Optimising medicines – prescribing and deprescribing proton pump inhibitors

Introduction

Much of a physician’s assessment of a patient ends in a prescription, when in actual fact this is only the beginning.¹ The safe and effective use of medicines should include regular medication review, particularly when a patient has been in hospital, or has been seen by another healthcare professional, whether referred by a general practitioner or not. The National Institute for Health and Care Excellence (NICE) in the UK provides useful guidance on when and for whom medicine reviews are particularly needed.² While the emphasis is frequently on polypharmacy in the older patient, medication review should also prioritise younger adults, children and adolescents with chronic conditions.

An important part of any medicine review is involving the patient in decision-making, particularly when considering changes to medication for a chronic condition or in conditions where symptoms occur intermittently, such as gastro-oesophageal reflux disease (GORD or GERD). If a medicine review is physician led, this needs to be individualised and well documented on patient records.

Self-management plans are generally reserved for those patients who want to be involved in managing their condition(s) and their medicines. Patient education is key, as deprescribing or reducing medication doses may cause concern as patients are less accustomed to this type of intervention.

This is the first in a series of deNovo Medica modules that will focus on optimising medication in chronic care.
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Prescribing proton pump inhibitors

PPIs are most commonly prescribed for GI disease, particularly GORD, but also for gastroprotection in at-risk patients receiving regular doses of nonsteroidal anti-inflammatory drugs (NSAIDs) and oral anticoagulants. Other GI indications that lead to PPI prescriptions are peptic ulcer disease, Barrett’s oesophagus, oesophagitis and gastritis.

Chronic PPI use is common, with some studies showing up to 65% of patients receiving ongoing therapy after hospitalisation without any evidence-based indication for treatment.

Brief review of GORD

The most recent classification of GORD is defined as its occurring in patients with reflux-oesophagitis confirmed by endoscopy and in association with increased exposure to gastric acid as confirmed by functional tests. The diagnosis of GORD is confirmed by gastroscopy (low sensitivity, but high specificity – 90-95%). However, the majority of patients with reflux symptoms have normal endoscopy results; ambulatory pH-monitoring is also performed to confirm that reflux is actually occurring. The latter test is more sensitive but does not confirm all cases of gastric reflux.

It is useful to distinguish between erosive reflux disease (ERD) and non-erosive reflux disease (NERD) since this may have treatment implications.

Optimising the PPI prescription

Ten key tips for consideration when prescribing PPIs:

1. Patients should be instructed properly about the timing of PPI intake relative to eating. Best results are achieved if the PPI is taken within one hour before a meal as these agents only inhibit actively secreting proton pumps

2. When initiating PPIs for GORD or mild-to-moderate (grade A or B) oesophagitis, therapy should be prescribed for 4-12 weeks and reviewed at four weeks to identify non- or partial responders
3. Doubling the PPI dose in partial responders or switching to alternative PPIs to try to improve symptom control has limited success as many of these patients will have functional reflux.

4. Lifestyle modifications in GORD should be motivated by the clinician at the time of initiating therapy for suspected GORD (raising head end of the bed, avoiding meals within three hours of bedtime, weight loss).

5. Adults with dyspepsia or reflux symptoms who are being sent for a test for Helicobacter pylori should stop the PPI for a two-week period prior to the test.

6. The standard triple therapy for H. pylori is a PPI, clarithromycin and amoxicillin for 14 days.

7. The long-term use of PPIs is warranted for severe oesophagitis, where there is a documented history of bleeding GI ulcer, Barrett’s oesophagus, and chronic NSAID, aspirin and anticoagulant users with a determined bleeding risk.

8. PPIs can be safely used on demand in patients with mild forms of GORD or NERD.

9. Patients with extra-oesophageal reflux manifestations (e.g. chronic cough, laryngo-pharyngeal reflux and asthma exacerbations), should use double the standard PPI doses for at least 8-12 weeks.

10. Discontinuing PPI therapy abruptly may lead to a rebound increase in reflux symptoms due to elevated gastrin levels and gastric acid output.

**Best practice when considering PPI deprescription**

The Canadian Guidelines development team has evaluated published randomised clinical trials, including a thorough assessment of outcomes regarded as important by patients, in order to develop evidence-based clinical deprescribing guidelines. As some patients are fearful of fully discontinuing treatment, evidence concerning alternative management strategies such as stepping down and reducing PPI use to either a lower dose or on-demand use was also evaluated (Table 1 describes the categories of PPI deprescription).

### Table 1. Choices in PPI deprescribing

<table>
<thead>
<tr>
<th>Deprescribing can include stopping, stepping down or reducing doses</th>
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</thead>
<tbody>
<tr>
<td><strong>Stopping</strong> can be done either via abrupt discontinuation or a tapering regimen</td>
</tr>
<tr>
<td><strong>Stepping down</strong> involves abrupt discontinuation or tapering of the PPI followed by prescription of an H2RA (any H2RA at any approved dose and dosing interval according to the drug monograph)</td>
</tr>
<tr>
<td><strong>Reducing</strong> includes the following subcategories:</td>
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<tr>
<td>• Intermittent PPI use, which is defined by the Canadian Consensus Conference as ‘daily intake of a medication for a predetermined, finite period (usually 2-8 weeks) to produce resolution of reflux-related symptoms or healing of oesophageal lesions following relapse of the individual’s condition’</td>
</tr>
<tr>
<td>• On-demand PPI use, which is defined by the Canadian Consensus Conference as ‘the daily intake of a medication for a period sufficient to achieve resolution of the individual’s reflux-related symptoms; following symptom resolution, the medication is discontinued until the individual’s symptoms recur; at which point, medication is again taken daily until the symptoms resolve’</td>
</tr>
<tr>
<td>• Lower dose, which represents a reduction from a standard dose to a maintenance dose</td>
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H2RA: histamine-2 receptor antagonist
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What issues should be dealt with when deprescribing PPIs?

1. Are there indicators or risk factors that support continued use?

Assessing the patient’s history is key to decision-making and determining the original indication for the PPI and whether there are ongoing risks for the patient (Figure 1). Patients with Barrett’s oesophagus, grade C or grade D oesophagitis or a documented history of bleeding GI ulcers are unlikely to benefit from stopping PPIs. Advice from a gastroenterologist should be sought in these patients when considering PPI deprescription (Table 2).

Figure 1. PPI deprescribing algorithm

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**Figure 1. PPI deprescribing algorithm**
Table 2. Los Angeles classification for the endoscopic assessment of reflux oesophagitis

<table>
<thead>
<tr>
<th>Classification</th>
<th>Grade A</th>
<th>Grade B</th>
<th>Grade C</th>
<th>Grade D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Consider PPI continuation</td>
<td>One or more mucosal breaks no longer than 5mm, none of which extends between the tops of the mucosal folds</td>
<td>One or more mucosal breaks more than 5mm long, none of which extends between the tops of two mucosal folds</td>
<td>Mucosal breaks that extend between the tops of two or more mucosal folds but that involve less than 75% of the oesophageal circumference</td>
<td>Mucosal breaks that involve at least 75% of the oesophageal circumference</td>
</tr>
<tr>
<td>Do not deprescribe without intervention</td>
<td></td>
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</tr>
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</table>

Figure 2. The schematic of the GORD Los Angeles classification is a useful memory tool

2. How should tapering be approached?

There is some evidence that abrupt discontinuation does increase symptom relapse. Therefore, it is prudent to reduce the PPI to the lowest effective dose before discontinuation. The patient should be provided with a symptom management strategy (and information aid) to provide for on-demand PPI usage. Clinicians may elect to introduce gradual dose reduction (from twice to once daily; from high to low dose, from daily to every other day) (Table 3).

“Unfortunately, GORD is a very heterogeneous condition and there is no reliable evidence-based or validated functional classification.”

Dr Letier
Table 3. PPI availability

<table>
<thead>
<tr>
<th>PPI</th>
<th>Standard dose (healing) (once daily)*</th>
<th>Low dose (maintenance) (once daily)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Omeprazole (Losec®) – Capsule (Omez, Altosec)</td>
<td>20mg or 40mg</td>
<td>10mg or 20mg</td>
</tr>
<tr>
<td>Esomeprazole (Nexiam®) – Tablet (Nesopram)</td>
<td>20mg or 40mg</td>
<td>20mg</td>
</tr>
<tr>
<td>Lansoprazole (Prevacid®) – Capsule (Lansoloc, Lansoloc OTC)</td>
<td>30mg</td>
<td>15mg</td>
</tr>
<tr>
<td>Pantoprazole (Tecta®, Pantoloc®) – Tablet (Prazoloc, Prazoloc OTC)</td>
<td>40mg</td>
<td>20mg</td>
</tr>
<tr>
<td>Rabeprazole (Pariet®) - Tablet</td>
<td>20mg</td>
<td>10mg</td>
</tr>
</tbody>
</table>

*non-erosive reflux disease; areflux oesophagitis
*Can be sprinkled on food
*Standard dose PPI taken BID only indicated in treatment of peptic ulcer caused by H. pylori; PPI should generally be stopped once eradication therapy is complete unless risk factors warrant continuing PPI (see guideline for details)

Engaging patients and caregivers

Patients and/or caregivers may be more likely to engage if they understand the rationale for deprescribing (risks of continued PPI use; long-term therapy may not be necessary), and the deprescribing process

Tapering doses

• No evidence that one tapering approach is better than another
• Lowering the PPI dose (e.g. from twice daily to once daily, or halving the dose, or taking every second day) OR stopping the PPI and using it on-demand are equally recommended strong options

Choose what is most convenient and acceptable to the patient

On-demand definition

Daily intake of a PPI for a period sufficient to achieve resolution of the individual’s reflux-related symptoms; following symptom resolution, the medication is discontinued until the individual’s symptoms recur, at which point, medication is again taken daily until the symptoms resolve.

3. What monitoring needs to be done and how often?

Typically, patients are seen at four and 12 weeks after deprescription, whether it is gradual reduction or stopping therapy; thereafter at six months or annually. If symptoms intervene, the patient should be educated on how to manage these with on-demand PPIs and the use of H2RA therapy, or other over-the-counter agents. Non-pharmacological interventions, such as weight loss, have been shown to be useful. Inclusion of a pharmacist within the interdisciplinary team is important in strategy definition and ongoing support. Pharmacist involvement will support patient understanding, implementing dose changes, monitoring and alerting the prescriber to the development of symptoms.
Conclusion

Overuse of medication is a key contributor to polypharmacy. While PPIs are generally regarded as safe and well-tolerated medications, side effects such as diarrhoea, Clostridium difficile infection, increased pneumonia risk, hip fracture risk, impaired B12 absorption and hypomagnesaemia can be troublesome, particularly in the elderly patient. The clinician’s involvement in deprescribing should be focused on stopping medication that might no longer be needed, or that might cause harm or interfere with other medication and result in additional unnecessary cost.

References

Click on reference to access the scientific article

1. Laloo UG, Director of Enhancing Care Foundation, Durban. deNovo Medica module published May 2017.
2. NICE Guideline: Medicines optimisation: The safe and effective use of medicines to enable the best possible outcomes. 4 March 2015 (nice.org.uk/guidance/ng5).
Case study – Deprescribing PPIs

Patient: 82-year-old retired woman

History:
- Osteoporosis
- Osteoarthritis
- Systolic hypertension
- Lower segment deep vein thrombosis after total knee replacement 10 years before.

Medication:
- Rx – losartan 50mg/d
- Enteric-coated aspirin 100mg/d
- Celecoxib 200mg/d
- Alendronate 70mg/week
- Vitamin supplements.

On examination:
- Patient presented to her GP and was referred to a general surgeon six months prior with dyspepsia and progressively worsening reflux symptoms not responding to antacids
- Upper GI endoscopy showed a normal oesophagus, stomach and duodenum
- Campylobacter-like Organism (CLO) test for H. pylori was negative
- Patient was started on esomeprazole 40mg/d and ulsanic suspension 1g TDS and referred back to the GP with no specific instructions.

Two months later:
- She presented to the ER with severe epigastric pain and an ultrasound revealed a thick-walled gallbladder with multiple calculi and a slightly dilated common bile duct
- Her symptoms resolved completely after a laparoscopic cholecystectomy
- Patient was given a seven-day course of antibiotics prior to surgery for presumed cholecystitis.

One week later:
- The patient had persistent diarrhoea a week after discharge from hospital and stool C. difficile toxin PCR was positive; treatment was commenced with oral vancomycin 125mg QID for 14 days
- Her reflux symptoms had resolved completely on the PPI therapy and she was still on the same dose
- Her GP then referred her for gastroenterology consultation.

13. What is the best timing for PPI dosing?
A. About half an hour before breakfast
B. Two hours post dinner with a snack
C. Just before bedtime
D. During the day with a small amount of orange juice

14. What are the risk factors for C. difficile infection in this patient?
A. PPI use
B. Hospitalisation
C. Recent antibiotic therapy
D. All of the above

15. What is the most appropriate PPI deprescribing regimen?
A. Reduce esomeprazole to 20mg/d and continue lifelong
B. Increase the esomeprazole to 80mg/d for six months and then taper by 10mg/month for the next six months
C. Switch to omeprazole and reduce to 20mg daily initially, then reduce the dose to the minimum that controls reflux, and eventually use on-demand or discontinue completely or change to H2RA or antacids if required
D. Switch to pantoprazole 20mg daily