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Treating Gastroesophageal Reflux Disease (GERD): When Proton Pump Inhibitors Fail

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Abstract

Gastroesophageal reflux disease (GERD) is a very common disease, and one that practitioners will encounter on a regular basis in the clinical setting. Understanding the pathophysiology of GERD, and the effect that proton pump inhibitors (PPI) play in treating acid reflux states is a vital part of understanding what clinical decision making steps to take in the event of limited or no symptomatic relief while taking a PPI. The practitioner must be skilled at assessment and correct diagnosis of GERD as PPIs will only treat gastric acid secretion, and not mechanical functional problems of the esophagus. Consensus of the medical community supports a step-wise approach to treating suspected cases of GERD, and has agreed to considering treatment failure or refractory GERD upon limited or no reduction of symptoms in eight to twelve weeks of PPI therapy. Understanding when referral to gastroenterology is necessary to assess for lower esophageal sphincter (LES) dysfunction, is critical to avoid prolongation of ineffective medication therapy with PPI. While PPIs can control reflux symptoms, and do aid in the healing of esophageal and gastric erosions, they do not seem to reduce the risk of malignant transformation of the mucosa of the distal esophagus, such as Barrett's esophagitis or esophageal adenocarcinoma. PPIs are not without side effects, and careful consideration of the patients with multiple comorbidities, such as osteoporosis, must be considered when long term PPI therapy is deemed appropriate.

Background

Treatment failure on proton pump inhibitors (PPI) is common in clinical practice. Reasons for failure can be associated with patient non-compliance, non-optimized dosing, or taking a PPI at the wrong time of day. PPI failure can also be the direct result of lower esophageal dysfunction. Herregods, Troelstra, Weijnenborg, Bredenoord, & Smoot (2015) found that the true etiology in many patients suffering from refractory reflux symptoms was non-erosive reflux disease (NERD), or functional heartburn. Katz, Gerson, & Vela (2013) report that persistent heartburn and regurgitation while on a PPI occurs in about 40% of patients. Factors found to contribute to failure include duration of disease, obesity, hiatal hernia, other comorbidities such as diabetes mellitus, and patient non-compliance with medications. Proton pump inhibitors (PPIs) have been available for clinical use for over twenty-five years and have greatly improved the lives of countless patients suffering from acid-related diseases (Strand, Kim & Peura, 2016). PPIs have essentially become the go to drug, so to say, to treat patients with several conditions: GERD; peptic ulcers; eosinophilic esophagitis; *H. pylori* infection; Zollinger-Ellison syndrome; and prevention of gastrointestinal ulceration due to non-steroidal anti-inflammatory use (Scarapignato et al., 2016). As with any medication, treatment failure does occur. Additionally, side effects of PPIs have become a growing concern, especially among the elderly, who may have many comorbid conditions and an increased risk of drug-drug interactions due to polypharmacy.

The case study presented will demonstrate a typical patient presenting with GERD and a common approach to treating the problem, such as prescribing a once-daily PPI which in this case is omeprazole. Upon four-week follow-up examination, if the patient is still reporting

reflux symptoms on a once-daily dose of a PPI, what actions can the provider take next to fully control acid reflux symptoms?

The purpose of this paper is to discuss the management of the patient for whom initial treatment with a PPI is not effective. To fully understand this patient population, there will be further elucidation of the common symptoms of acid reflux and its etiologies, the length of treatment, reasons for treatment failure, and indications for referral to gastroenterology.

Case Study

History of present illness: An 88-year-old Caucasian female presents to clinic with complaints of a persistent non-productive cough for the past three months. She reports the cough is worse at night, especially when lying supine. She describes a “tickling” sensation in her throat without sore throat or nasal symptoms or post nasal drip. Further discussion of the problem reveals complaints of frequent, almost daily episodes of heartburn, for which she uses over-the-counter antacids to control. She does describe frank reflux of acidic/sour contents in her mouth, and water brash. She denies any fever, chills, night sweats, shortness of breath, weight loss, or abdominal pain. She reports regular soft bowel movements without any blood in stools, or bleeding from rectum. She does report being treated for bronchitis with antibiotics approximately two months ago, but the cough is persisting.

Review of systems is essentially benign except as stated in history of present illness. She has no known drug allergies. Past medical history includes hypertension, for which the patient has taken Lisinopril 10 mg daily for several years. She denies any surgical history. Social history reveals an elderly female who lives in a single-family dwelling with her spouse. She reports she quit smoking ten years ago after having smoked since her early twenties. She denies

any illicit drug use, but does report having two to three alcoholic beverages nightly, and has done so for quite some time.

Physical exam reveals stable vital signs and an essential negative exam. Oral mucosa and pharynx is pink and moist; dentures are in place. No oral lesions or erosions are appreciated. Lungs reveal clear and equal bilateral breath sounds without wheezes, rhonchi or rales. Heart rate is regular with normal S1 S2, without murmur, rubs, clicks or gallop. TED hose are being worn for 2+ chronic dependent edema. Capillary refill time is less than 2 seconds, and no JVD is present. Pulses are 2+ and intact in all extremities. Abdomen is round and soft, with no tenderness, rebound, or guarding. No masses or hepatosplenomegaly is appreciable. Bowel sounds are present in all four quadrants. Skin is warm and dry, without lesions or rashes.

Initial clinical diagnosis of this patient is gastroesophageal reflux disease, which is presumed to be secondary to daily alcohol consumption. Treatment will begin by prescribing the patient Omeprazole 20mg, 1 capsule by mouth daily. After discussion, the patient is willing to begin lifestyle modifications, which includes cessation of alcohol intake. Patient was also instructed to elevate head of bed with commercially available blocks at least 6 inches. She will avoid eating at least three hours before bedtime, and avoid spicy or greasy food, or any other food she knows will incite reflux, or dyspepsia. She will follow up in clinic in one month, and sooner for any fever, vomiting, abdominal pain, or passing blood in her stools.

Review of Literature

Utilizing the University of North Dakota Harley French Health Sciences Library, the medical database was searched to identify observational studies, randomized controlled trials, systematic reviews, and meta-analysis. The initial literature search utilized the PubMed database. Search parameters in PubMed included the search terms “proton pump inhibitors”,

with “MeSH” terms “treatment failure”, and “refractory GERD”. The search was limited to the English language, articles on human subjects, and limited to the past ten years. A total of 406 journal articles were found. Of these, 42 were relevant to the topic, reviewed, and ten were set aside. Further review of these ten relevant articles, and review of their references and associated bibliographies yielded five additional articles with great topic specificity. CINAHL database search yielded no specifics due to its specificity for nursing and allied health. Cochrane review was also queried, with limited findings on treatment failure management.

GERD

GERD is the symptoms or subsequent complications that occur by the reflux of acidic stomach contents into the esophagus, oral cavity, and/or the lungs. GERD can be further classified into symptomatic with erosions present (ERD), or symptomatic non-erosive disease (NERD) (Katz, Gerson, & Vela 2013). It is a very prevalent disease affecting 27.8% of North American’s (Herregods et. al., 2015), or as many as 10-20% of the population of the Western world (Katz, Gerson, & Vela, 2013). The underlying cause of GERD has been established as inappropriate transient lower esophageal sphincter (LES) dysfunction. According to Tebala (2016), GERD can cause:

- Classical esophageal syndromes, including typical reflux symptoms (regurgitation) and chest pain (heartburn).
- Complicated esophageal symptoms including esophagitis, Barrett’s esophagitis, adenocarcinomas, and esophageal strictures.
- Extra-esophageal syndromes, involving the upper and lower respiratory tract.

Typical symptoms of GERD include the following:

- Heartburn, regurgitation, water brash, dysphagia.

- Odynophagia, belching, sour taste in the mouth.
- Coughing, hoarseness, wheezing (usually at night).
- Substernal/retrosternal chest pain-not induced by activity.

Atypical symptoms have been identified as:

- Epigastric pain, and dyspepsia.
- Nausea, bloating, and belching.

These atypical symptoms may be suspicious for or indicative for GERD, but may coincide or overlap with other disease conditions, such as cholelithiasis (Katz, Gerson, & Vela, 2013).

Effective treatment of GERD is to provide control of reflux symptoms and to maintain esophageal mucosal healing (Kroch, & Madanick, 2017). Other benefits of treatment include prevention of esophageal ulceration, esophageal stricture, Barrett's esophagus, pulmonary aspiration, and upper gastrointestinal bleeding (Dunphy, Winland-Brown, Porter, & Thomas, 2015).

Diagnosis of GERD can be made clinically, with heartburn and regurgitation being the usual chief complaint. Empirical treatment with a PPI, and subsequent resolution of reflux symptoms help establish the diagnosis of GERD. Prior to initiation of treatment for GERD, red flag symptoms should be ruled out. Red flags include the following: abdominal pain; especially epigastric and right upper quadrant pain or tenderness, blood in stools, hematemesis/coffee ground emesis, and dysphagia/achalasia. Chest pain must also be differentiated as occurring with or without activity to rule out cardiac etiology.

A brief review of the pharmacokinetics and pharmacodynamics of PPIs will help elucidate specific reasons for treatment failure with PPIs with relation to patients' disease state. To date, there are currently five PPIs approved by the FDA: lansoprazole, pantoprazole,

rabeprazole, esomeprazole, and dexlansoprazole. All have very similar pharmacologic properties and efficacy. PPIs function by acting upon activated parietal cells and act upon hydrogen/potassium ATPase to inhibit production of acid secretion. With each dose, approximately two-thirds of active proton pumps are inhibited, reducing acid production, and with each subsequent meal, continue to attenuate proton exchange (Strand, Kim, & Peura, 2017). The less acidic the stomach becomes, the greater the absorption of PPIs. Three to five days is needed for gastric acid levels to return to normal, as the hydrogen/potassium/ATPase must again be synthesized in the parietal cells.

Refractory GERD

Several studies in current literature define reflux symptoms as refractory to PPIs when eight to twelve weeks of therapy results in less than 50% resolution of symptoms (Richter, 2014). Determining this rate of failure is difficult in clinical practice as each patient's perception of GERD symptoms is very subjective. Herregods, et. al. (2015) studied patients in the gastroenterology setting who were deemed refractory to PPIs and underwent stationary esophageal monitoring and ambulatory pH-impedance monitoring. Results showed that nearly one-third of patients in the study were found not to have GERD. These findings demonstrate that patients with NERD, or non-erosive reflux, and functional heartburn (FH) make up a large percentage of patients who are failing treatment with PPIs. Some controversy exists in defining refractory patients. Many investigators state that GERD patients who continue to have reflux symptoms on a twice-daily PPI should be considered refractory, where other researchers contended that lack of response to daily PPI therapy is sufficient to be described as refractory (Hershcovici & Fass, 2010).

A nested case-control analysis by Ruigomez, Johansson, Wernersson, Fernandez, & Garcia (2012) found that there may be an association between treatment failure or partial response to PPI therapy and the following variables: The female gender, a diagnosis of anxiety or depression, the initial severity of GERD symptoms at the time of diagnosis, and taking six or more medications at the time of diagnosis. Overall, one in five patients newly diagnosed with GERD in this study showed only partial response to PPIs. Any changes in PPI therapy such as dosage increase or switching PPIs were regarded as partial response or refractory.

Katz, Gerson, & Vela, (2013) conclude that the initial step in management of persistent GERD is optimization of PPI pharmacotherapy by ensuring dosage optimization and patient compliance. It must be noted that research data supporting patient lifestyle modifications is limited (Kroch, & Madanick, 2017). As with many disease conditions, the severity of the patients symptoms should guide the course of treatment.

Lifestyle modifications should remain at the cornerstone of GERD treatment, and practitioners should continue to emphasize basic modifications to improve their symptoms. Modifications include weight loss, especially in patients with BMI greater than 25. Additionally, the following should be avoided: Large meals that will increase gastric pressure and increase the likelihood of reflux, reclining or supine positioning after meals, caffeine in all forms as it has the tendency to relax the LES, trigger foods, and discourage alcohol consumption and use of tobacco products.

Step Wise Approach

Begin GERD management with a step-wise approach based upon severity, or persistence of symptoms. Dunphy, et. al., (2015) detail an algorithm for a step-up/step-down approach: Initial therapy for mild intermittent symptoms may only require lifestyle modifications, the use

of antacids, or the occasional use of an H₂ receptor antagonist, such as ranitidine. Begin with this course of treatment for one month, then step-up for persistent or worsening symptoms with continued diet/lifestyle modifications, and begin scheduled dosing of an H₂ receptor antagonist, or initiate therapy with a once-daily PPI for one month. If reflux symptoms are persisting, step-up to twice-daily PPI, or consider changing to a different PPI. Consider PPI failure after this 8-week course of treatment and refer to surgeon or gastroenterologist. Commonly, after referral to an GI specialist, an EGD will be performed, but in up to 90% of the cases, test results will be normal (Richter, 2014).

Other Agents to Treat Reflux

Since their inception, PPIs have been an interest of study in patients across all ages and of different disease conditions. Tebla (2016), finds that one third of patients with reflux symptoms are symptomatic due to non-acid reflux, from transient relaxation, or mechanical failure of the lower esophageal sphincter, which will be unaffected by PPIs. Tebla (2016), reports that despite the fact that long term PPI therapy is vital to treating acid reflux and helping to prevent associated esophageal mucosal changes and progression to Barrett's esophagus. It is also important to note that the incidence of esophageal adenocarcinoma is on the rise across the world despite the high use of PPIs, and reminds us that PPIs offer protection, but are not appearing to reduce the risk of esophageal or gastric cancers. Additional pharmacologic agents have been studied, such as metoclopramide, to speed gastric transit to alleviate reflux symptoms, but has not shown efficacy (Kroch & Madanick, 2017), especially if no gastroparesis exists. Baclofen has shown effectiveness in reducing transient lower esophageal sphincter relaxations, but its use is limited by its central nervous system side effects which includes dizziness and excessive sedation.

Considerations in Elderly Patients

Many elderly patients often wind up on PPI therapy indefinitely due to their efficacy, and are not monitored and re-evaluated to ensure they are on the lowest effective dose. The Beers criteria in 2015 recommends limiting treatment length to eight weeks except for high risk patients (Merel & Paauw, 2017), due to risks of bone loss and a growing concern for correlation between *Clostridium difficile* infection and PPIs. H2 receptor antagonists use should be observed carefully in elderly patients with renal insufficiency as metal status changes may occur (American Geriatrics Society, 2015). Concerns over decreased calcium, iron, magnesium, and vitamin B12 absorption, decreased bone density and fracture risk, as well as dementia and acute and chronic kidney disease should be prompting clinicians to more carefully consider long term PPI use in the elderly (Merel & Paauw, 2017). Evaluation of the patients quality of life must be considered when opting for long term PPI therapy in patients with osteoporosis, renal insufficiency, high risk for falls, and dementia.

Patients having significant reflux symptoms or chronically taking NSAIDS or corticosteroids should still be treated with PPIs under close monitoring. Long term or chronic treatment with PPIs to decrease gastric acid production is critical in healing gastroesophageal erosions, and preventing the formation or progression of Barrett's esophagus. Nonetheless, research is demonstrating an increasing incidence of esophageal adenocarcinoma throughout the world. PPIs therapy can control GERD symptoms, but a significant number of patients are still progressing on to develop Barrett's esophagus and adenocarcinoma despite PPI treatment (Tebala, 2016).

Review

GERD is very common problem that is encountered in primary care. Patients of all ages can suffer from reflux symptoms. It is important to tailor care to the individual patient. Prior to starting drug therapy, the practitioner should review and encourage lifestyle modifications, when feasible, to help decrease the frequency and severity of acid reflux symptoms. Common lifestyle modifications include:

- Avoid large meals 2-3 hours before bed.
- Alcohol and tobacco cessation.
- Elevate head of bed (6 inches).
- Avoid trigger foods; such as greasy, spicy, caffeine, chocolate, alcohol etc.
- Weight loss as indicated.
- Avoid tight fitting clothing.
- Caution use of NSAIDS, ASA, steroids, or other GI irritants.

Over-the-counters (OTCs), can be useful for patients with rare or very infrequent reflux or dyspepsia. H2 blockers such as cimetidine, ranitidine, or famotidine can be used and are quite effective but do not inhibit acid production as the PPIs do, and are ineffective at healing esophageal erosions. H2 blockers can be used with patients taking a PPI, especially those with nocturnal reflux symptoms. Caution should be taken in the elderly patient due to increased incidence of polypharmacy and increased likelihood of drug-drug interactions. Typical length of treatment is 8-12 weeks when using PPIs, at which time efforts should be made to look at optimizing the patients medication and dosage, and limiting it to the lowest effective dose possible utilizing a step-wise approach to symptomatic relief. Referral to a GI specialist may be

indicated in individuals who are refractory to PPIs for further management and other treatment options (Figure 1).

Take Away Points

Proton pump inhibitors remain very effective medications to treat patients with GERD.

Treatment failure is common, so consider the following points in clinical practice:

- Like nearly all medications, start low and go slow. Titrate the drug to lowest effective dose utilizing a step-wise approach. Chronic use has the potential for risks, but must be weighed against quality of life.
- If suspected, rule out cardiac etiology before initiating therapy with a PPI.
- It is safe to initiate PPI therapy empirically if GERD is suspected and may help confirm the diagnosis.
- If PPI therapy is not completely effective, ensure compliance and that dosing is given half an hour before a meal to optimize acid inhibition. You may consider increasing or doubling the dose, or trying a different PPI, and as always, promote lifestyle modifications.
- Consider treatment failure if limited or no response after 4 weeks of once-daily dosing PPI, or 8 weeks on twice-daily dosing of a PPI.
- Refer patients with persistent GERD symptoms despite lifestyle modifications and PPI therapy to gastroenterology for further treatment and evaluation as indicated.
- Diagnostic testing is not indicated in patients with typical GERD symptoms.

Summation

This author concludes that as providers, reinforcement of lifestyle and diet modifications should occur with every visit for the patient with GERD. GERD symptoms will vary widely

from patient to patient. A common thread in the literature continues to point to the patient's subjective interpretation of GERD symptoms and the incidence of refractory PPI therapy. The step-wise treatment approach has become standardized in assisting with proper diagnosis of GERD and appropriate treatment of patients with acid reflux symptoms. If symptoms are bothersome to the patient after eight weeks of PPI therapy at twice-daily dosing, then referral to a gastroenterologist is warranted. Elderly patients do pose special concerns, but their quality of life should not be overlooked.

References

- American Geriatrics Society (2015). American geriatrics society 2015 updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatric Society*, 63(11), 2227-2246
- Dunphy, L. M., Winland-Brown, J. E., Porter, B. O., & Thomas, D. J. (2015). *Primary care: The art and science of advanced practice nursing* (4th ed.). Philadelphia, PA. F. A. Davis Company.
- Herregods, T. V. K., Troelstra, M., Weijenborg, P. W., Bredenoord, A. J., & Smout, A. J. P. M. (2015). Patients with refractory reflux symptoms often do not have GERD. *Neurogastroenterology & Motility*, 27(9), 1267-1273. doi:10.1111/nmo.12620
- Hershcovici, T., & Fass, R. (2010). Management of gastroesophageal reflux disease that does not respond well to proton pump inhibitors. *Current Opinion in Gastroenterology*, 26(4), 367-378.
- Katz, P. O., Gerson, L. B., & Vela, M. F. (2013). Guidelines for the diagnosis and management of gastroesophageal reflux disease. *American Journal of Gastroenterology*, 108, 308-328. doi:10.1038/ajg.2012.444
- Kroch, D.A. & Madanick, R.D. (2017). Medical treatment of gastroesophageal reflux disease. *World Journal of Surgery*. doi:10.1007/s00268-017-3954-2
- Merel, S. E., & Paauw, D. S. (2017). Common drug side effects and drug-drug interactions in elderly adults in primary care. *Journal of the American Geriatrics Society*. doi:10.1111/jgs.14870

- Richter, J. E. (2014). Current diagnosis and management of suspected reflux symptoms refractory to proton pump inhibitor therapy. *Gastroenterology & Hepatology*, 10(9),547-555.
- Ruigomez, A., Johansson, S., Wernersson, B., Fernandez Cantero, O., & Garcia Rodriquez, L. A. (2012) Gastroesophageal reflux disease in primary care: Using changes in proton pump inhibitor therapy as an indicator of partial response. *Scandinavian Journal of Gastroenterology*, 47(7), 751-761.
- Scarpignato, C., Gatta, L., Zullo, A., & Blandizzi, C., for the SIF-AIGO-FIMMG Group, and on behalf of the Italian Society of Pharmacology, the Italian Association of Hospital Gastroenterologists, and the Italian Federation of General Practitioners. (2016). Effective and safe proton pump inhibitor therapy in acid-related diseases- A position paper addressing benefits and potential harms of acid suppression. *BMC Medicine*, 14(179).
<http://doi.org/10.1186/s12916-016-0718-z>
- Strand, D. S., Kim, D., & Peura, D. A. (2017). 25 years of proton pump inhibitors: A comprehensive review. *Gut and Liver*, 11(1), 27–37. <http://doi.org/10.5009/gnl15502>
- Tebbas, G. D. (2016). Gastroesophageal reflux disease: Are we acting in the best interest of our patients? *European Review for medical and pharmacological sciences*, 20(21), 4553-4556.

Figure 1.

Refractory GERD Management Algorithm.

Reproduced from Hershcovici & Fass, 2010.

