Analysis of Nonformulary Use of PPIs and Excess Drug Cost in a Veterans Affairs Population

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ABSTRACT

BACKGROUND: In the Veterans Affairs (VA) health care system, a formulary-based approach without beneficiary cost-share incentives is used to limit the pharmacy cost of proton pump inhibitors (PPIs). However, the effectiveness of this approach in reducing the cost of PPIs is unknown.

OBJECTIVES: To (a) compare cost differences between the formulary PPI (generic omeprazole) and nonformulary PPIs and (b) evaluate reasons for nonformulary PPI use in order to identify opportunities to increase formulary drug use and discourage unnecessary use of nonformulary PPIs.

METHODS: A list of patients with receipt of PPIs from July 1, 2008, through June 30, 2009, was obtained from the Loma Linda VA Healthcare System pharmacy. Subjects with receipt of at least 120 units (capsules or tablets) of any PPI in the study period were considered long-term users.

Demographic information was collected. Pharmacy consult records were reviewed to identify reasons for nonformulary use and dosing regimen of the formulary PPI prior to the switch. Cost analysis was done based on the VA contract prices for the drugs at the time of the study.

RESULTS: Of 58,605 unique patients seen in this VA health care system in the 12-month period from July 1, 2008, through June 30, 2009, 13,713 (23.4%) received a PPI, and of these, 10,483 (76.4%) received at least 120 PPI units and were defined as long-term users. Of the long-term users, 9,462 (90.3%) were on the formulary PPI generic omeprazole, and 1,021 were nonformulary PPI users. Use of nonformulary PPIs (esomeprazole, pantoprazole, lansoprazole, rabeprazole) accounted for 10.5% of the PPI units and 9.7% of the users but 57.3% of total PPI cost. This pattern resulted in \$570,263 in excess spending (i.e., \$570,263 would have been saved in the study period if the nonformulary PPI users had used the formulary drug). The most common reason for nonformulary long-term PPI use was persistent symptoms ($n=901$, 88.2%). Adverse reaction was cited by 111 (10.9%) of nonformulary PPI users, 33.3% ($n=37$) of whom reported diarrhea. Of those who switched to a nonformulary PPI due to persistent symptoms, 363 (40.3%) were on once-daily dosing prior to the switch; 379 (42.1%) were on twice-daily dosing; and 159 (17.6%) were transfers from other places in which prior dosing information was not available in the hospital pharmacy records.

CONCLUSIONS: One-year PPI use prevalence was 23% in this VA population, and long-term use prevalence was 18%. Nonformulary PPI use accounted for 10.5% of the PPI units and 9.7% of the users but 57.3% of total PPI drug cost. Opportunities to reduce nonformulary PPI use in order to reduce overall expenditures on PPIs include verification of optimal formulary PPI use, titration to twice-daily dosing, and confirmation of adverse reaction as being attributable to PPI use.

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What is already known about this subject

- In studies conducted from 1991 to 2003, between 0.5% and 5.0% of the population used antisecretory medications on a long-term basis and were identified using a variety of definitions ranging from 1 repeated prescription over 12 months to continuous therapy for periods ranging from 4 to greater than 12 months.

What this study adds

- In a sample of veterans using PPIs long term (defined as receipt of 120 units or more during a 1-year period), the 10% who used a PPI other than the formulary PPI, generic omeprazole, accounted for 57% of PPI cost.
- Reported reasons for nonformulary PPI use included persistent symptoms (88%) and adverse reaction to the formulary PPI (11%). Although the Veterans Affairs health care system requires a pharmacy consult to permit nonformulary PPI use, there is no clear guideline for what constitutes therapeutic failure or intolerance, and there are opportunities to reduce nonformulary PPI use that include verification of optimal use of the formulary drug and investigation of whether a reported adverse reaction is attributable to the PPI.

More than 119 million prescriptions for proton pump inhibitors (PPIs) were filled in 2009, making this class of drugs, at \$13.6 billion in sales, the third-highest in sales in the United States.¹ PPIs are primarily used for the management of gastroesophageal reflux disease (GERD) and its complications. Most users of PPI are long-term users, which varies from 1 repeated prescription over 12 months to continuous therapy for periods ranging from 4 months to more than 12 months.² There is currently no consensus definition of long-term users,² and intermittent PPI use is often included in the definition of "long-term" use. Various studies conducted between 1991 and 2003 have found that between 0.5% and 5.0% of the population used antisecretory medications on a long-term basis.³⁻¹⁰

The Veterans Affairs (VA) health care system, unlike most private health systems, does not use beneficiary cost-share incentives for formulary management. In incentive-based formularies, the patient's copayment increases for the use of more expensive nonformulary medications. At the VA, however, the patient's copayment is the same regardless of the formulary

status of the medication. The VA health system has formulary and nonformulary PPI use without a clear guideline on what constitutes a formulary PPI failure. To use a nonformulary PPI, a pharmacy consult is required in which the prescriber is required to state the PPI currently being used by the patient, the dose, the reason for the change to a nonformulary PPI, and the name and dose of the nonformulary PPI. The nonformulary drug is usually approved if the reason for change is persistent symptoms or presence of an adverse reaction (e.g., nausea, diarrhea, abdominal pain).

At a large VA health system, the formulary PPI is generic omeprazole. At the time of the study, the cost to the VA of omeprazole 20 milligrams (mg) was \$0.13 per capsule, while the costs per unit for nonformulary PPIs were \$0.82 for pantoprazole 20 mg, \$2.72 for rabeprazole 40 mg, \$3.01 for lansoprazole 15 mg, and \$3.19 for esomeprazole 20 mg. It is unknown whether use of a nonformulary PPI without beneficiary cost-share incentives is effective at limiting PPI expenditure. The aim of this study was to compare cost differences between the formulary PPI and nonformulary PPIs and to identify reasons for use of a nonformulary PPI in order to identify opportunities to increase formulary drug use and discourage unnecessary nonformulary use of PPIs.

Methods

Study Design and Patient Population

The study was a cross-sectional assessment of patients seen at the Loma Linda VA Healthcare System. The Loma Linda VA Healthcare System consists of a medical center affiliated with a major university and 5 community clinics. The study sample included all unique patients with receipt of at least 120 units of PPI between July 1, 2008, and June 30, 2009. The definition of long-term use was similar to the one used by Reimer and Bytzer (2009) in which patients with receipt of prescriptions for at least 120 tablets of any PPI in the previous 12 months were considered long-term users.⁵ This definition includes on-demand (intermittent) users of PPI, who on average use 1 tablet or capsule of PPI every 3-4 days, equivalent to at least 120 tablets or capsule per year.^{11,12} Because 90-day supplies may be dispensed in the VA clinic pharmacies or by mail order, long-term PPI users in the present study could include patients with as little as 1 dispensing.

Data Collection and Analysis

A clinical informatics pharmacist provided a list of all patients who received a PPI from July 1, 2008, through June 30, 2009, including the name of the PPI and the total number of PPI units dispensed to each patient. The list was revised to include only those patients who received at least 120 units of PPI in the study period. Demographic information including age, gender, and ethnicity was obtained from the electronic medical record.

Pharmacy consults (part of the patient's medical record) for nonformulary PPI were reviewed by the investigators to iden-

tify the reason for switching to a nonformulary PPI. The dosage regimen of the PPI used prior to the switch was noted.

The cost comparison was based on PPI units dispensed in the study period and the unit price of the PPI (according to the VA contract price at the time of the study). This study was approved by the Institutional Review Board (IRB) of the Loma Linda VA Healthcare System.

Results

Of the 58,605 unique patients seen in this VA health care system in the 12-month period from July 1, 2008, through June 30, 2009, 13,713 (23.4%) received a PPI. Of these PPI users, 10,483 (76.4%) received at least 120 PPI tablets and were defined as long-term users. Therefore, the prevalence of long-term PPI use was 17.9% in this patient population. The mean (standard deviation) age was 67 (13) years; 92% were aged 50 years or older; and 94% were male. Ethnicity was documented as known in only 3,647. Of these, whites were 76%, and the rest were nonwhites.

Overall, 9,462 (90.3%) of long-term PPI users were on generic omeprazole, indicating that most patients were prescribed the formulary PPI. Pantoprazole was used by 731 (7.0%) and lansoprazole by 176 (1.7%). Rabeprazole and esomeprazole were each used by 57 (0.54%) of long-term PPI users. In total, 1,021 (9.7%) of long-term PPI users were on a nonformulary PPI. A total of 3,577,635 capsules of generic omeprazole was dispensed in the study period. The number of nonformulary PPI units dispensed was 419,406. Formulary and nonformulary PPI costs accounted for \$465,092.55 and \$624,785.46 respectively (Table 1). Formulary (omeprazole) PPI use accounted for 89.5% of the PPI units and 90.3% of the users but only 42.7% of total PPI drug cost. The 1,021 nonformulary PPI users (10.7%) accounted for \$570,263 in excess spending (i.e., \$570,263 would have been saved in the study period if the nonformulary PPI users had used the formulary drug; Table 1).

The reasons for switching from generic omeprazole to a nonformulary PPI were persistent symptoms ($n=901$, 88.1%), adverse reactions ($n=111$, 10.9%), and presence of percutaneous endoscopic gastrostomy (PEG) tube ($n=9$, 0.9%). Of those who switched to a nonformulary PPI due to persistent symptoms, 363 (40.3%) were on once-daily dosing prior to the switch; 379 (42.1%) were on twice-daily dosing prior to the switch; and 159 (17.6%) were transfers from other settings in which prior dosing information was not available in the hospital pharmacy records. The most common adverse reactions were diarrhea (37, 33.3%), nausea and vomiting (20, 18.0%), abdominal pain (16, 14.4%), headaches (10, 9.0%), rash (5, 4.5%), hives (4, 3.6%), and edema (3, 2.7%). Dizziness, gynecostasia, lethargy, bloating, and flatulence had 2 (1.8%) cases each. Myalgia, tachycardia, pruritus, cough, lightheadedness, and constipation each contributed 1 (0.9%) adverse reaction case.

TABLE 1 Cost Differences Between Formulary and Nonformulary Long-Term PPI Users (July 1, 2008 – June 30, 2009)

Proton Pump Inhibitor	Patients n (% Total)	Mean [Median] Units Per Patient	Units Per Year	Cost Per Unit (\$) ^a	Total PPI Cost (\$)	Excess PPI Cost in \$ (% Total Excess Cost)	Mean Cost Per Patient Per Year (\$)
Formulary							
Omeprazole 20 mg	9,462 (90.3)	378 [360]	3,577,635	0.13	465,093	-	49
Nonformulary							
Pantoprazole 40 mg	731 (7.0)	396 [360]	289,480	0.82	237,374	199,741 (35.0)	325
Lansoprazole 30 mg	163 (1.6)	474 [390]	77,186	3.01	232,330	222,296 (39.0)	1,425
Rabeprazole 20 mg	57 (0.5)	421 [360]	23,970	2.72	65,198	62,082 (10.9)	1,144
Esomeprazole 40 mg	50 (0.5)	427 [360]	21,330	3.14	66,976	64,203 (11.3)	1,340
Lansoprazole 15 mg	13 (0.1)	353 [360]	4,590	3.01	13,816	13,219 (2.3)	1,063
Esomeprazole 20 mg	7 (0.1)	407 [450]	2,850	3.19	9,092	8,721 (1.5)	1,298
Nonformulary subtotal		412.8 [360]	419,406	2.65	624,785	570,262 (100.0)	1,094
Total			3,997,041		1,089,878		

^aVA contract price.

mg = milligram; PPI = proton pump inhibitor; VA = Veterans Affairs.

Discussion

In this study, the prevalence of long-term PPI use was 18%. This prevalence rate was higher than most published estimates. Previous studies reported a prevalence rate between 0.5% and 5.0%.³⁻¹⁰ The definition of long-term use varied among the published studies, and some earlier studies included histamine-2 (H2) receptor blockers in the overall estimates. Lassen et al. (2004) considered at least 180 daily doses of antisecretory medication (PPI or H2-blocker) per patient per year as long-term use.³ Jacobson et al. (2003) considered patients on more than 90 days of PPI or H2-blocker as “chronic” use.⁴ Goudie et al. (1996) defined long-term antisecretory use as at least 1 repeat (refill) prescription,⁶ and Hungin et al. (1999) defined long-term PPI use as at least 1 repeat prescription in the last 12 months.⁷ Ryder et al. (1994) considered continuous treatment for 6 months or more.⁸ Boutet et al. (1999) considered all repeat prescriptions.⁹ Rubin et al. (1995) considered patients who had received continuous treatment (10-month supply in the previous year) and intermittent therapy (6-10 month supply in the previous year) as long-term use.¹⁰

Using the same definition of long-term use as in the present study (i.e., at least 120 PPI units in the past year), Reimer and Bytzer (2009) found a prevalence of 2.1% long-term PPI use,⁵ compared with 18% in the present study. The reasons for this unusually high prevalence of long-term PPI use in the present study are unknown. One possible explanation was the low threshold for definition of long-term use in the present study (e.g., 120 units could have been dispensed in 1 prescription with twice-daily dosing and a 60-day supply). Second, the veteran population is typically older, obese, male-dominated, and with high prevalence rates of alcohol and tobacco use.¹³⁻¹⁵ These characteristics are often associated with prevalence of GERD. The age and gender distribution seen in this study

closely resembles that of the overall VA population in this health system.

As expected, the most common reason for switching from a formulary PPI to nonformulary PPI was persistent symptoms. When adverse reaction was cited as a reason for switching to a nonformulary PPI, it was mostly gastrointestinal in nature. Lansoprazole has a disintegrating formulation that is less likely to clog PEG tubes and is recommended in patients with PEG tubes. Less than 1% of patients on nonformulary PPI had a PEG tube. Forty percent of those who switched to a nonformulary PPI as a result of persistent symptoms were on a once-daily dosing regimen, and the dosing regimen of 18% of the patients was unknown. This pattern is not consistent with the American Gastroenterological Association (AGA; 2008) definition of treatment failure, in which only patients whose symptoms have not adequately responded to twice-daily PPI therapy (daily dose is not mentioned) should be considered treatment failures.¹⁶

The VA health care system requires a pharmacy consult to permit use of a nonformulary PPI, but there is no clear guideline for what constitutes therapeutic failure or intolerance to the nonformulary PPI. In this setting, only 9.7% of all long-term PPI users received nonformulary PPI. However, the majority of PPI cost was still attributable to nonformulary PPI use because the mean cost per patient was higher for nonformulary PPI. The VA contract prices for nonformulary PPIs would have to be significantly lower for the total expenditure to be lower. VA contract prices for PPIs reflect differences between brand and generic drugs. Before the entire class of PPIs become available in generic form and, therefore, are less expensive, we suggest that there is an opportunity to reduce nonformulary PPI use and avoid excess drug cost.

Methods to Reduce Nonformulary PPI Use

Before a nonformulary PPI consult is placed, prescribers should verify optimal use of the formulary PPI. Even though labels on PPI bottles instruct patients to take the medication 30 minutes before a meal, studies suggest that among patients with persistent GERD symptoms, up to 54% of patients use PPIs suboptimally.¹⁷ Patients who report persistent symptoms on a once-daily PPI regimen should have their dosing increased to twice-daily before a nonformulary consult is placed. A review by Liu and Saltzman (2009) suggested that up to 25% of patients with refractory symptoms on once-daily PPI treatment would respond to an increase to twice-daily PPI dosing.¹⁸ A position statement from the AGA also recommends twice-daily dosing in patients with persistent symptoms on once-daily dosing.¹⁶

When adverse reaction is cited as a reason for nonformulary PPI consult, a careful review of the symptoms and all medications the patient is taking should be done. Some of the adverse reactions attributable to PPI use in this study may not have been due to PPI use. The reason for PPI use should be included in the pharmacy consult. Finally, prescribers should be made aware of cost differences between the various PPIs, particularly because no PPI has been shown to be superior to other PPIs.

Limitations

First, the present study was conducted in 1 VA health care system in the Pacific region composed of 1 medical center and 5 community clinics. Our findings may not be generalizable to commercial health plans. Second, the study may not have captured all PPI use because PPI prescriptions could have been filled outside the VA system, and the VA does not cover over-the-counter (OTC) drugs, such as omeprazole OTC. Third, because we did not assess both units dispensed and days supply, it is possible that patients were included in the present study who received as little as 1 prescription of PPI with twice-daily dosing (e.g., 120 units dispensed as a 60-day supply). Fourth, the study did not look at differences in symptom control, health-related quality of life, or lost productivity between long-term formulary and nonformulary PPI users. These factors may contribute to indirect cost.

Conclusions

The study revealed an unusually high prevalence of long-term PPI use among veterans. Most veterans used the formulary PPI. However, based on actual incurred pharmacy costs, nonformulary PPI users accounted for greater PPI cost. Opportunities to reduce nonformulary PPI use in order to reduce overall expenditures on PPIs include verification of optimal PPI use, titration to twice-daily dosing, and confirmation of adverse reaction attributable to PPI.

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DISCLOSURES

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