DE-ESCALATION OF PROTON PUMP INHIBITORS

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INTRODUCTION

Acid suppression through the use of proton pump inhibitors has revolutionised the treatment of acid related disease in the oesophagus, stomach and duodenum. Unfortunately, PPI prescription has become the victim of its own success. Multiple studies have shown that rates of potentially inappropriate prescribing have been increasing over the years. In clinical practice this is often seen as patients given short term courses of PPI for undiagnosed epigastric symptoms turning in to long term therapy, maintenance of PPI therapy for non-acid related foregut symptoms after exclusion of the diagnosis of reflux or other conditions, and inappropriate and sustained dose escalation of PPI therapy without planning for alternate therapies or dose de-escalation.

Because of this the PBS have taken the rather unusual step of requiring an authority script for patients prescribed PPI therapy which unfortunately leads to an extra workload for clinicians.

While the absolute risk of harm to individuals from PPI prescription is low the very high and rising prescription of these medications has created the risk of significant impacts at a population level.

The aim of this article is to provide information to help practitioners reduce prescription rates. Unfortunately, widespread withdrawal of H2 blockers from the Australian market limits therapeutic options in patients who are allergic to PPI's or who suffer renal injury from them.

INDICATIONS FOR CHRONIC PPI USE

There are a number of indications for long term PPI use including severe Barrett's oesophagus with oesophagitis, eosinophilic oesophagitis, at risk individuals on dual antiplatelet agents or patients with antiplatelet agent associated peptic ulceration and endoscopically proven significant and resistant oesophageal gastric or duodenal ulcer disease. Recent studies however have shown that probably only about a third of patients receiving long term PPI therapy are receiving it in keeping

with current guidelines. Risk factors for over prescription include younger age and diagnosis of functional conditions. Under prescription will occur in some patients however in these same studies.

POTENTIAL HARMS OF PPI THERAPY

1. C. difficile infection and potentially campylobacter and salmonella gastroenteritis.
2. Increase fracture risk related to alterations and absorption of calcium. Deficiencies in iron, magnesium and B12 are also possible.
3. Renal injury. Acute interstitial nephritis will occur in approximately 0.01 % of prescriptions however chronic kidney disease from other mechanisms may also occur.
4. PPI therapy can also interfere with other medications. The most prominent of this is Clopidogrel where PPI therapy can significantly reduce its antiplatelet effects.

MINIMISING OVERPRESCRIPTION

The PBS changes to prescription are effectively a blunt form of drug stewardship. It is clearly possible for clinicians however to undertake this in more clinically balanced and nuanced ways. While it is probable that some patients will seek to purchase over-the-counter PPI therapy it is likely that this will decrease over time especially for maintenance therapy.

CLINICAL SYNDROMES

1. Dyspepsia. Undiagnosed dyspepsia is a common cause for PPI prescription. Lifestyle factors such as smoking, alcohol consumption and weight gain can be contributors as can certain drugs such as calcium channel blockers, bisphosphonates, antiplatelet agents and non-steroidal anti-inflammatory drugs. For these patient's lifestyle change and drug substitution are a possibility. If patients are prescribed a PPI, then dose duration should be discussed at the time of initial prescription.
2. Ulcer Healing. PPI remains the "gold standard" for ulcer healing however, once the cause of the ulcer has been removed and the ulcer has been proven to have healed there is usually no indication for ongoing therapy.
3. Prophylactic therapy. PPI as prophylaxis can be required in patients having long term antiplatelet agents or NSAIDS. Testing for an eradication of Helicobacter will ameliorate risk in a significant number of these patients. Higher risk patients are those over the age of 65 years, with a history of peptic ulcer disease or GI haemorrhage or patients taking multiple medications that are known to cause GI adverse effects.
4. Reflux disease. While symptoms of gastro-oesophageal reflux are highly prevalent in the community, the condition itself is only injurious enough to be considered a significant disease state in a minority of patients. For example, the prevalence of Barrett's oesophagus is less than 5% in this population and only a small minority of patients with Barrett's progress to develop oesophageal neoplasia. The majority of patients with persisting reflux symptoms do not have ulcerative oesophagitis on endoscopy so their symptoms are not associated with acid related

injury, and amongst patients with diagnosed oesophagitis, a reasonable majority are Grade A or 1 oesophagitis which is a variant of normal and not indicative of a sustained oesophageal injury. In patients under the age of 50 with a putative diagnosis of gastro-oesophageal reflux and disruptive symptoms it is still reasonable to consider prescription of PPI therapy however consideration of alternate diagnoses and a conversation about the lifestyle factors associated with reflux are important as is a discussion about a plan to cease prescription after a certain period of time. In patients over the age of 50 with new symptoms suggesting reflux disease an endoscopy should be considered reasonably early while formulating a management plan as well as a conversation about lifestyle factors. In patients with rebound symptoms after deprescription it might be reasonable to consider simple antacids however there will be some patients with recurrent reflux symptoms after PPI deprescription who should also be considered for endoscopy and other diagnostic tests to establish the severity and therefore likely chronicity of their reflux condition so that long term PPI therapy and other potential therapeutic options can be discussed.

REFLUX DIAGNOSTIC TESTING

1. Endoscopy. Endoscopy is a gold standard test for diagnosing the complications of reflux as well as other conditions of the oesophagus, stomach and duodenum. In the absence of Grade B or above oesophagitis however it does not establish a diagnosis of reflux disease.
2. Barium swallow. Barium x-rays are becoming less accessible due to relatively poor remuneration relative to the expense of performing the test. Barium swallows are not diagnostic for reflux disease, but they can be very effective screening procedures for patients where access to endoscopy is limited.
3. Nuclear Medicine reflux tests. These tests are not specific enough to provide useful diagnostic information for the majority of patients.
4. Oesophageal physiology tests. Measurements of oesophageal function (manometry) and oesophageal acidification (pH testing or pH impedance testing) are the Gold Standard for reflux and other oesophageal diseases. While the tests are very cheap compared with endoscopy or long-term PPI prescription the tests are viewed by patients as being relatively invasive, so they are only performed when there is a diagnostic dilemma or when escalated therapy is being considered. The majority of these tests are outpatient catheter based tests that require no anaesthesia, however endoscopically placed catheter free pH testing probes are also available for patients who wish to avoid catheter based studies and can afford to cover the costs of the implantable capsule.

INDICATIONS FOR PHYSIOLOGY TESTING

1. Significant symptoms attributed to reflux, not responsive to PPI therapy.
2. Any patient being considered for anti-reflux or hiatus hernia surgery.
3. Patients with unexplained dysphagia and a normal endoscopy.

PPI ALTERNATIVES

1. Reinforcement of lifestyle. Encouragement of weight loss and avoidance of reflux precipitants are a powerful tool for the majority of patients with acid related symptoms. Simple antacids are appropriate if they are required on a PRN basis however if patients are requiring multiple doses a day then they can be viewed as potentially ineffectual. Prokinetics such as Domperidone are another option.
2. Anti-Reflux surgery. Due to concerns about long term toxicity from PPI use there are some patients who may request anti-reflux surgery as an alternative to long term PPI use.

INDICATIONS FOR ANTI-REFLUX SURGERY

1. To manage disruptive reflux symptoms in patients with proven reflux diagnosis and poor symptom control. Patients for example with persisting disruptive heartburn, especially if associated with regurgitation of fluid will generally make good candidates for surgery. Patients with extra oesophageal or less well-defined symptoms will have less sustained duration of response to surgery.
2. Surgery for the complications of reflux. Patients with aspiration pneumonia associated with reflux, persisting significant ulceration or complicated Barrett's with ulceration or Barrett's neoplasia requiring endoscopic treatment.
3. Large hiatus hernias. Large hiatus hernias with an intrathoracic stomach in a retrocardiac position are known to cause exercise limiting shortness of breath due to atrial and coronary sinus compression. They can also cause chest pain and obstructed eating with the risk of gastric volvulus and strangulation. Usually for these patients reflux is not the primary indication rather surgery is for restoration of normal eating and exercise function.

CONCLUSIONS

More and more patients are likely to seek PPI de-escalation, either because of concerns about long term PPI use or because of the difficulty of obtaining PPI prescription especially escalated dose prescription. While there will be some patients where it is medically sound to continue long term or lifelong PPI therapy there are many alternate options available for patients.