Cost Reduction and Optimization of Proton Pump Inhibitor Therapy

Introduction

The average Canadian family physician devotes an estimated 7% of their practice to the management of dyspepsia, a condition thought to affect 29% of the general population in Canada[1]. Dyspepsia is defined as a "symptom complex of epigastric pain or discomfort thought to originate in the upper gastrointestinal tract, and may include any of the following symptoms: heartburn, acid regurgitation, excessive burping/belching, increased abdominal bloating, nausea, feeling of abnormal or slow digestion, or early satiety"[1]. Several organic causes of dyspeptic symptoms exist: duodenal or gastric ulcers, reflux esophagititis or gastroesophogeal reflux disease (GERD), and gastric or esophageal cancer. In Canada, the overall frequency of GERD is 20-40%, and has surpassed ulcers as the most probable cause of dyspeptic symptoms[1].

The majority of patients presenting to primary care physicians with dyspeptic symptoms are treated empirically. Endoscopy is generally reserved for those patients with refractory or alarm symptoms (dysphagia or bleeding), and may actually be misleading as greater than 50% of patients with GERD show no abnormalities on endoscopy[1-2].

The Canadian Dyspepsia Working Group considers both proton pump inhibitors (PPIs) and H_2-receptor antagonists (H_2-RAs) first line agents in the treatment of dyspepsia[1]. However, evidence continues to suggest PPI efficacy profiles are superior to H_2-RAs both for dyspeptic symptom relief and ulcer healing. Because of this, PPIs are now considered the drugs of choice in managing patients with peptic ulcer disease (PUD) and GERD[2-4].

All five PPIs available in Canada (esomeprazole, lansoprazole, omeprazole, pantoprazole, and rabeprazole) appear to have equivalent efficacy and side effect profiles, and similar dosing regimens. To date, there is no solid evidence to establish one agent as superior to the others[3-4]. Where the difference exists between these agents is in their individual acquisition costs. As can be seen in Table 1, rabeprazole has a significantly lower acquisition cost than the other agents. In Saskatchewan, all PPIs require Exceptional Drug Status (EDS) before the provincial government will assume any of their costs. EDS criteria for the PPIs can be found in Appendix I.

In an era of limited healthcare spending, drug costs to both the individual patient and the healthcare system (namely through provincial drug plans) are significant. The purpose of this study is to measure the clinical response, as well as the individual and provincial cost savings of patients currently on PPI therapy who are switched to the less costly rabeprazole.

Table 1 –Comparative Costs of PPIs Listed on Saskatchewan Formulary*

Drug	Acquisition Cost (per dose)
Omeprazole 10mg	1.8988
Omeprazole 20mg	2.3900
Lansoprazole 15mg or 30mg	2.1700
Pantoprazole 40mg	2.0615
Rabeprazole 10mg	0.7053

*Saskatchewan Health Formulary 53rd ed. July 2003-July 2004.

Methods

Patient Selection

The local community pharmacy database was searched, and patients were selected based on the following criteria: older than 18 years of age, currently taking either lansoprazole, omeprazole or pantoprazole, currently under the care of one of the participating physicians, refilling PPI medication on a regular monthly basis. Patients who were pregnant or breastfeeding were not included. It should be noted that patients currently receiving esomeprazole were not included in the study, as esomeprazole is not eligible for coverage by the Saskatchewan Drug Plan.

The compiled lists were then sent to each of the respective participating physicians for their review. Any patients they felt who would not benefit from this study were excluded. A standing order was then given by each physician to switch the selected patients from their current PPI therapy to the appropriate rabeprazole dose (Appendix II). The standing order also included a protocol for re-initiating previous PPI therapy should the patient not respond to rabeprazole. Medication changes were made when the patient refilled their PPI at the pharmacy, or during their next physician visit, whichever came first. At the time of the medication change, each patient was given a consent letter outlining the purpose of this study, their physician's approval, a protocol should they experience any adverse effects, and an estimate of their potential cost savings (Appendix III). If the patient agreed to participate in the study one copy of the consent letter was signed and retained, and one copy was sent with the patient.

Outcomes

The primary clinical outcome of this study is the relief of dyspeptic symptoms. The primary economical outcome was the actual dollar savings to the individual patient, the Saskatchewan Prescription Drug Plan (SPDP), and third party payers.

Outcome Measurements

Patients' history of dyspepsia, including initial presenting symptoms, was collected from a medical chart review done by the clinical primary care pharmacist. If this information was unavailable from the chart, it was obtained from the patient. The clinical outcomes were measured using a patient questionnaire. At the time of the medication change, patients were given a short questionnaire evaluating their symptom relief and any adverse effects experienced (Appendix IV). Patients were instructed to complete the questionnaire during the next four weeks and return it to the pharmacy when they collected their next month of medication.

The economical outcomes were calculated manually by subtracting the cost of a patient's rabeprazole therapy from the cost of their previous PPI therapy. Cost savings to the SPDP and third party payers were calculated in the same way, based on the percentage that they contributed. Dispensing fees were calculated at the maximum provincial fee, although they vary between pharmacies. For those patients who pay a flat rate for each prescription regardless of the medication, only cost savings to the SPDP and/or third party payers could be calculated.

Results

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References

1. van Zanten V, Flook N, Chiba N, et al. An evidence-based approach to the management of uninvestigated dyspepsia in the era of *Helicobacter pylori*. CMAJ. 2000; 162: S3-S22.

2. van Pinxteren B, Numans M, Lau J, et al. Short-term Treatment of Gastroesophageal Reflux Disease – a Systematic Review and Meta-analysis of the Effect of Acid-suppressant Drugs in Empirical Treatment and Endoscopy-negative Patients. J Gen Intern Med. 2003; 18: 755-763.

3. Vakil N, Fennerty B. Systematic Review: Direct Comparative Trials of the Efficacy of Proton Pump Inhibitors in the Management of Gastro-Oesophageal Reflux Disease and Peptic Ulcer Disease. Aliment Pharamcol Ther. 2003; 18: 559-568.

4. Welage LS, Berardi RR. Evaluation of Omeprazole, Lansoprazole, Pantoprazole, and Rabeprazole in the Treatment of Acid-Related Diseases. J Am Pharm Assoc. 2000; 40: 52-62.

<u>Appendix I</u> -- Saskatchewan Prescription Drug Plan (SPDP) Exceptional Drug Status (EDS) Criteria for Proton Pump Inhibitors

(a) For a maximum of 8 weeks in treatment of peptic ulcer disease, which includes gastric and duodenal ulcers, in patients not responding or experiencing unusual or severe adverse reactions to a reasonable trial with H_2 blockers, sucralfate or misoprostol. *Coverage for a repeat treatment will be approved only after a 3-6 month period of no treatment or prophylaxis with an H_2 blocker, sucralfate or misoprostol*.

(b) For one year in treatment of symptoms of gastroesophageal reflux disease (GERD). *It was noted that patients with non-erosive GERD could potentially be reduced to step-down therapy with an H_2 antagonist depending on symptom resolution*.

(c) For one year in treatment of severe erosive esophagitits and Zollinger-Ellison Syndrome. *This is renewable on a yearly basis*.

(d) For one week for eradication of H. pylori-related infections in individuals with peptic ulcer disease. *Provisions will be made for additional coverage in treatment failures.*

(e) First-line prevention of gastroduodenal hemorrhage in high-risk patients with prior history of gastroduodenal bleeds for whom anticoagulant, glucocorticosteroid or NSAID therapy cannot be avoided. *Coverage is renewable on a yearly basis for patients if discontinuation of offending agents or replacement with less damaging alternatives is not feasible.*

(f) For a maximum of 8 weeks in patients discharged from hospital, on a proton pump inhibitor, following a gastroduodenal bleed.

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*Criteria taken directly from SPDP Formulary (July 2003 – July 2004)

*Note that esomeprazole (Nexium®), pantoprazole 20mg are not eligible for EDS in Saskatchewan

<u>Appendix II</u> – Physician Standing Order for Switching Patients to Rabeprazole

Stueck Pharmacy Ltd.

Box 400 Leader, Sk. S0N 1H0
Ph(306)628-3744 Fax(306)628-4378

Cost Reduction and Optimization of PPI Therapy

Dr. X

January 2004

Please switch the following patients' current PPI therapy to rabeprazole 20mg (Pariet®) daily *x* 8/52. At the end of this 8-week period, patients will be reviewed to assess whether a dose reduction to rabeprazole 10mg OD is appropriate.

Should patients experience a recurrence of dyspeptic symptoms, or any adverse effects related to the rabeprazole, previous PPI therapy is to be re-initiated.

<u>Omeprazole 20mg (Losec®)</u> Patient X

<u>Pantoprazole 40mg (Pantaloc®)</u> Patient X

<u>Lansoprazole 30mg (Prevacid®)</u> Patient X

_____ _____

Dr. X Date

Appendix III – Patient Consent Form

Stueck Pharmacy Ltd.

Box 400 Leader, Sk. S0N 1H0
Ph(306)628-3744 Fax(306)628-4378

Cost Reduction and Optimization of PPI Therapy

January 2004

Dear _____,

Together, with the physicians at the Leader Medical Clinic, we are conducting a small study to determine the cost savings to patients and drug plans when certain stomach, or ulcer, medications (Losec®, Pantaloc®, and Prevacid®) are changed to a similar yet less expensive alternative (Pariet®). Pariet® works to relieve heartburn and help heal ulcers in exactly the same way, and has the same potential side effects as the other three medications. However, Pariet® costs considerably less. We have estimated your monthly savings to be approximately _____.

Because you are currently taking _____, we are asking you to participate in this study. Should you agree, your doctor has approved your _____ be changed to Pariet®. If at any time you feel that Pariet® is not working for you, or that you are experiencing any intolerable side effects, simply let us know, and you will be changed back to your original medication.

All data collected and reported throughout this study will contain no personal information, and confidentiality is assured. Please note that your participation in this study is totally voluntary and you are able to withdrawal from the study at any time. If you have questions or concerns, please do not hesitate to contact the pharmacy.

By signing below you are agreeing to participate in the study, and are verifying that you have read and understood the above information.

_____	_____	_____
Patient	Witness	Date

Appendix IV – Patient Symptom and Side Effect Questionnaire

Stueck Pharmacy Ltd.

Box 400 Leader, Sk. S0N 1H0
Ph(306)628-3744 Fax(306)628-4378

Cost Reduction and Optimization of PPI Therapy

January 2004

Please rate your symptoms since switching to Pariet® based on the following scale:

1	No symptoms at all
2	Once or twice in a month
3	Once weekly
4	Two to four times in a week
5	Almost every day

1. How often did you experience heartburn?

   1 2 3 4 5

2. How often did you experience acid regurgitation?

   1 2 3 4 5

3. How often did you experience excessive burping or belching?

   1 2 3 4 5

4. How often did you experience abdominal bloating?

   1 2 3 4 5

5. How often did you experience nausea?

   1 2 3 4 5

6. How often did you experience a feeling of abnormal or slow digestion?

1 2 3 4 5

7. How often did you experience a feeling of early satiety (feeling “full” after eating)?

1 2 3 4 5

8. How often did you experience headaches?

1 2 3 4 5

9. How often did you experience diarrhea?

1 2 3 4 5

Please list any other symptoms or side effects you feel are related to taking the Pariet®:

_____

_____

_____

_____

_____

_____

Thank you for taking the time to fill out this questionnaire. Please return this form to the pharmacy next time you refill your medication.