Step-Down Treatment of Uncomplicated Gastroesophageal Reflux Disease in Patients Taking Twice-Daily Lansoprazole

Cameron C. Lindsey, PharmD, Maqual R. Graham, PharmD, and Lauri A. Witt, PharmD

ABSTRACT Gastroesophageal reflux disease (GERD) is a common medical problem in which clinical guidelines exist to provide an effective stepwise or step-up approach to therapy. Little information exists in the literature, however, to guide practitioners in initiating step-down therapy in patients whose symptoms are controlled.

A protocol was developed to incorporate efficacious, cost-effective step-down therapy for patients who had been receiving proton pump inhibitor (PPI) therapy at an inappropriate dose and to assess symptom control after a dose reduction. As part of a medication utilization review, a retrospective study involved patients who received a one-month supply of lansoprazole (Prevacid®), TAP, administered twice a day between January 1 and December 31, 1999, at the Kansas City Veterans Affairs Medical Center. Primary care provider notes and esophagogastroduodenoscopy (EGD) results were reviewed for diagnosis of uncomplicated GERD. Patients were contacted by telephone at baseline and at weeks two and four to assess the course of their symptoms following a dose reduction of lansoprazole to once a day.

Forty-seven patients met criteria for step-down therapy. The dose was decreased to once daily in 34 patients (72%); 65% of patients maintained control of GERD symptoms with a once-daily PPI at week two, and 62% maintained control with this regimen at week four. A step-down protocol for patients receiving twice-daily lansoprazole resulted in successful symptom control during this project.

KEY WORDS: gastroesophageal reflux disease (GERD), proton pump inhibitor (PPI), lansoprazole.

INTRODUCTION

The Medical Advisory Panel for the Veterans Health Administration Pharmacy Benefits Management Strategic Healthcare Group (PBM SHG) coordinates the development of guidelines for the pharmacological management of common disease states treated within the Veterans Affairs (VA) system. These documents are based on nationally recognized treatment guidelines and current literature with the purpose of assisting primary care practitioners in clinical decision-making. As a result, if drug therapy is standardized, patient outcomes improve and the use of cost-effective medication is enabled.1

Current guidelines for the treatment of GERD follow a stepwise, or step-up, approach. The first tier consists of nonpharmacological modalities, including lifestyle changes and behavior modification (Table 1).2–4 If a patient does not experience symptomatic relief after a trial of nonpharmacological measures, an antacid is recommended on an as-needed basis.2 A histamine receptor antagonist (H2RA) is then initiated at a standard dose, titrated to the manufacturer’s recommended maximum dose.2–4 If symptoms persist with a maximum dose of an H2RA, a prokinetic agent or a once-daily dose of a proton pump inhibitor (PPI) is recommended to replace the H2RA.2–3 Although it is the standard practice in some institutions to increase the PPI dose to twice daily after unsuccessful once-daily dosing, no published recommendations are available for routine treatment of uncomplicated GERD with twice-daily dosing of PPIs.

Other treatment guidelines, including JNC VI and the Expert Panel Report 2,5 outline a step-down approach to medication management after a patient’s hypertension and asthma, respectively, are stabilized. In contrast, there is no consensus about therapeutic step-down treatment for GERD.

To assess the appropriateness of twice-daily dosed PPIs, a retrospective medication use evaluation (MUE) was completed at the Kansas City Veterans Affairs Medical Center during September 1999 and was then compared with the PBM SHG guidelines. The guidelines suggest twice-daily PPIs and include (1) treatment of complicated GERD, Barrett’s esophagus, GERD refractory to alternate regimens, and hypersecretory conditions and (2) therapy as part of Helicobacter pylori infection.1 For this MUE, the PBM SHG randomly selected 45 patients from a population of 309 at our facility whose prescriptions had been filled, during April 1999, for either oral delayed-release capsules of omeprazole (Prilosec®, AstraZeneca) or oral delayed-release capsules of lansoprazole (Prevacid®, TAP), administered twice daily. By means of the electronic medical record system, patients’ charts were reviewed for indications, endoscopic findings, and previous medications prescribed for the treatment of GERD.

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<table>
<thead>
<tr>
<th>Lifestyle Modifications for Patients with Gastroesophageal Reflux Disease1–4</th>
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<tr>
<td>1. Elevate the head of the bed six inches.</td>
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<tr>
<td>2. Avoid fatty foods.</td>
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<tr>
<td>3. Eat smaller meals.</td>
</tr>
<tr>
<td>4. Avoid eating for at least three hours before lying down.</td>
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<td>5. Lose weight.</td>
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</table>
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Sixty percent (n = 27) of the patients reviewed had an accepted indication for the use of PPIs twice daily. Extrapolated to the whole population of 309, these data indicate that 186 of those patients (60%) whose PPI prescriptions were filled in April 1999 also had acceptable indications for the use of PPIs twice a day.

It is unclear whether the remaining 40% (n = 123) of the total population (n = 309) could have benefited from a dose reduction. If patients could tolerate such a reduction, and assuming that most patients were taking lansoprazole, the institution could potentially save more than $80,000 annually in direct drug costs by stepping down therapy in this remaining 40%.

To provide continual symptom control of GERD while minimizing costs, a protocol was developed locally to implement step-down therapy in patients with uncomplicated GERD who were receiving PPIs twice a day.

METHODS

Patients

This project reviewed Kansas City VA Medical Center patients identified as part of an MUE. In order to obtain an adequate group, all patients receiving a one-month supply of the formulary PPI, lansoprazole, and with a quantity of 60 doses or greater from January 1 to December 31, 1999, were evaluated. Criteria for step-down therapy included an active prescription or a refill within six months of lansoprazole administered twice daily and a diagnosis of uncomplicated GERD based on EGD results and/or primary care provider notes.

Excluded from the study were patients with evidence of strictures, varices, Barrett’s esophagus, or esophagitis on EGD examination. Patients were also excluded if the VA Medical Center was not their primary health care institution. The P&T committee at the VA Medical Center approved the protocol.

Procedures

Patients were identified and then contacted. During the initial assessment, the pharmacist explained step-down therapy and the follow-up telephone schedule. After the initial contact, letters were mailed to patients to provide written instructions regarding the step-down therapy, the follow-up schedule, some general information about GERD, nonpharmacological ways to reduce symptoms, and the pharmacist’s phone number should any questions arise. Patients’ prescriptions were edited in the computer system to reflect the new dosing schedule for future refills. The pharmacist completed follow-up phone calls at two and four weeks after the initial conversation or bimonthly until symptoms were controlled.

Patients were asked questions that were derived from the Gastroesophageal Reflux Disease—Health-Related Quality of Life (GERD–HRQL) Scale to assess severity, frequency, and time of day at which the symptoms occurred, if present, following dose reduction. According to the protocol, if patients’ symptoms worsened, 150 mg of ranitidine (Zantac®, GlaxoSmithKline) was added at bedtime to their regimens and titrated to a maximum dose of 300 mg twice daily. If no relief was achieved at the maximum dose, patients were referred to the gastroenterology service and scheduled for EGD before reinitation of lansoprazole therapy twice daily. Medication profiles were also reviewed for age, weight, height, length of treatment with a PPI, and concomitant medications that might have exacerbated symptoms of GERD.

A Student’s t-test was used to calculate mean and standard deviation (SD) for interval data.

RESULTS

Forty-seven patients who met inclusion and exclusion criteria participated in the project. Thirteen patients either did not have a telephone or were not willing to take part in the project. The remaining 34 patients were contacted by telephone and were subsequently stepped down to lansoprazole administered once a day.

Participants were between the ages of 46 and 83 years (mean ± SD, 64 ± 10.5 years), and most were men (97%). The body mass index (BMI) of the 32 patients, with a recorded height and weight, ranged from 19 to 42 kg/m² (mean ± SD, 28 ± 5.5 kg/m²). The length of treatment with a PPI prior to step-down treatment had ranged from four to 38 months (mean ± SD, 23 ± 10.2 months). A review of the medication profile revealed that 24 patients (71%) were receiving concomitant drug therapy, including calcium channel blockers, exogenous hormone therapy, and theophylline, that was known to relax lower esophageal sphincter (LES) tone, thereby leading to an increase in GERD symptoms.

Twenty-two patients (65%) reported no increased frequency of GERD symptoms during the two-week follow-up call. Four patients (12%) required the addition of ranitidine after experiencing heartburn during the overnight hours. Eight patients (23%) resumed and maintained the twice-daily dose of lansoprazole prior to the follow-up call and could not specify the number of times a day they had experienced heartburn, which they felt was continual throughout the day.

At the four-week follow-up, one patient (3%) who had previously been started on a bedtime dose of ranitidine resumed taking lansoprazole twice daily after symptoms increased from nightly to continuous throughout the day. A total of 10 patients (29%) resumed twice-daily PPIs by the four-week follow-up call. Twenty-one patients (62%) remained symptom-free taking once-daily doses throughout the monitoring period (Table 2).

DISCUSSION

MUEs conducted on frequently prescribed, expensive drug therapy help to identify misuse of medications. Protocols that empower pharmacists to accurately assess treatment can improve patient care while minimizing direct drug costs.

None of the 10 patients whose step-down therapy had failed were started on a medication known to relax LES tone while they

<table>
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<tr>
<th>Follow-up</th>
<th>Once-Daily PPI</th>
<th>Once-Daily PPI + Bedtime H₂RA</th>
<th>Twice-Daily PPI</th>
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<tbody>
<tr>
<td></td>
<td>No. (%)</td>
<td>No. (%)</td>
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<tr>
<td>2 weeks</td>
<td>22 (65%)</td>
<td>4 (12%)</td>
<td>8 (23%)</td>
</tr>
<tr>
<td>4 weeks</td>
<td>21 (62%)</td>
<td>3 (9%)</td>
<td>10 (29%)</td>
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H₂RA = histamine receptor antagonist; PPI = proton pump inhibitor.
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were participating in the step-down program. Furthermore, compared with the sample population, they showed no differences in BMI, length of treatment with a PPI, or use of gastrointestinal-exacerbating medications such as prednisone and nonsteroidal anti-inflammatory drugs (NSAIDs).

Another way to relieve symptoms of GERD is through lifestyle modifications. One such change that can reduce symptoms is weight loss. The National Institutes of Health (NIH) has defined obesity as a BMI of ≥28 kg/m² or greater;⁹ therefore, most of the patients contacted were at increased risk for GERD symptoms as a result of their obesity.²,⁶

Our attempt to develop step-down therapy may have been limited by the method of communication that was chosen. Bias may have been introduced, because only patients who were accessible by telephone were included. Therefore, potentially successful candidates may have unintentionally been excluded. Face-to-face interaction might be superior to telephone conversation in attempts to educate patients about their drug therapy. Objective evaluation of patients’ understanding of verbal directions was not addressed and is a concern because low literacy levels are common among this population. Written directions might have benefited the hearing-impaired.

Compliance is essential to evaluate the success of a step-down program; unfortunately, pill counts were not implemented as part of this protocol because interaction with patients was performed by telephone. Obtaining refill histories would not have been an accurate method of determining adherence, because only short-term assessments were required for completion of the protocol.

Another barrier to evaluating compliance might be the inability to change the directions on the current prescription bottle label. Most veteran patients exhibit polypharmacy, which can impede compliance. Therefore, if patients were confused, they might have reverted to the instructions originally printed on the label instead of implementing the regimen discussed by telephone.

Future research incorporating a step-down approach to PPI therapy should include baseline symptomatology coupled with more objective questioning regarding lifestyle modifications and other medications used to treat symptoms. Using the validated GERD-HRQL scale during both baseline and follow-up questioning would provide a more objective assessment of symptom severity and frequency, increase internal consistency, and provide replicable measurements.⁷

Although cost should never be the sole determining factor in prescribing medication therapy, it may be a limiting factor and should be considered. Lansoprazole accounted for more than 12,000 prescriptions filled and almost $780,000 of the VA Medical Center’s pharmacy budget for 1999. The results of this study are extrapolated to an annual per-patient savings in direct drug cost of $504 for patients who were stepped down to daily lansoprazole therapy.

CONCLUSION

Although it is common for practitioners to continue prescribing therapeutic drugs that have benefited patients, it is most often appropriate to incorporate the use of the lowest effective dose into the clinical decision-making process in order to avoid adverse drug events and to minimize the costs. Guidelines may assist practitioners in providing optimal care, but they do not always indicate the use of the lowest effective drug dose.

Although limitations exist with our process, we suggest that once-daily dosing of lansoprazole is as effective as twice-daily dosing in approximately 60% of our patients and that this plan is also more economical. If symptoms persist with a once-daily PPI, patients may benefit from the addition of another, less expensive medication, such as ranitidine.

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REFERENCES