Mr SH: A 41 year old man with GORD

- Moderate retrosternal heartburn
- Sometimes feels liquid in the back of his throat
- Mild bloating
- 1-2 episodes per day, mostly at night mild impact on quality of life
- No other associated symptoms, weight stable
- Diet: Often has fried chicken and fatty foods, 2-4 coffees per day, a beer after dinner some nights, often skips lunch

Medical History: BMI 28 kg/m2, dyslipidaemia

Family History: IHD

Medications: PRN antacids occasionally with relief



Characterising reflux symptoms

- Volume symptoms
- Dyspeptic symptoms and location
- Timing of symptoms
- Other symptoms, such as bloating and abdominal pain

How I think about GORD

Acidity

- Dietary: Acidic foods (citrus, tomato, vinegar), caffeine, alcohol, protein, dairy
- Medications: NSAIDs, steroids

Lower oesophageal sphincter tone

- Dietary: Alcohol, caffeine, fat, chocolate
- Anatomical: Age, variation, hiatus hernia

Pressure

- Dietary: Fat, insoluble fibre, large/solid particles, calorie dense
- Delayed gastric emptying: GLP1s, opiods, anticholinergics, CCBs, marijuana
- Body habitus (extrinsic)



Treating Mr SH's reflux

- **Symptom relief:** Encourage antacid use for symptoms, could consider PRN H2RA or PPI for more severe symptom periods
- Anti-reflux dietary changes:
 - Reduce dietary fat intake
 - Smaller more frequent meals, avoid skipping meals
 - Avoid regular pre-bed beer
 - Reduce caffeine intake, especially in the afternoon
- Lifestyle changes: Weight loss



Anti-reflux lifestyle changes





A few years later...

- Moderate dyspeptic symptoms increased in frequency despite daily antacid use
- Symptoms during the day and at night
- Mild volume symptoms
- Has continued with dietary modifications "there's nothing more I can do"
- Weight increased a bit more to BMI 30 kg/m2
- Saw a different GP a few months ago commenced omeprazole 20mg daily with moderate improvement. Symptoms remain significant.



What next?

- PPI optimisation
 - Dose
 - Formulation
 - Timing of administration
- Re-explore dietary contributors
- Weight loss strategies

[n.b. GLP1s, sleeve gastrectomy, intragastric balloons may worsen GORD]



Which PPI is most efficacious?

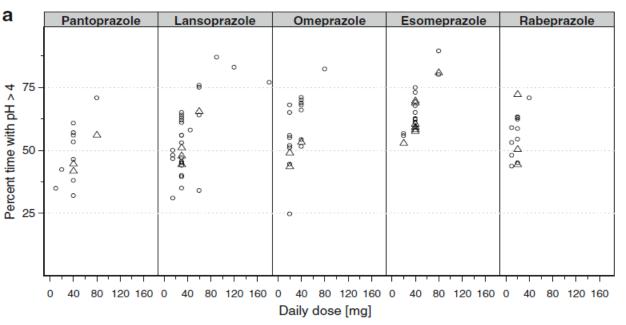
What is the efficacy end point?

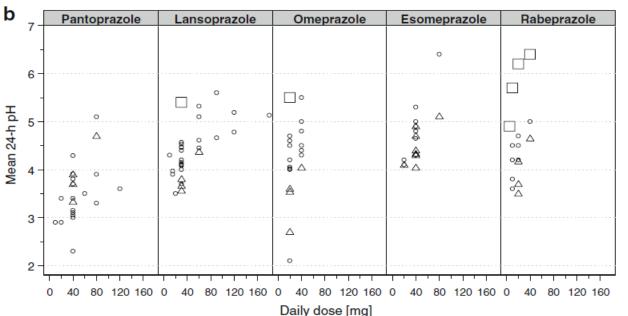
- Intragastric pH variable results, including inter and intraindividual variability
- Symptoms no high quality evidence of superiority of one over other
- Oesophagitis no comparative difference (except esomeprazole superior to omeprazole)



Fig. 2 The upper figure (a) shows the percentage of 24-h time at which gastric pH was above 4.0 in relation to the dose of the PPI. Only data from multiple dosing studies are shown. The lower figure (b) shows the mean 24-h gastric pH measurements from all multiple dose studies analyzed in the present review. These data are the basis of the nonlinear regression analysis presented in Fig. 3 and Table 3. Data measured in healthy volunteers are shown as circles, data from patients with GERD are shown as triangles and data from Helicobacter pylori positive healthy volunteers are shown as squares

Which PPI is most efficacious?





Kirchheiner et al. Relative potency of proton-pump inhibitors, Euro Clin J Pharmacol (2009).



Which PPI is most efficacious?

Efficacy affected by patient factors

- H pylori status greater reduction in gastric acid secretion with PPIs than non-H.P. infected
- GORD status baseline lower gastric pH
- CYP2C19 polymorphisms slow vs rapid metabolisers ?implications for incomplete acid reduction and nocturnal symptoms

Optimising PPI Therapy

- More frequent dosing may be more efficacious
 - Improved nocturnal acid breakthrough / better acid reduction
- Double / maximise the dose
- → Both have similar symptomatic improvement

- **↑ frequency**
 - ↑ dose

- Timing
 - 30-60 mins before meals to allow prodrug activation relies on acidic environment
 - Do not take with H2RAs or antacids → suggest take PPI pre-meals and H2RA post meals

Symptom relief with PPI modification

Changed to pantoprazole 40mg BD, with complete resolution of symptoms



Q: But Doc...I've heard PPIs are bad for you. Do I need this

medication long term?



Busting myths surrounding PPIs

- Lazarus et al (2016): PPIs associated with a 20-50% increased risk of CKD with prolonged use
- Xie et al (2016): PPI users had a significantly higher risk of developing ESRF than H2RA users
- Moayyaedi et al (2019): Identified possible associations with gastric cancer, nutrient deficiencies, bone fractures
- Blank et al (2014): Documented cases of AIN
- Yu et al (2017): Linked long term PPI use to gastric cancer

Mostly retrospective, observational studies... potential confounding by indication and comorbidities, overuse of PPIs, no definitive causal link





The more important questions:

Does this patient need long-term PPI?

What is the risk-benefit balance?



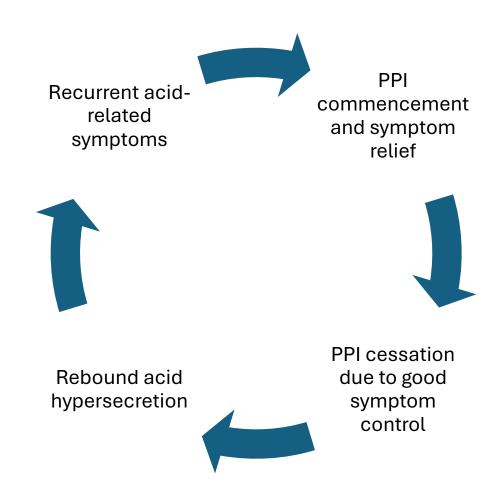
So...When should PPIs not be stopped?

- Barrett's oesophagus: Process initiated by acid/bile exposure, driving inflammation and the metaplastic process
 - Some medium quality evidence to suggest that PPI may reduce the risk of adenocarcinoma and dysplasia
- Severe erosive oesophagitis: Reduce the risk of Barrett's and complications such as strictures [?without significant modifiable RFs]
- Zollinger-Ellison syndrome
- High risk PUD prophylaxis: History of gastric ulceration or GI bleeding without other reversible factors (e.g. need for long term NSAIDs or antiplatelets)
 - Testing for and eradicating H pylori before prescribing NSAIDs or aspirin can reduce the risk of PUD



Breaking the vicious cycle of long-term PPIs

- May occur after 4-8 weeks of PPI use
- Generally symptoms occur 5-14 days post-withdrawal
- Physiological changes may persist for 1-4 weeks
- ? Taper may be of benefit evidence unclear
- ? Use of on demand PPI / H2RA / antacids for symptoms, rather than regular PPI recommencement



Wean PPI over 3 months

- Continued 40mg pantoprazole BD for 4 weeks, 20mg BD for 2 weeks, 20mg daily for 2 weeks, 20mg every second day for 2 weeks, then continued PRN for 2 weeks
- Remained well off PPI; continued with lifestyle modification
- Ongoing unsuccessful attempts at weight loss



Another few years later (age 61)

- Again reporting increased GORD despite weight loss (BMI now 24kg/m2)
- Recommenced pantoprazole 40mg BD near-complete resolution of dyspeptic symptoms
- Severe ongoing volume symptoms multiple times a day
- Severe impact on QoL "I can't live like this Doc!"



When to refer for an endoscopy?

Urgent if dyspepsia AND:

- GI bleeding
- Clinically significant unexplained weight loss
- Dysphagia
- Persistent or recurrent vomiting
- Unexplained iron deficiency

Semi-urgent: Significant PPI refractory GORD

- Is it actually GORD?
- Are there any complications from GORD?
- Could this patient require surgery in the future?

Also exclude other potential causes. If abdominal pain, should have some imaging (US would suffice)

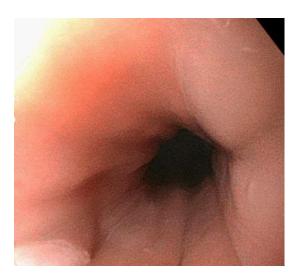


Referred for an endoscopy

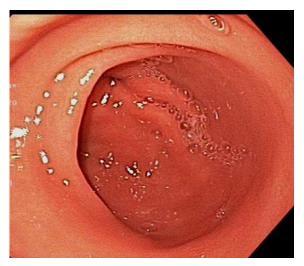
Normal oesophagus (no erosive changes), no erosive oesophagitis or Barrett's oesophagus

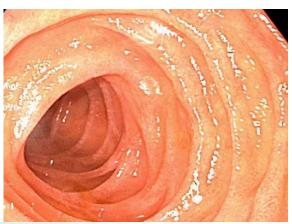
2cm hiatus hernia

Stomach and duodenum normal











Other medical treatment options??

Antacids -> neutralise acid, excess use can cause diarrhoea depending on formulation

H2RAs → more useful if ongoing dyspeptic symptoms despite optimised PPI

Prokinetics → may provide some mild improvement in volume related symptoms by reducing intragastric pressure

Sucralfate → persistent erosive oesophagitis despite PPI and H2RA → a protective barrier +/- repair



Antacids are effective for symptom control

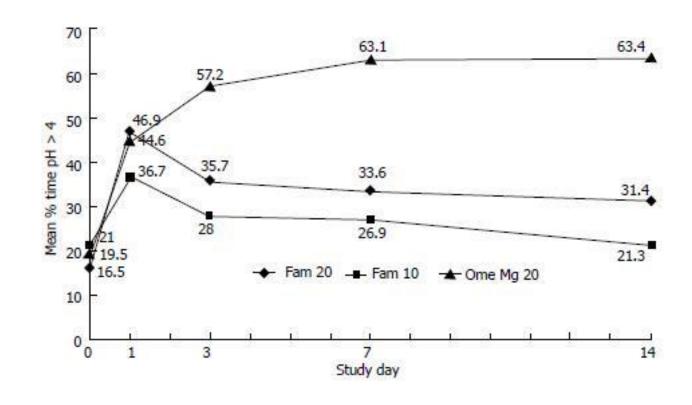
- Brand/formulation
 - Acid-reducing efficacy / buffer function: relevant, but difficult to ascertain
 - May be some value in trying a different type if limited response to one particular brand

- ?Mode of delivery no evidence regarding tablets vs liquid
 - Acid neutralisation effect similar
 - My thoughts: Perhaps liquid may offer better oesophageal protection



H2RAs work better when used intermittently

- Remember ranitidine had issues related to NDMA – now removed and back on the market
- Famotidine and nizatidine are alternatives
- Some data older suggesting an increased risk of gastric cancer, however more recent data suggests otherwise

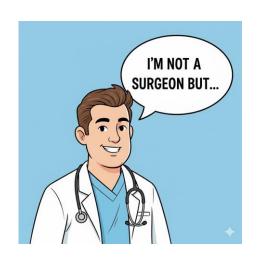


McRorie JW, Kirby JA, Miner PB. Histamine2-receptor antagonists: Rapid development of tachyphylaxis with repeat dosing. World J Gastrointest Pharmacol Ther. 2014 May 6;5(2):57-62. doi: 10.4292/wjgpt.v5.i2.57. PMID: 24868486; PMCID: PMC4023325.



What's the threshold for surgery?

- Symptoms impacting quality of life
 - PPI refractory volume or dyspeptic GORD
 - Refractory severe oesophagitis
 - Peptic inflammatory stricture requiring repeated dilation
 - Significant mechanical/anatomical issue, esp with volume Sx
- Objective evidence of true reflux: Barrett's oesophagus +/oesophagitis +/- pH studies demonstrating GORD
- Exclude oesophageal dysmotility: No major dysmotility on barium swallow and manometry



Underwent surgery

- pH studies confirmed NERD and manometry excluded oesophageal motility disorder
- Underwent successful laparoscopic fundoplication and hiatus repair
- Remains off therapy now 5 years down the track

Questions?







Brisbane North

Lifestyle and Preventive Care Medical

Assault or Abuse

Cardiology

Dermatology Diabetes

Endocrinology

Acute Abdominal Pain in Adults

B12 Deficiency

Gastroenterology

Bowel Cancer Screening

Chronic Abdominal Pain in Adults

Bowel Polyp Surveillance

Coeliac Disease in Adults

Colorectal Symptoms

Constipation in Adults

Diarrhoea in Adults

Dysphagia

Dyspepsia and GORD

Enteral Feeding Tubes in Adults

Inflammatory Bowel Disease (IBD)

Irritable Bowel Syndrome (IBS)

Liver Conditions

Abnormal Liver Function Tests

Fatty Liver

Hepatitis B

Hepatitis C (HCV)

Hereditary Haemochromatosis and Raised Ferritin

Incidental Liver and Spleen Lesions

Gastroenterology Requests

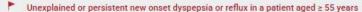
Q Search HealthPathways

♠ / Medical / Gastroenterology / Dyspepsia and GORD



Dyspepsia and GORD

Red flags



Dysphagia (difficulty swallowing) or odynophagia (painful swallowing)

Unexplained weight loss (> 5% of body weight in the previous 6 months)

Iron deficiency in males and post menopausal women, or unexplained iron deficiency in premenopausal women

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Persistent or protracted vomiting

Background

About dyspepsia and gastro-oesophageal reflux disease (GORD) ✓

Assessment

- 1. Take a history:
 - · Symptoms:
 - o Ask about frequency, severity, and duration of symptoms.
 - o Check for potential triggers ∨ and use of medications that can cause dyspepsia ∨.
 - o Try to determine whether symptoms are predominantly dyspepsia or GORD ▼.
 - Concerning features ∨.
 - Family history of gastrointestinal malignancy (first-degree relative).
- 2. Examine the patient:
 - Measure height and weight and calculate BMI ▼.
 - · Check vital signs.
 - Look for jaundice.
- Palpate abdomen, looking for epigastric tenderness, masses, or enlarged organs.
- Consider differential diagnosis ➤.
- 4. Arrange investigations V.
- Consider other investigations if contemplating differential diagnosis:
 - ECG (if suspected ischaemic heart disease)
 - Ultrasound abdomen (looking for gallstones)



Home / Refer your patient / Gastroenterology / Dyspepsia/heartburn/reflux

Dyspepsia/heartburn/reflux

Emergency department referrals

All urgent cases must be discussed with the on call Gastroenterology Registrar to obtain appropriate prioritisation and treatment. Contact through

- Royal Brisbane and Women's Hospital (07) 3646 8111
- . The Prince Charles Hospital (07) 3139 4000
- Redcliffe Hospital (07) 3883 7777
- Caboolture Hospital (07) 5433 8888

Urgent cases accepted via phone must be accompanied with a written referral and a copy faxed immediately to the Central Patient Intake Unit: 1300 364 952.

If any of the following are present or suspected, refer the patient to the emergency department (via ambulance if necessary) or seek emergent medical advice if in a remote region.

- · Potentially life-threatening symptoms suggestive of:
 - · acute upper GI tract bleeding
 - · acute severe lower GI tract bleeding
 - o oesophageal foreign bodies/food bolus
 - acute Severe Colitis*
 - bowel obstruction
 - abdominal sepsis
- · Severe vomiting and/or diarrhoea with dehydration

*Acute severe colitis as defined by the Truelove and Witts criteria – all patients with ≥ 6 bloody bowel motions per 24 hours plus at least one of the following:

- temperature at presentation of > 37.8°C,
- · pulse rate at presentation of > 90 bpm,
- haemoglobin at presentation of < 105 gm/l, CRP >30mg/dl at presentation (or ESR > 30 mm/hr)

Does your patient wish to be referred? ②

Minimum referral criteria

Does your patient meet the minimum referral criteria?

Category 1

Appointment within 30 days is desirable

- Any patient with significant impact on activities of daily living, unexplained, persistent, or recent-onset symptoms (treatment-resistant) with any of the following concerning features:
 - gastrointestinal bleeding
 - weight loss, ≥5% of body weight in previous 6 months
 - difficulty swallowing
 - persistent and/or recurrent vomiting
 - iron deficiency in males and postmenopausal women or unexplained iron deficiency in premenopausal women

Category 2

Appointment within 90 days is

 Any patient with significant, unexplained, persistent, or recent-onset symptoms (treatment-resistant) without concerning features Other Gastroenterology conditions

Send referral

Hotline: 1300 364 938

Electronic:

GP Smart Referrals (preferred) eReferral system templates

Medical Objects ID: MQ40290004P HealthLink EDI: gldmnhhs

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Metro North Central Patient Intake Aspley Community Centre 776 Zillmere Road ASPLEY QLD 4034

Health pathways 🔞

Access to Health Pathways is free for clinicians in Metro North Brisbane.

For login details email:

healthpathways@brisbanenorthphn.

org.au

Login to Brisbane North Health Pathways:

brisbanenorth.healthpathwayscomm

unity.org

Locations

Caboolture Hospital

Redcliffe Hospital

Royal Brisbane and Women's Hospital

The Prince Charles Hospital

Resources

Specialists list

General referral criteria