Implementation of a proton pump inhibitor stewardship program

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Purpose. The development and implementation of a proton pump inhibitor (PPI) stewardship program at a single institution are described.

Summary. Due to the overuse of PPIs and the increasing awareness of the adverse drug events associated with long-term PPI therapy, the pharmacy and internal medicine services of a medical center implemented a PPI stewardship program. All patients admitted to the internal medicine service were evaluated by the PPI stewardship team to determine if they had an appropriate indication for PPI continuation in the hospital as well as after discharge. If patients did not meet specified criteria for continuation of PPI use during hospitalization, PPI therapy was suspended and replaced by as-needed acid suppressive therapy, and the patients received discharge counseling regarding the implemented medication regimen changes. Challenges encountered during program development included establishing appropriate criteria for PPI continuation and determining the best method for discontinuing PPIs in order to reduce the risk of rebound hyperacidity.

Conclusion. In an effort to reduce unnecessary PPI use, a PPI stewardship program was developed and implemented to ensure appropriate continuation of PPIs for patients admitted and discharged from an internal medicine service.

Keywords: antacids, anti-ulcer agents, gastric acid, gastroesophageal reflux, gastrointestinal tract, proton pump inhibitor

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The prevalence of symptomatic gastroesophageal reflux disease (GERD) in the Western world has been estimated to be as high as 20%.[1,2] Proton pump inhibitors (PPIs) are effective agents for the treatment of GERD and other acid-related disorders and are widely prescribed for these indications. PPIs act on the parietal cells in the stomach, inhibiting the $\text{H}^+/\text{K}^+$-adenosine triphosphatase pump, thus suppressing gastric acid secretion.[3]

PPIs, while effective when used appropriately, are also a greatly overused class of medications, as studies have found that up to 30-60% of prescriptions for PPIs may not have an evidence-based indication.[4,5] The reason for the overuse may be that the optimal duration of PPI therapy is not always clear for many conditions. For instance, guidelines for the management of GERD recommend 8 weeks of once-daily PPI therapy to allow symptom relief and healing from erosive esophagitis; however, the guidelines stipulate that, for some patients, twice-daily dosing is appropriate if there is a partial response to once-daily therapy and that maintenance PPI therapy can be continued if they experience symptoms after the PPI is discontinued or have certain complications.[2] Similarly, after an upper gastrointestinal (GI) bleed, the duration of PPI therapy is based on the etiology of the upper GI bleed, which can be unclear.[5,7] Given these and other examples, it is often difficult for clinicians to determine if continued PPI
therapy is appropriate, particularly if the patient is unable to provide an accurate medication history or is in a setting where his or her primary care records are not readily available; this can lead to concern that stopping the PPI may cause harm if a valid indication exists, ultimately resulting in prescribing “inertia” and the long-term continuation of PPIs.

This is a significant concern given that PPIs are not benign drugs and their long-term use has been associated with hypomagnesemia, pneumonia, bone fractures, and enteric infections, such as *Clostridium difficile* infection (CDI) and spontaneous bacterial peritonitis. In addition, there have been some retrospective studies indicating that mortality may be higher in elderly patients treated with PPIs. PPIs have also been identified in the “Beers criteria” as potentially inappropriate medications, with a recommendation to avoid PPI use for more than 8 weeks in patients over 65 years of age unless the benefits outweigh the risks.

Considering these factors, it would be advantageous if facilities could create programs to reduce unnecessary PPI use. We describe our experience with the implementation of a PPI stewardship program at our institution.

**Problem**

The Lexington Veterans Affairs (VA) Medical Center is a 99-bed facility with emergency and inpatient medical-surgical services as well as acute mental health and intensive and progressive care units. There are 2 critical care clinical pharmacy specialists who split their time between the critical care and internal medicine services. In addition, our facility has a team of 5 pharmacists who are responsible for conducting medication reconciliation during transitions of care; this includes conducting admission interviews of all patients to obtain an accurate medication history and performing discharge counseling, with provision of written instructions regarding any changes to the home medication regimen. There are a total of 12 full-time hospitalists working at the medical center who provide care to approximately 250 patients admitted to the internal medicine services each month.

An interprofessional team of hospitalists, pharmacists, and nurses meet on a monthly basis to discuss ways to optimize care in patients admitted by the internal medicine service. The issue of PPI overuse was addressed during one of these meetings because internal analyses had determined that up to half of veterans admitted to the Lexington VA Medical Center were taking a PPI prior to admission. Informal chart reviews and anecdotal reports from physicians and pharmacists suggested that up to 20% of these patients did not have a clear, documented indication for the medication, which is consistent with published research findings.

The benefits of antimicrobial stewardship programs in reducing inappropriate antimicrobial use and healthcare-associated infections are well documented. Our group reasoned that a PPI stewardship program targeting patients admitted to an internal medicine service at our facility could serve a similar purpose, as it would reduce the prescribing of inappropriate PPIs, particularly in our population of patients over 65 years of age, and might reduce the risk of healthcare-associated infections, such as pneumonia and CDI, and prevent adverse drug events associated with long-term PPI use. To develop and implement this program, a PPI stewardship team consisting of 2 pharmacists and 1 hospitalist, with input from 1 gastroenterologist, was created at our facility in January 2016.

**Analysis and resolution**

**Initial planning.** The stewardship team reviewed the literature to determine if there were any published reports of successful PPI stewardship programs or PPI “deprescribing” efforts at other facilities. We also discussed the logistics of the program to evaluate the resources required to undertake such a project. With an estimated 250 patients admitted to the internal medicine services each month and approximately half of those patients taking PPIs regularly, it was determined that a daily review of all patients taking PPIs at the time of admission would be reasonable.

The next step was to determine which criteria would preclude the discontinuation of PPIs at the time of admission. Since there is no evidence to support stress ulcer prophylaxis in noncritically ill patients, it was decided that the only acute care patients who would continue to receive a PPI during hospitalization would be those at an increased risk for GI complications with even brief PPI therapy interruptions. These criteria were largely based on the expert opinion of the gastroenterologists at our facility and the limited evidence available.
The PPI stewardship team determined that patients with Barrett’s esophagus and those with acid-related complications (e.g., upper GI bleeding, erosive esophagitis, ulcers) diagnosed in the 8 weeks before admission (or longer than 8 weeks before admission if there was documentation of persistent symptoms of GERD) would be at increased risk for rebleeding or other GI complications with even short-term discontinuation of PPI therapy. Additionally, the risks of PPI discontinuation in patients with hypersecretory disorders or with esophageal strictures secondary to acid reflux were felt to outweigh any possible benefits from temporarily stopping PPI use. Patients with previous esophageal or gastric surgery (except total gastrectomy), including gastric bypass surgery, were also continued on their PPIs to reduce the risk of complications or marginal ulcer development. Any patients of the VA gastroenterology clinic with a documented indication for PPI therapy were also continued on home PPI regardless of indication, as were any patients whose differential diagnosis at the time of admission included a potential acid-related disorder. In addition, patients with documented previous failed attempts at weaning from PPIs were continued on PPI therapy along with all patients receiving a PPI as part of treatment for Helicobacter pylori infection.

While chronic kidney disease (CKD) alone is not an indication for PPI use, there was concern expressed among the group that discontinuation of PPIs in patients with CKD might prompt them to overuse antacids, some of which contain aluminum or magnesium, which can accumulate in patients with renal impairment. Given that concern, the PPI stewardship team decided that patients with stage 4 or 5 CKD would be excluded from the stewardship program population and that they would instead be referred to the facility’s nephrology pharmacist for evaluation. Also excluded were any patients actively receiving treatment for cancer; all decisions regarding PPI regimens in those patients would be made by the hematology–oncology pharmacist.

**Implementation.** With the patient selection criteria established, the PPI stewardship program was implemented in March 2016. Each day, a report listing all internal medicine patients admitted to the hospital over the preceding 24 hours was generated. For all patients receiving home PPI therapy, a chart review by 1 of the 2 pharmacists on the PPI stewardship team was conducted to determine if there was an appropriate indication for continuation of PPI during hospitalization. Progress notes written by the primary care provider (PCP) and gastroenterologists were reviewed, as were results of past procedures such as esophagogastroduodenoscopy (if available). If the patient met the criteria for continuation of PPI use, there was no intervention. If the patient did not meet the criteria, the team discontinued the PPI and placed orders for 2 acid-suppressive therapies to be used as needed if patients experienced dyspepsia or heartburn symptoms. One order was for an antacid, which was to be used as the first-line agent for symptom relief, and the other order was for a histamine H₂-receptor antagonist to be used if symptoms were not relieved by the antacid; the latter was used as a second-line agent because there have been studies suggesting an association between the use of H₂-receptor antagonists and CDI. In addition, a “placeholder” order indicating that the patient’s PPI had been discontinued was added to the electronic medication administration record. The placeholder order stated that the medication had been discontinued by the PPI stewardship team in an attempt to reduce adverse events associated with PPIs, and providers were directed to use antacids and H₂-receptor blockers in patients with symptoms of dyspepsia or heartburn.

The PPI stewardship team recognized that there may be instances when the primary care team felt a patient would benefit from PPI continuation for reasons that would not necessarily be captured in a chart review. Therefore, whenever a PPI order was discontinued, a PPI stewardship note was entered in the patient’s electronic chart. The attending physician in charge of caring for the patient was alerted to this note so that he or she could use his or her discretion in resuming the PPI as appropriate—for example, if a patient reported previous failed attempts to discontinue PPI therapy or was receiving care for an acid-related complication outside the VA system. In addition, education describing the stewardship program and emphasizing that nurses should contact the primary care team if symptoms of dyspepsia or heartburn persisted despite antacid and H₂-receptor blocker use was provided to the clinical nurse specialists and managers.

The PPI stewardship program also addressed PPI prescribing in the outpatient setting. The PPI stewardship team recognized that there were patients who would not be harmed due to temporary discontinuation of PPI therapy during hospitalization but would benefit from resumed PPI therapy over the long term. To this end, the PPI stewardship team created separate criteria for PPI resumption on discharge. In other words, some patients with discontinued inpatient orders for PPIs were counseled to resume PPI use on discharge, while other patients were counseled to attempt a trial of permanent discontinuation; decisions about which recommendation to make were based on whether there was an evidence-based indication for continuation of postdischarge PPI use. There is clear evidence to support long-term PPI therapy in patients with a history of peptic ulcer disease, erosive esophagitis, or upper GI bleeding; so while their PPIs may have been withheld temporarily during hospital admission, these patients were instructed to resume PPI use upon discharge. In addition, patients taking specified therapies, including anticoagulants, chronic
nonsteroidal antiinflammatory drugs, dual antiplatelet therapy, and chronic steroids, were told to resume PPI use on discharge from the hospital, as there is evidence to support the use of PPIs to decrease the long-term risk of acid-related complications associated with the use of these medications.\textsuperscript{18-21} Based on current evidence,\textsuperscript{22} it appears that chronic steroid use alone does not require gastroprotection. Despite this, patients with chronic steroid use were counseled to resume PPIs on discharge, as the PPI stewardship team found that our population of patients often had additional risk factors, such as NSAID use or a history of ulcers.

If patients did not meet any of the criteria for long-term use of PPIs, they were counseled to attempt a trial of permanent PPI discontinuation on discharge. The team of medication reconciliation pharmacists played an important role in this aspect of the program, as they reviewed PPI stewardship notes and incorporated these recommendations into discharge counseling and documentation. Patients encouraged to attempt a trial of PPI discontinuation were offered an antacid and informed that they could use nonprescription antacids for management of symptoms related to heartburn and dyspepsia; however, these patients were instructed to resume their PPI regimen or talk with their PCP about alternative treatment options if their symptoms persisted. As most patients follow up with their PCP soon after discharge, education about the PPI stewardship program was provided to the facility’s PCPs to ensure continuity of care so that PCPs could reinforce medication regimen changes and facilitate the prescribing of alternative agents if patients experienced rebound symptoms not relieved by antacids.

An additional component of the PPI stewardship program was a pilot program wherein any patient discharged by an internal medicine team with a prescription for an antibiotic was counseled by the medication reconciliation pharmacists to suspend PPI use for the duration of antibiotic therapy (patients who met criteria for inpatient PPI use were exempted). The rationale for this approach was that since antibiotics are associated with the development of CDI, it is possible that concomitant use of PPIs and antibiotics may increase the risk of CDI. That rationale is supported by a recent study that found a significantly higher incidence of CDI in patients taking PPIs along with “high-risk” antibiotics.\textsuperscript{23} It is important to note that currently there is no evidence that this strategy can reduce the risk of CDI or that suspending PPI use for the duration of antibiotic therapy is enough, as there is evidence that the risk of CDI exists for several months after antibiotic receipt.\textsuperscript{24} Future studies will be needed to validate this practice. In cases in which PPI use was suspended due to concurrent antibiotic therapy, the reason for putting PPI therapy on hold was explained to the patient on discharge both orally and in writing, and he or she was instructed to take nonprescription antacids (or provided with a prescription for antacids on request) to relieve symptoms of rebound hyperacidity. After the antibiotic course was completed, patients who met the specified criteria were instructed to resume PPI use; those not meeting the criteria were instructed to continue with the suspension of PPI use, particularly if their symptoms were controlled or could be relieved with use of antacids.

\textbf{Discussion}

Several challenges were encountered during the development of the PPI stewardship program. Before program implementation, the stewardship team had to determine the best approach for PPI discontinuation, as most evidence suggests that some patients may experience rebound hyperacidity after abrupt discontinuation of these agents.\textsuperscript{25} The team spent considerable time researching the literature and, based on the available evidence, determined that a discontinuation strategy involving the tapering of PPI doses or the use of antacids or H\textsubscript{2}-receptor antagonists to control rebound hyperacidity was likely to be the most successful approach.\textsuperscript{26,27} Since part of the stewardship program involved suspension of PPI use in patients receiving antibiotics (a situation that would not lend itself to a PPI taper), the decision was made to simply stop PPI use in patients without an appropriate indication and provide them with antacids and H\textsubscript{2}-receptor antagonists on an as-needed basis.

Another challenge encountered was related to the fact that we could identify no published reports on studies evaluating the risks versus benefits of short-term PPI discontinuation, so it is not known whether this intervention will translate into improved patient outcomes; however, we felt that the possible benefits outweighed any theoretical risks. Moreover, the long duration of PPI pharmacologic action supports the argument that many patients do not require additional doses of PPIs while they are hospitalized, particularly if the length of stay is short. Withholding an unnecessary medication confers several benefits. First, it is consistent with best practices to withhold a medication without an indication.\textsuperscript{28} It also reduces the chance for a medication error to occur and reduces overall healthcare costs and resource utilization. Another benefit is that it may illustrate to patients that they truly do not need a PPI, which is important considering that the placebo effect is thought to play a role, to a certain extent, in the clinical improvements reported by some patients with GERD.\textsuperscript{29}

The PPI stewardship team also recognized that while we had established criteria for appropriate inpatient and outpatient continuation of PPI use, there would invariably be situations in which patients did not technically meet the criteria but in whom continuation would be appropriate due to extenuating circumstances. For example, a patient entering the hospice program may not meet the criteria;
however, if that patient feels that PPI use will make him or her more comfortable, then it certainly might be reasonable to continue PPI therapy. To this end, the PPI stewardship team remained flexible in their implementation of the criteria and used clinical judgment when discontinuing PPI therapy.

The PPI stewardship team also anticipated that the overall rate of outpatient discontinuation of PPI use might be lower than intended, for several reasons. First, despite discharge counseling to suspend PPI use, patients can choose to resume PPI use upon discharge and will presumably still have a supply of the medication at home. In addition, the team did not discontinue the outpatient prescription in the VA system if the patient had any refills remaining in that event, the prescription was placed on hold. That meant that the medication would not be automatically refilled and mailed to the patient but would instead be refilled upon patient request.

Conclusion

In an effort to reduce unnecessary PPI use, a PPI stewardship program was developed and implemented to ensure appropriate continuation of PPIs for patients admitted and discharged from an internal medicine service.

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Additional information

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