

Background

Proton pump inhibitors (PPIs) are a class of drugs which suppress gastric acid secretion by inhibiting the H^+/K^+ ATP pump in parietal cells. They decrease the acidity of the gastro-intestinal tract. The 5 drugs in this class include esomeprazole (Nexium®), lansoprazole (Prevacid®), omeprazole (Losec®), pantoprazole (Pantoloc®), and rabeprazole (Pariet®). At equivalent doses, all PPIs have similar efficacy rates and safety profiles.

PPIs are highly effective for the treatment of a variety of conditions that are caused or aggravated by acid. They are used to treat ulcers, GERD, and erosive esophagitis. They are also often given before anesthetic to reduce the risk of acid aspiration pneumonia. The length of time that PPI therapy is needed depends on the condition being treated. For treatment of an ulcer, GERD, or erosive esophagitis, therapy should extend for 4-8 weeks. If the PPI was given pre-anesthetic, therapy is generally continued for one month. If the medication is used in conjunction with an *h. pylori* eradication regimen, therapy should continue for 7-14 days. There are some patients who require long-term PPI therapy, such as those with Zollinger-Ellison syndrome, or patients at high risk for a GI bleed in whom anticoagulant, NSAID, or glucocorticosteroid therapy cannot be avoided.

PPI therapy is expensive. The monthly cost ranges from \$26.42 (rabeprazole 10 mg) to \$89.78 (lansoprazole 30 mg) per patient. The vast majority of patients who start taking PPIs require these medications for a limited period of time (ex: 4-8 weeks) but never stop taking them. This is a huge economic drain and is money that could be used elsewhere. As well, the Saskatchewan Health Drug Plan and Extended Benefits Branch Exception Drug Status (EDS) Program Criteria for Proton Pump Inhibitors usually only provides coverage for up to 8 weeks. Therefore, many patients on long-term PPI therapy do not have coverage for their medications, and are paying out of pocket for them. Furthermore, even if patients are approved for EDS coverage, if they have been prescribed a PPI which exceeds the Maximum Allowable Cost (MAC) Policy, they are still paying for some of the cost of their medication. In addition to the economic implications, patients taking PPIs unnecessarily are complicating their medication regimens and exposing themselves to the side effects of the medication.

Literature Review

T.J Lee et al¹ conducted a systematic review to investigate whether some GERD patients are receiving maintenance treatment with a PPI unnecessarily, and whether these patients are taking unnecessarily high or unnecessarily frequent doses. They found that a substantial portion of patients with GERD can be managed with treatment that is less intensive than daily PPIs. Stepping down to no therapy may also be acceptable in endoscopy negative reflux disease (ENRD). However, the authors emphasize that a reduction in the cost of treatment is desirable, but is only acceptable if symptom control is not compromised.

A double-blind, placebo controlled trial by E. Bjornsson et al² investigated the proportion of patients on long term PPI therapy who are able to discontinue without developing symptoms. Participants underwent upper endoscopy and were excluded if endoscopic findings indicated that they could not safely discontinue their PPIs. This trial found that GERD patients had more difficulty discontinuing long-term PPIs than non-GERD patients (ex: those taking the medications for ulcer prophylaxis, dyspepsia, or peptic ulcer disease). Discontinuation of PPIs was successful in 27% of long-term PPI users in this trial, although there were no recommendations given on the most successful method of discontinuation.

An economic analysis by D.A. Hughes et al³ of 7 placebo-controlled trials evaluated the cost effectiveness of on-demand PPI therapy in patients with endoscopy-confirmed non-erosive reflux disease (NERD). They compared the costs and effectiveness of the five PPIs in previously symptomatic patients whose heartburn symptoms had resolved completely after 4-weeks of acute PPI treatment. This trial intentionally did not look at other cost-minimization ways to manage NERD. The results suggest that on-demand rabeprazole can be a cost-effective choice among PPI-responsive patients with endoscopy-confirmed NERD.

N.J. de Wit et al⁴ investigated the effectiveness of H. pylori testing and treatment in discontinuation of maintenance therapy (H₂RA or PPI). As virtually all non-NSAID ulcers are caused by H. pylori, patients with a confirmed ulcer who were not taking NSAIDs were tested for H. pylori, and 87% of these patients tested positive for the bacteria. 3 months after eradication therapy (with omeprazole 20 mg bid, amoxicillin 1 g bid, and clarithromycin 500 mg bid x 7 days), 32 of the 36 patients (89%) treated with H. pylori eradication remained free of acid-inhibiting medications, and after 1 year 78% were still free from acid-suppression therapy. This suggests that H. pylori eradication is an effective way to halt long-term use of acid suppressing medications.

Based on a review of the literature, we have decided to target patients who are taking proton pump inhibitors

1. As an extension of a post-anesthetic or in-hospital prescription; or
2. After treatment with an h. pylori eradication regimen; or
3. For greater than 8 weeks to heal an ulcer and are not at risk for ulcer recurrence; or
4. For treatment of GERD which is currently controlled; or
5. With no indication for PPI use.

For patients who are found to be suitable candidates for PPI discontinuation, we will fax their doctor for approval. This will be followed with a recommendation that they start working towards PPI discontinuation, initially using their PPI every other day and Gaviscon® to help with rebound acid hyper-secretion. If their symptoms are still successfully controlled after a period of decreased PPI therapy, we will encourage them to try stopping their PPI medications altogether.

Methods

We prepared a consent form for eligible patients (*Appendix A*), as well as a weekly survey for patients after they started decreasing their PPI use (*Appendix B*). We then wrote a letter to nurse practitioner and physicians at the Leader Medical Clinic explaining the purpose of our trial and asking for their input (*Appendix C*).

Using our medication records, we identified 220 patients at our pharmacy who had taken a PPI since July 1, 2007. We then looked for patients with known contraindications to PPI discontinuation and removed them from our list of targets. After printing an article in the Leader News to raise awareness of our program, a copy was sent to 192 patients (*Appendix D*) who we thought may be eligible for PPI discontinuation. When these patients came in to the pharmacy, we evaluated whether they were potential candidates for decreased PPI use. If they met the criteria, we faxed their doctors for approval, then recommended that they try decreasing their use to every other day, and using Gaviscon® for relief of symptoms due to initial rebound acid hypersecretion. If these patients were able to control their symptoms after a month of decreased PPI use, they were encouraged to discontinue their PPIs altogether.

Results

Coming Soon!

Appendix A Patient Screening Tool

Decreasing the Unnecessary Use of PPI's

February 2008

Patient's Name _____

Taking PPI _____

1. How long have you been taking this medication for?

2. Why did you start taking this medication?

3. Is this condition under control?

4. Would you be willing to try discontinuing this medication?

Name _____

Date _____

Appendix B Patient Symptom Questionnaire

Decreasing the Unnecessary Use of PPI's

Name _____

Date _____

Please rate your symptoms since discontinuing your proton pump inhibitor. We encourage you to complete this questionnaire weekly. However, we understand this may not be possible, but please ensure that you date each form that you complete.

1. Did you experience any heartburn this week?

Yes

No

2. If yes, how would you rate it?

- Mild (only an annoyance)

- Moderate (caused some discomfort)

- Severe (caused significant pain)

3. Did you experience any acid regurgitation this week?

Yes

No

4. Did you experience excessive burping or belching this week?

Yes

No

5. Did you experience any abdominal bloating this week?

Yes

No

Did you experience anything else out of the ordinary that you feel may be due to decreasing/discontinuing your proton pump inhibitor? If yes, please explain.

Thank you for taking the time to fill out this questionnaire. Please save these forms and return them to Stueck Pharmacy the next time you are in.

Appendix C Letter To Physicians

Stueck Pharmacy Ltd.
Box 400
Leader SK
S0N 1H0
Phone – (306) 628-3744
Fax – (306) 628-4378

Dear Dr. _____

February 2008

We at Stueck Pharmacy are interested in decreasing the unnecessary use of proton pump inhibitors in community pharmacy. This will reduce costs to both patients and the provincial drug plan. It will also simplify medication regimens and stop exposing these patients unnecessarily to potential side effects of proton pump inhibitors (including, among others, headache, diarrhea, constipation, and predisposition to hip fractures).

Target patients are those who are taking PPI's for the following reasons:

1. As an extension of a post-anesthetic prescription
2. Following H. pylori eradication
3. Used the PPI for up to 8 weeks to heal an ulcer
4. Without a clear indication for PPI use

We understand that there are instances that necessitate the use of PPIs. Patients will not be included in this trial if they have been diagnosed with an esophageal stricture, Barrett's esophagus, or are presumed to have extra-esophageal manifestations of GERD (such as asthma symptoms, non-cardiac chest pain, or chronic cough). Participation in this trial is completely voluntary, and we will encourage treatment in those who experience symptoms, although we may recommend that they try something else before resuming PPI therapy.

We would like to evaluate patients on PPI therapy and determine if they are candidates for discontinuation. We will reach these patients primarily when they come in to refill their prescription, but would appreciate if you would spread the word to suitable patients in your clinic as well. With your approval, we will encourage those patients who we feel do not require therapy, to attempt to discontinue their PPI. Of course, if at any time the participants or you feel that PPI therapy is vital, it will be immediately resumed.

If you have any questions or comments regarding this proposed program, please do not hesitate to contact the pharmacy. We welcome any input and suggestions you can offer!

Thank you,
Erica Peterson, BSP candidate 2008



This is a copy of an article which was printed in the Leader News. I think that it may be of interest to you. You have received this letter because our records indicate that you have taken a proton pump inhibitor.

Proton pump inhibitors (PPIs) are a class of drugs which decrease the acidity of your stomach. Drugs which are included in this class include esomeprazole (Nexium®), lansoprazole (Prevacid®), omeprazole (Losec®), pantoprazole (Pantoloc®), and rabeprazole (Pariet®). PPIs are used to treat ulcers, heartburn, and gastroesophageal reflux disease (GERD). They are often given before general anesthetic to reduce stomach acidity.

The length of time that you should take a PPI varies. If the medication is treating an ulcer, heartburn, or GERD, therapy may extend 4 – 8 weeks. If you have been given a PPI prior to anesthetic, therapy is generally for a month. Long-term PPI use is appropriate in some instances, such as for prevention of stomach bleeding in high risk patients, and treatment of complications due to GERD.

The problem is that people often start treatment with a PPI for a condition that does not require indefinite PPI therapy, but never stop taking it. This complicates their medication regimens, carries significant economic implications, and exposes them to the side effects of PPIs (which include, but are not limited to, headache, diarrhea, stomach pains, gas, and impaired absorption of Vitamin B₁₂ and iron). The monthly cost ranges from \$26.42 (rabeprazole 10 mg) to \$89.78 (lansoprazole 30 mg) per patient. The vast majority of patients do not require long term therapy with PPIs, and when people continue taking these medications forever, the only real winners are the drug manufacturers. Studies have indicated that it is possible, safe, and cost effective to avoid long-term use of PPIs.

We at Stueck Pharmacy believe in evidence based, appropriate use of medications. If you are taking a PPI, we encourage you to consult with us the next time you are in the pharmacy. If you are willing and a suitable candidate for PPI discontinuation, we will work with you and your physician to discontinue this medication.

We will pilot this program in our pharmacy, and see how many patients are able to successfully discontinue their PPIs. Our next goal will be to see if we can get each pharmacy in Saskatchewan to encourage a minimum of 3 patients to discontinue PPIs.

Assuming that there are 345 pharmacies in Saskatchewan:

$$\underline{\$89.78 \text{ (lansoprazole 1 month)} + \$26.42 \text{ (rabeprazole 10 mg 1 month)}} = \underline{\$58.10/\text{month}}$$

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345 pharmacies x \$58.10 per PPI prescription x 3 patients per pharmacy = \$60,133.50 savings per month to Saskatchewan people and the health system, which translates to \$721,602.00 per year. If you were to extrapolate this nationally, savings could range as high as 25 million dollars annually. This is a step in the right direction to limiting expenditures for unnecessary prescription drugs.

Thank you! Erica Peterson, BSP candidate 2008

References

1. Lee TJ, Fennerty MB, Howden CW. Systematic review: is there excessive use of proton pump inhibitors in gastro-oesophageal reflux disease? *Alimentary Pharmacology & Therapeutics* 2004; 20:1241-1251.
2. Bjornsson E, Abrahamsson H, Simren M, Mattson N, Jensen C, Agerforz A, Kilander A. Discontinuation of proton pump inhibitors in patients on long-term therapy: a double-blind, placebo-controlled trial. *Alimentary Pharmacology & Therapeutics* 2006; 24, 945-954.
3. Hughes DA, Bytzer P, de Herdt D, Dubois D. Economic Analysis of On-Demand Maintenance Therapy with Proton Pump Inhibitors in Patients with Non-Erosive Reflux Disease. *Pharmacoeconomics* 2005; 23(10): 1031-1041.
4. De Wit NJ, Quintero AO, Numans ME. Helicobacter pylori treatment instead of maintenance therapy for peptic ulcer disease: the effectiveness of case-finding in general practice. *Alimentary Pharmacology & Therapeutics* 1999; 13: 1317-1321.