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BACKGROUND AND OVERVIEW	
Article Title/Citation	Hansen AN, Bergheim R, Fagertun H, Lund H, and Moum B. A randomized prospective study comparing the effectiveness of esomeprazole treatment strategies in clinical practice for 6 months in the management of patients with symptoms of gastroesophageal reflux disease. <i>J Clin Pract.</i> 2005; 59: 665-671.
Study objectives/purpose	The objective of this study was to compare continuous esomeprazole, on demand esomeprazole, and continuous ranitidine in terms of effectiveness and costs (indirect and direct).
Brief background	One of the most common chronic conditions treated today is gastroesophageal reflux disease (GERD). Proton Pump Inhibitors (PPIs) and H ₂ blockers are both common treatments for GERD. Current literature supports continuous PPIs as the superior treatment for relieving and preventing symptoms of GERD.
Funding sources	AstraZeneca
METHODS	
Study design and methodology	This study was a prospective, randomized, open, parallel group study. The first 4 weeks of the study was the control phase followed by a 6 month follow-up phase. For the first 4 weeks, patients received esomeprazole 40mg daily. After the completion of those 4 weeks patients who were symptom free (<1 day with mild heartburn in 7 days) were randomized to one of the three study groups for 6 months. Patients received either esomeprazole 20mg every day, esomeprazole with symptoms only, or ranitidine 150mg twice daily. Patients were asked about their satisfaction and symptoms after the control phase (esomeprazole 40mg daily) but before initiation of the follow-up phase and at 3 and 6 month intervals. Satisfaction of treatment and symptom severity was measured with separate 7 point Likert scales, while the frequency of heartburn was recorded as the number of days with episodes during the last 7 days. If patients needed a change in therapy the clinic would adjust the treatment based on which medication regimen the patient was on. The patients with recurring symptoms receiving either esomeprazole regimen were given esomeprazole 40mg daily for 4 weeks, while the patients with recurring symptoms on ranitidine were changed to 4 weeks of ranitidine 300mg twice daily. After that 4 weeks, if the patients were symptom-free (<1 day with mild heartburn in 7 days) they switched back to the treatment that they were originally randomized to.
Patient selection & enrollment	Patients over 18 with GERD symptoms for 3 or more days in the 7 days before the study were eligible. Recruitment was from 281 Norwegian General Practitioner clinics.
Outcome measures/endpoints	This study was conducted to look at the effectiveness and cost of treating GERD. This study had the initial 4 week control phase with treatment of esomeprazole 40 mg daily, then the follow-up phase lasted 6 months.
RESULTS	
Summary of study results, focusing on primary and secondary outcomes	<p>After 4 weeks of esomeprazole 40mg 88% (1902 patients) were symptom free. Before the initiation of the follow-up phase, >90% of patients were completely or very satisfied with the esomeprazole 40mg treatment. After the completion of the follow-up period the patients who were completely/very satisfied decreased: 82.2% in the esomeprazole 20mg continuous, 75.4% in the esomeprazole 20mg on demand, and 33.5% in the ranitidine 150 BID treatment group. The esomeprazole continuous treatment group was significantly better (p<0.01) than the esomeprazole on demand therapy. Both the esomeprazole groups had patients stay on the assigned treatment significantly longer than the ranitidine group (p <0.0001). The esomeprazole 20mg continuous group stayed on the assigned therapy an average of 170 days continuously, while the esomeprazole on demand group continued therapy for 171 days compared to 125 days for the ranitidine group. The number of patients who sought medical treatment for GERD was less in both esomeprazole groups (7% continuous and 10.9 on demand) than the ranitidine group (34.4%). This was significant with a p <0.0001. The ranitidine group had the 250 patients discontinue the study, while the esomeprazole had 73 from the continuous and 64 from the on demand group stop the trial due to lack of efficacy.</p> <p>The adverse events were similarly report among the treatment groups. The esomeprazole groups has the fewest patients stop the trial due to an adverse event.</p> <p>Esomeprazole 20mg on demand had a lower cost in terms of direct medical and total costs. Ranitidine had lower direct medical costs, but had a higher cost in every other way.¹</p>
DISCUSSION	
Brief summary of authors' main discussion points	The authors note that the 40mg esomeprazole daily for 4 weeks resolved a lot of GERD symptoms. Esomeprazole was superior to ranitidine on both a continuous and as needed basis. Continuous 20mg esomeprazole use led to the greatest patient satisfaction. The number of patients who relapsed and had to be restarted on standard dosing was higher in the ranitidine group. In the cost analysis, both esomeprazole groups were cheaper than the ranitidine group. ¹

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Study strengths	<ul style="list-style-type: none"> -The study groups were similar based on average patient age, percentage of males and females and degree of symptoms. -Type-1 errors were corrected using Duncan's test. -Patients were followed for six months. -This study had 2,156 patients. -Patient relapse did not disqualify them from the study, there was a protocol to increase the medication. -The study to follow what happens in the current clinical setting by empirically treating symptoms without performing an endoscopy, but during the trial the physician could request one to be done.
Study limitation	<ul style="list-style-type: none"> -Patients received 4 weeks of 40mg esomeprazole initially and 88% (1902 patients) were symptom free. -The study was sponsored by AstraZeneca, the makers of Nexium (esomeprazole). -This was not a blinded study. -The Likert scale to assess patient satisfaction was unbalanced, favoring satisfied with treatment. -If a patient discontinued the study, the last patient satisfaction score was carried forward. This study was preformed in Norway, not the United States.
Applicability and impact on pharmacists/ healthcare providers	This study has the potential to change prescribing for treatment of GERD. H ₂ blockers are a common treatment, and this study shows that even esomeprazole as needed is superior in both cost and efficacy.
CONCLUSIONS	
Author's conclusions	Esomeprazole both continuous and on demand are a superior treatments than ranitidine. Patient satisfaction was higher while the cost was lower. Ranitidine had a lower acquisition cost.
Evaluator/student's conclusions	This study was a fairly large study that did show esomeprazole being a superior treatment in both efficacy and cost for patients. This study shows promise because some patients already take their PPI on an as needed basis since other OTC items are taken that way. I do feel like there were several limiting factors in this study and would like to see another study done addressing efficacy without having the control phase.
Biggest take home message(s) in 3 sentences or less	-This trial proved that after a 4 week treatment with esomeprazole 40mg, esomeprazole 20mg daily and esomeprazole 20mg as needed were better than ranitidine 150mg twice daily in both cost and efficacy. Patient satisfaction was higher with the as needed PPIs than the scheduled ranitidine.

Abbreviations Used:

GERD- GastroEsophageal Reflux Disease
 PPI-Proton Pump Inhibitor
 OTC-Over The Counter

¹ Hansen AN, Wahlqvist P, Jorgensen E, Bergheim R, Fagertun H, Lund H, and Moum B. Six-month management of patients following treatment for esophageal reflux disease symptoms-a Norwegian randomized, prospective study comparing the costs and effectiveness of esomeprazole and ranitidine treatment strategies in a general medical practitioners setting. J Clin Pract. 2005; 59: 655-664.