Webstercare®

CONTINUING EDUCATION

Consultant Pharmacist Continuing Education Series

December 2023

Proton pump inhibitors

Proton pump inhibitors (PPIs) are one of the most commonly used classes of medicines. They are mostly used for symptoms of gastro-oesophageal disease (GORD). People living in residential aged care facilities (RACFs) are at high risk of medication-related harm and may be prescribed potentially inappropriate medicines. Long-term use of PPI in RACFs is common and often not necessary.

PPIs include:
- Esomeprazole
- Lansoprazole
- Omeprazole
- Pantoprazole
- Rabeprazole

Indications

PPIs are used in a range of conditions with excessive acid production and damage to upper gastrointestinal tissue. They are also prescribed as gastroprotection for patients being treated with medications which increase the risk of ulceration, such as non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids (prednisone, prednisolone). Used as part of triple therapy for the eradication of *H pylori* infection, PPIs improve cure rates and reduce comorbid symptoms of long-term dyspepsia.

Indications for use include:
- Peptic ulcer disease
- GORD
- Dyspepsia
- Zollinger-Ellison syndrome
- *H. pylori* eradication
- Prevention and/or treatment of upper gastrointestinal adverse effects of NSAIDs
- Stress ulcer prophylaxis

Some medicines may cause or worsen GORD symptoms. These include NSAIDs, bisphosphonates, tetracycline antibiotics, nitrates and calcium channel blockers. PPIs are often co-prescribed in people taking NSAIDs to reduce the risk of upper GI bleeds. However, they are also often inappropriately continued once NSAIDs have been ceased.

All PPIs have similar efficacy and adverse effects. They are more effective than histamine 2 receptor antagonists (e.g., famotidine, nizatidine) for treating GORD.

Stress and anxiety can play a part in perception of reflux symptoms, and should be managed appropriately with lifestyle, cognitive and medications (if needed).

Dose

For functional dyspepsia, a standard starting dose for oral omeprazole is 20 mg once daily, trialled for four weeks. Typical starting doses for other PPIs are esomeprazole 20mg, lansoprazole 30mg, pantoprazole 40mg and rabeprazole 20mg daily. After initial symptom control, the lowest dose and frequency that provides ongoing symptom control should be the goal. The STOPPFrail criteria recommend reducing the dose after 8 weeks therapy, except when symptoms persist.

For people with severe oesophagitis, higher dose may be indicated, such as omeprazole 40mg daily, as well as a longer treatment period.

No dose reduction is required in renal impairment.

Diet and lifestyle modifications

Reflux symptoms are commonly caused by high-fat meals, alcohol, coffee, chocolate, citrus fruit, tomato products, spicy foods and carbonated beverages. If a person has these food triggers, they should be avoided. However, food restrictions should not be continued if symptoms do not improve.

Weight loss can be effective for improving reflux symptoms.

Other lifestyle measures include:
- eating smaller meals
- eating meals slowly
- avoiding lying down after eating
- avoiding eating or drinking for 2 to 3 hours before bedtime or vigorous exercise
- using a positional therapy device (e.g., wedge pillow) or elevating the head of the bed (if symptoms occur at night)
- stopping smoking

Adverse effects

PPIs are generally well tolerated. Short-term use (4-8 weeks) is safe and effective. Some common side effects include headache, nausea, vomiting, diarrhoea, abdominal pain, constipation, and flatulence.

Calcium and vitamin D status should be assessed before and whilst prescribed PPIs. In older people, PPIs have a higher rate of fracture compared to non-users. PPIs modestly increase the risk of fracture at the hip, spine and other sites after falling. Histamine 2 receptor antagonists do not appear to be associated with an increased fracture risk. In people at high risk of osteoporosis, adequate dietary calcium and sun exposure is needed, or if insufficient, supplements should be used.

With long-term use PPIs may cause decreased serum vitamin B12 concentration, pneumonia, fracture, iron deficiency and chronic kidney disease. Enteric infections (including *Clostridioides difficile*-associated disease) have been associated with PPI use. Some studies suggest an association between PPI use and pneumonia. A large study of people aged 65 years and over found for every 80 patients treated with a PPI, one extra patient would be hospitalised for pneumonia.

Long-term use of PPIs can also lead to hypomagnesaemia, which can lead to secondary hypoparathyroidism and hypocalcaemia.

The long-term use of PPIs has been associated with the development of both acute and chronic kidney injury.

As dietary iron absorption requires gastric acid, long-term use of PPIs may lead to iron deficiency and iron deficiency anaemia. The risk is greatest with high PPI doses and increasing duration of therapy. PPIs may also increase the risk of vitamin B12 deficiency.

There is also a significant link between PPIs and higher risk of cardiovascular events, especially with treatment more than 8 weeks.

There is conflicting evidence that PPIs are associated with an increased risk of dementia.

Drug interactions

Omeprazole and esomeprazole may decrease the efficacy of clopidogrel due to drug interactions. For people prescribed clopidogrel, lansoprazole, pantoprazole, or rabeprazole should be used.

Dose adjustments or PPI cessation may be required for patients at-risk of severe medication interactions, such as those taking citalopram, methotrexate and some cancer drugs.

Deprescribing

Ongoing use of PPIs should be assessed regularly. Choosing Wisely Australia recommend against long-term use of PPIs with uncomplicated disease without regular attempts at reducing dose or ceasing. The Beers criteria and STOPP/START criteria both recommend against full therapeutic dose for more than 8 weeks. It is estimated that 22% to 63% of PPI use in Australia is inappropriate.

If symptoms are well controlled, reducing the dose or stopping treatment should be considered. The lowest effective dose should be the goal for ongoing therapy. Intermittent or 'prn' use can be considered.

Rebound acid hypersecretion may occur with abrupt cessation of PPIs. Therefore, slow tapering of the PPI dose is recommended over 2 to 4 weeks. Occasional reflux or dyspepsia symptoms can often be managed with as-needed PPIs, alginate/antacid combination products, or antacids.

PPIs should not be ceased for people with ongoing high risk of bleeds or ulceration, chronic high-risk NSAID use, severe oesophagitis, and a history of bleeding gastrointestinal ulcer.

Information on the risk and benefits of deprescribing PPIs is available at https://www.primaryhealthtas.com.au/resources/deprescribing-resources/

Quality improvement

Quality improvement interventions should be routinely addressed in residential aged care homes. Pharmacists can conduct medication use audits to assess inappropriate long-term use of PPIs. PPIs should be prescribed for the shortest period necessary to achieve the greatest improvement in quality of life. Pharmacists can also play a key role in assessing the need for continuation of PPIs on a regular basis when conducting Residential Medication Management Reviews (RMMRs).

References
BMJ 2023;383:e070752.
J Clin Med 2022;11(17):5189.
BMC Geriatrics 2022;22:493.
J Fam Pract 2019;68(3);E18-E19.