Peer group

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Mr A

- 55 year old man with heartburn for 5 years
- Gained 10kg over 2 years
- No dysphagia, early satiety or melaena
- Smoker with 20 pack year history, drinks alcohol occasionally
- At follow up visit, reports that he is responding well to empirical PPI treatment & is trying to stop smoking and lose weight

Mr A

Which of the following would also be appropriate for this patient at this time?

a) No further investigations required
b) Barium swallow
c) Gastroscopy
d) Oesophageal pH monitoring
e) Oesophageal manometry

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Patients >40 years with chronic symptoms of GERD for 5 or more years should undergo screening for Barrett's oesophagus

What are the risk factors for Barrett's oesophagus?

- Duration of GORD for at least 5 years
- Age ≥50
- Male
- White race
- Obesity
- Nocturnal reflux
- Tobacco use (past or current)
- 1st degree relative with Barrett's and/or adenocarcinoma

Gastro-oesophageal reflux disease (GORD)

- Reflux of stomach contents causing troublesome symptoms +/- complications

- Pathogenesis
  - Relaxation of lower oesophageal sphincter

  - Low resting lower oesophageal sphincter pressure
    - Food: chocolate, alcohol, fatty meals, coffee, soda, tea, smoking
    - Meds: anticholinergics, B blockers, Ca channel blockers (nifedipine), OC pill, diazepam, nitrates etc etc

  - Increased gastric pressure

Gastro-oesophageal reflux disease (GORD)

- Classic symptoms: heartburn & regurgitation

- Atypical symptoms:
  - Chest pain
  - Globus sensation
  - Chronic cough
  - Hoarseness
  - Wheezing

Red flags – should be referred for endoscopy

- Age ≥ 50 years at 1st presentation for people of European ethnicity
  - Age ≥ 40 years for people of Maori, Pacific or Asian ethnicity

- GI bleeding
- Iron deficiency anaemia
- Dysphagia
- Unexplained weight loss
- Persistent vomiting
- Family history of gastric or oesophageal cancer(1st degree relative)
- Palpable abdominal mass

What are potential complications associated with GORD?

- Erosive oesophagitis
- Oesophageal stricture
- Barrett's oesophagus
- Oesophageal cancer

Mrs B

- 60 year old woman with persistent symptoms of heartburn despite PPI 20mg bd.
- Gastroscopy normal macroscopically & microscopically (no HP)
- BMI 30
- Social smoker while drinking alcohol

Mrs B

Which of the following management might also be appropriate?

a) Optimise PPI therapy
b) Add a prokinetic agent tds pre meals
c) Recommend lifestyle and dietary modification
d) Oesophageal pH monitoring
e) Add a H2 receptor antagonist

Refractory GORD

- ~10-40% of GORD patients fail to respond symptomatically to PPIs
- Most of these patients either have non erosive reflux disease (NERD) or functional heartburn
- Oesophageal pH monitoring should be considered if patients fail bd PPI and gastroscopy normal
  - Stop PPI if patients have atypical symptoms
  - Continue on PPI if patients have partial response to PPI
    - ? Continued pathological acid or non acid exposure despite PPI

Lifestyle & dietary modification

- Weight reduction
- Smoking cessation
- Avoiding trigger foods e.g. EtOH, coffee, spicy, fatty or acidic foods
- Smaller meals & avoiding meals 3-4 hours before bedtime
- Elevating head of bed
- Managing stress and anxiety

Refractory GORD – empirical treatment

- Optimise PPI therapy
  - Check patient adherence
  - Timing of PPI use
  - Trial increasing to 40mg bd
  - Switching to a different brand
- Add a prokinetic agent
- Add a H2 receptor antagonist at night

Table 1. Potency of PPIs Based on OE

Drug at lowest available dosage	OE
Pantoprazole 20 mg	4.5 mg
Lansoprazole 15 mg	13.5 mg
Omeprazole 20 mg	20 mg
Esomeprazole 20 mg	32 mg
Rabeprazole 20 mg	36 mg

NOTE. PPIs are listed in order of increasing potency.[17]
OE, omeprazole equivalent; PPIs, proton pump inhibitors.

Graham et al. Clin Gastroenterol Hepatol 2018; 16:800-808

Refractory GORD – post oesophageal pH study

- Residual acid reflux
  - Add H2 receptor blocker
  - Gaviscon
  - Anti-reflux surgery

- Non acid reflux (weakly acidic or alkaline reflux)
  - Baclofen 5-10mg bd (reduces transient LOS relaxation)
  - Pain modulators ie TCA, SSRI
  - Anti-reflux surgery

- Reflux hypersensitivity (symptoms a/w non pathologic acid exposure)
  - Pain modulators

Mr C

- 70 year old man with Barrett's oesophagus
- On PPI for many years and is asymptomatic
- His recent surveillance gastroscopy & biopsies showed Barrett's oesophagus with no dysplasia
- He came across an online article reporting significant side effects associated with long term PPI use

Mr C

- He has come to see you for a routine check up and asked if his PPI should be discontinued

- What would you do?

PPI use in older adults in NZ

- Omeprazole was the 3rd most commonly dispensed medication in NZ in 2018 after paracetamol and atorvastatin

- Between July 2017 and June 2018, 34% of people 65 years or older were dispensed a PPI

- Should not stop if patient has history of
  - Grade B, C or D oesophagitis noted on gastroscopy
  - Barrett's oesophagus
  - Peptic stricture
  - Zollinger-Ellison Syndrome

Adverse effects associated with long term PPI use

- Renal impairment
  - Acute interstitial nephritis (class effect)
  - Chronic kidney disease (CKD)
    - A meta-analysis of 5 studies including >600,000 people reported 16% and 39% higher risk of CKD and ESRF respectively in people taking PPIs c/w those who did not
    - Risk of CKD increased with PPI duration
      - PPI use for ≥2 years appeared protective against CKD
    - Estimated absolute risk increase in CKD for an individual is 0.1%-0.3% per year

Freedberg et al. Gastroenterology 2017; 152:706-15
Sun et al. Int Urol Nephrol 2018; 50:1835-43

Adverse effects associated with long term PPI use

- Fractures
  - Meta-analysis of 18 observational studies including >240,000 fracture cases found PPI use was associated with
    - 33% increase in RR for fracture at any site
    - 26% increase in RR for hip fractures
    - 58% increase in RR for spine fractures
  - Absolute risk increase for a bone fracture estimated to be 0.1-0.5% per year for an individual

Zhou et al. Osteoporos Int 2016; 27:339-47
Freedberg et al. Gastroenterology 2017; 152:706-15

Adverse effects associated with long term PPI use

- Infections
  - C.difficile
    - Observational studies show ~50% RR increase with PPI use
    - Absolute risk increase estimated to be 0.09% per year given low incidence
  - Community acquired pneumonia
    - A study of >75,000 people age ≥60 in primary care in UK found a significant association between PPI use longer than 1 year and pneumonia (adjusted hazard ratio = 1.82, 95% CI 1.27-2.54)

Freedberg et al. Gastroenterology 2017; 152:706-15
Zirk-Sadowski et al. J Am Geriat Soc 2018; 66: 1332-8

Adverse effects associated with long term PPI use

- Dementia
  - Association between PPI use and dementia is unclear
  - Increased risk reported in some studies but analysis may have been confounded by failure to control for potentially significant factors e.g. FHx of dementia, HTN etc

- Electrolyte disturbance
  - Severe hypomagnesaemia a/w hypocalcaemia (class effect)

Key messages

- Review PPI use to determine whether long-term treatment is still indicated

- Manage risks associated with long term PPI use
  - Fracture risk
    - Maintain adequate vitamin D and calcium intake
    - Strategies to reduce falls risk

  - Encourage pneumococcal vaccination in all older people

Key messages

- If stopping PPI is appropriate, a “step-down” approach is recommended
  - E.g. reduce dose, use every 2nd day or PRN then stop completely

- Patients should be warned about the possibility of rebound symptoms when stopping PPI & how to manage these

Mrs D

- A 50 year old woman with severe iron deficiency anaemia, intermittent dysphagia to solids and a history of heartburn which resolves with once daily PPI

- Gastroscopy showed a large hiatus hernia with Cameron's erosions (linear erosions on gastric folds at level of the diaphragm)

- Colonoscopy was normal

Mrs D

- Her PPI was increased to twice daily
- Unable to tolerate oral iron
- Her Hb remained low on follow up blood results at 4 and 8 weeks later

Mrs D

Which of the following is the most appropriate at this time?

a) Add metoclopramide
b) Add a H2 receptor antagonist at night
c) Iron infusion
d) Capsule endoscopy
e) Refer patient to surgical clinic for a fundoplication