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Is Esomeprazole (Nexium) More Effective than Omeprazole (Prilosec) in Reducing Heartburn and in Increasing the Rate of Esophageal Healing in Adults with Endoscopically Diagnosed Erosive Esophagitis (EE)?

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"Is Esomeprazole (Nexium) more effective than Omeprazole (Prilosec) in reducing Heartburn and in increasing the rate of esophageal healing in adults with endoscopically diagnosed Erosive Esophagitis (EE)?"

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ABSTRACT

OBJECTIVE: The objective of this systematic review is to determine whether Esomeprazole (Nexium) is more safe and effective than Omeprazole (Prilosec) in reducing Heartburn and in increasing the rate of esophageal healing in adults with endoscopically diagnosed Erosive Esophagitis (EE)

STUDY DESIGN: A review of all English language randomized controlled double blind comparative trials comparing the different forms of Proton Pump Inhibitors from 2006-2009. The studies included participants 18-85 years old with GERD and endoscopically diagnosed Erosive esophagitis.

DATA SOURCES: Randomized controlled Double Blind Comparative trials were Found using PubMed and Cochrane Databases.

OUTCOME MEASURED: Outcomes measured were reduction in GERD symptoms and healing of erosive esophagitis. Each Article measured symptoms based off of patient daily journals and symptoms criteria scales. Measurement of esophageal healing was done based off of the LA Classification scale. One article measured reduction of GERD symptoms after 5 days of treatment and the other two measured reduction after 4 weeks of treatment. Patients whos GERD symptoms were measured after 5 days of treatment were assessed based on a 6 point symptom scale (0: none; 1: mild; 2: mild-moderate; 3: moderate; 4: moderate-severe; 5: severe and/or intolerable).

RESULTS: All three RCTs in this review found that there were comparable effect on GERD Symptoms both after 4 weeks of treatment and after 5 days of treatment. One RCT found that Esomeprozole more rapidly decreased GERD symptoms compared to other PPIs but after 5 days showed no difference in efficacy. All trials also found that 40mg and 20 mg of Esomeprozole showed no significant difference in EE Healing compared with Omeprozole 20mg.

CONCLUSION: The Results of the three RCTs showed evidence that Esomeprozole was just as effective as Omeprozole 20mg after 7 days of treatment but had no difference in efficacy after 4 and 8 weeks of treatment. There was no evidence found that Esomeprozole had greater efficacy on Esophageal healing at 8 weeks with 20mg and 40 mgs compared to Ompeprozole 20mg.

KEYWORDS: Omeprozole, Esomeprozole, Erosive Esophagitis, GERD

Introduction:

GastroEsophageal Reflux Disease or GERD is a very common disease of the upper GI system that affects about 10-40% of the adult US population. If not treated this disease can progress into other serious conditions such as erosive esophagitis (EE), Barrots Esophagus and even Esophageal Cancer. In fact about 40-60% of patients with GERD will progress to these other serious conditions. Fortunately these subsequent diseases can be prevented with daily medication such as proton pump inhibitors with a prescription from your primary care practitioner. Not only would this medication be beneficial to prevent symptoms and disease progression but it would also reduce the cost that GERD has on society as a whole. Currently GERD and its associated diseases is costing American businesses $75 billion per year in workforce productivity due to the 16 million people scheduling doctors appointments and diagnostic procedures, keeping people from work; not to mention the amount Americans spend on treatment and diagnostic studies alone.

GERD results when there is weakening and relaxation of the lower esophageal sphincter leading to gastric contents to enter the esophagus. As a result the acidic contents of the stomach causes irritation and erosion of the esophageal lining. Over time this erosive esophagitis may lead to Barrot's esophagus in which the lining of the esophagus goes through histologic changes from squamous cells to columnar cells. Individuals with barrots are more prone esophageal cancer as a result of this histologic change. All of these issues could easily be avoided by many

preventable measures such as measures such as weight loss, change in eating habits, smoking cessation and elevating the head while sleeping.

Though all of these measures help in reducing GERD symptoms not one of them measures up to the effectiveness of PPIs such as Esomeprozole (Nexium) or Omeprozole (Prilosec). PPIs work to reduce the amount of HCL produced by the parietal cells of the stomach, ultimately reducing the acidity of the stomach and as a result reducing acid reflux symptoms.

Since PPIs have been developed there have been multiple additions to the PPI family such as esomeprozole, lansoprozole and Pantoprozole to name a few. With each new one created there is question of their efficacy when compared to the others. A prime example is the difference between the safety and efficacy of Esomeprozole and Omeprozole in treating GERD and GERD related diseases. The answer to this question is beneficial because Omeprozole is often a cheaper alternative to Esomeprozole. In order to answer this question a systematic review was conducted, comparing three RCTs. The SR was done to determine if there is a difference in safety and efficacy in relieving GERD symptoms and in the healing of erosive esophagitis.

Objective:

The objective of this systematic review is to determine whether Esomeprazole (Nexium) is more safe and effective than Omeprazole (Prilosec) in reducing Heartburn and in increasing the rate of esophageal healing in adults with GERD and endoscopically diagnosed Erosive Esophagitis (EE).

Method:

All three trials selected for this systematic review included randomized controlled trials (RCTs) with adult patients anywhere from 18-85 years old (age range depending on study) who have been endoscopically diagnosed with Erosive Esophagitis (EE). Each study included an intervention of Esomeprozole 20-40mg QD, using Omeprozole 20mg QD as the control group. Some variation did exist between studies. Although all three trials endoscopically measured the difference in the healing of EE after 8 weeks and the reduction of GERD symptoms, specifically heartburn. Two of the studies had treated patients for 8 weeks and one of the studies for only 7 days. Also, the two 8 week trials measured effects on heartburn after 4 weeks of treatment and the 7 day study measured the effects on heartburn every day up until day 5 of treatment. Further specific variations in study are mentioned below.

In the Lightdale, 2006 study, the experimental group was given Esomeprozole 20mg QD for 8 weeks and the control group was given omeprozole 20mg QD for 8 weeks. The study measured the patients change in GERD symptoms at 4 weeks but measured the rate of Esophageal healing at 4 and 8 weeks. The Schmitt 2006 study was conducted in the exact same format except that Esomeprozole 40mg was used as the experimental treatment instead of Esomeprozole 20mg.

The Zheng 2009 study was conducted in a slightly different fashion. The time frame of this study was 7 days in duration with results recorded using the acid

reflux score; specifics of this scoring system can be found in the "Outcomes Measured" section. Scores were recorded on days 1 through 5 using Esomeprozole 40mg QD as the experimental group and Omeprozole 20mg as the control group. Pantoprozole and Lansoprozole were also used in this trial as experimental groups but these results were disregarded from the review for simplicity sake.

All three article were English speaking and have been written in peer reviewed journals. Keywords used in the literature search Esomeprozole, Omeprozole, GERD and Erosive Esophagitis using PubMed and Chochrane Databases to perform the search. Articles were excluded if not POEMs, RCTs, written before 2005 and if it did not include symptom based outcomes. Statistics used in the studied included P values, RRR, ARR NNT and CI.

Outcomes Measured:

Outcomes measured were reduction in GERD symptoms and healing of erosive esophagitis. Each Article measured symptoms based off of patient daily journals and symptoms criteria scales. Measurement of esophageal healing was done based off of the LA Classification in all three the articles. One article measured reduction of GERD symptoms after 5 days of treatment and the other two measured reduction after 4 weeks of treatment. Patient participants of the 7 day treatment were assessed based on a 6 point subjective symptom scale (0: none; 1: mild; 2: mild-moderate; 3: moderate; 4: moderate-severe; 5: severe and/or intolerable).

Table 1 - Demographics & Characteristics of included studies

Study	Type	#Pt	Age(y	Inclusion	Exclusion	W/	Intervent

		s	rs)	criteria	Criteria	D	ions
Lightdale, C.J.; 2006	A Multicenter, Randomized, Double-Blind, 8-Week Comparative	1176	18-65	an endoscopic diagnosis of erosive essophagitis that tested negative for H. pylori	positive for *H. pylori* by serology at screening; GI bleeding detected at the time of the; and a H/O of gastric surgery. H/O of Zollinger-Ellison syndrome. esophageal motility disorder, stricture, or any serious medical condition, including cancer and Barrett's esophagus.	70	Daily Administration of Esomeprazole 20mg for 4-8 weeks and Daily Administration of Omeprazole 20mg for 4-8 weeks
Schmitt, C; 2006	A Multicenter, Randomized, Double-Blind, 8-Week Comparative Trial	1148	18-65	an endoscopic diagnosis of erosive essophagitis that **tested negative for H. pylori**	Same as Lightdale, C.J. 2006 publication	28	Esomeprazole 20mg QD for 4-8 weeks and Omeprazole 20mg QD for 4-8 weeks
Zheng, R.N.;2009	Randomized comparative study based on efficacy and safety of treatment on all 4 medications.	274	36-85	**endoscopically diagnosed reflux essophagitis**	Active PUD, upper GI CA, CA of other organs, cardiac, hepatic, or renal diseases, anemia, pregnant and/or lactating.	10	Pts to receive either 40mg QD Esomeprazole X 8 weeks or 20mg QD Omeprazole for 8 weeks

Results:

This Systematic review was done on three randomized controlled trials; two of which were 8 week comparative trials and one a 7 day trial. All three included omeprozole 20 mg daily as the control and esomeprozole as the experimental dosed at either 20mg or 40 mg daily. Patients included in each study were between the ages of 18-85 and endoscopically diagnosed with Erosive Esophagitis. All participants were tested for H. Pylori and were only included in the study if test results came back negative for H. Pylori.

In the Lightdale, 2006 study, after 4 weeks there was found to be no significant difference in efficacy between the two PPIs in resolving heartburn ($p=0.995$); Esomeprozole having 60.6% efficacy and Omeprozole 60.5% efficacy. Similarly the difference between the two treatments found no statistical significance in EE healing after 8 weeks ($p=0.621$); with Esomprozole being 90.6% effective and Omeprozole being 88.3% effective.

The Schmidt 2006 study, similar data was collected that found no statistical significance between the experimental and the control group. At 4 weeks, Esomeprozole 40mg was 65.0% effective and Omeprozole 20mg was 63.1% effective with a P-value of 0.480. Similarly, At 8 weeks, there was no statistical significance on the rate of EE healing for either treatments ($p=0.552$); Esomeprosole 40mg being 92.2% effective and Omeprozole 20mg being 89.8% effective.

The Zheng 2009 study concluded that during the first few days of treatment some variation existed on GERD symptom reduction showing that Esomeprozole was of greater efficacy than Omeprozole. By day 5 there was no statistical

difference in efficacy between the two treatments (p=0.0069). After 8 weeks patients were brought back in for endoscopic measurement of EE healing. Endscopic results showed that there was no statistical difference in the rate of esophageal healing between the two treatments (esomeprozole at 95.4% and Omeprozole at 87.7%).

Table 2: Esomeprozole vs. Omeprozole on the reduction of GERD symptoms.

	Esomeprozole (EER)	Omeprosole (CER)	P Value	RBI	ABI	NNT
Lightdale, 2006 (4 weeks)	60.6%	60.5%	0.995	0.00165	0.001	1000
Schmidt, 2006 (4 weeks)	65.0%	63.1%	0.48	0.0292	0.019	52.6
Zheng, 2009 (5 days)	N/A	N/A	0.0069	N/A	N/A	N/A

Table 3: Esomeprozol vs. Omeprozole in Esophageal healing at 8 weeks of treatment.

	Esomeprozol (EER)	Omeprosole (CER)	P Value	RBI	ABI	NNT
Lightdale, 2006 (8 weeks)	90.6%	88.3%	0.621	0.026	0.023	43.5
Schmidt,	92.2%	89.8%	0.552	0.027	0.024	41.7

2006 (8 weeks)						
Zheng, 2009 (5 days)	95.4%	87.7%	N/A	0.088	0.077	12.99

To understand why the authors of the article deemed the differences between each treatment stastistically insignificant the RBI, ABI and NNT were calculated for each study. This was done by taking the efficacy rates for each treamtment; Esomeprozole being the Experimental Event Rate (EER) and omeprozole being the Controled Event Rate (CER). Both were used to calculate the Relative Benefit Increased (RBI) and the Absolute Benefit Increase (ABI). The ABI was then used to calculate Numbers Needed to Treat (NNT). Numbers needed to treat will tell us how many patents need to be treated in order to have Esomeprozole show some statistical significance in efficacy over Omeprozole.

In Lightdales study, in order for Esomeprozole to have show significant benefit over Omeprozole for treating heartburn about 1000 people would need to be treated and about 43.5 people would need to be treated to show a benefit for EE healing. In the Schmidt 2006 study, 52.6 patients would need to be treated to show a greater benefit in heartburn treatment and 41.7 for EE healing. The Zheng 2009 study, it wasn't possible to calculate NNT for Heartburn treatment but it did show that Esomeprozole was slightly more beneficial than Omeprozole with an NNT of 12.99.

Safety: Only the Lightdale 2006 and Schmidt 2006 studies documented Adverse Effects of their treatments. Both studies showed similar results in safety between the experimental and control. Four of the most common side effects of both drugs were HA, Gastritis, Diarrhea and Respiratory infection. In both studies, Esomeprozole and Omeprozole yielded similar percentages in Adverse Effects(AE) with Esomeprozole having slightly higher incidences of AE in all types. Specific numbers and percentages can be found in tables 4 and 5. Despite a few Adverse side effects reported by some patients overall the two drugs were very well tolerated during the study.

Table 4: Common Adverse Effects of Esomeprozole and Omeprozole from Lightdale 2006.

	Headaches	**Gastritis**	**Diarrhea**	**Resp. Infection**
Esomeprozole	58 (9.9%)	31 (5.3%)	27 (4.6%)	27 (4.6%)
Omeprozole	37 (6.3%)	18 (3.1%)	28 (4.8%)	25 (4.3%)

Table 5: Common Adverse Effects of Esomeprozole and Omeprozole from Schmidt 2006 Study

	Headaches	**Gastritis**	**Diarrhea**	**Resp. Infection**
Esomeprozole	59 (10.2%)	28 (4.9%)	38 (6.6%)	26 (4.5%)

Omeprozole	39 (6.8%)	18 (3.2%)	31 (5.4%)	16 (2.8%)

Discussion:

Historically PPIs are very safe and effective drugs used to treat GERD and other gastric diseases such as ulcers and H. Pylori infections. These studies have indicated that PPIs are also effective in treating Erosive Esophagitis. EE is a disease that is often a result of chronic GERD and heartburn. As a result of these observations, it can be hypothesized that aggressive treatment of GERD with PPI therapy ultimately reduces the damaging affects of GERD on the esophagus and allows for prevention and quicker healing of erosive esophagitis.

Other similar studies may be performed to test this hypothesis and to provide more concrete evidence that PPI therapy is a safe and effective treatment for erosive esophagitis. If enough evidence is collected, it will be easier to educate patients on the effectiveness of PPI therapy an adequate preventative treatment of erosive esophagitis and other diseases caused by GERD. This type of preventive measure would not only reduce the uncomfortable and dangerous problems individual patients have with Esophageal disease. It can also reduce the amount of money American spends each year on GERD and related diseases.

Conclusion:

After reviewing all three articles and comparing the results, it has been concluded that there is no overall, statistically significant difference between

Esomeprozole and Omeprozole for the treatment of GERD symptoms or for EE Healing. From the Zheng 2009 study results, it is possible that Esomeprozole might provide reduction GERD symtoms quicker than Omeprozole in the first 1-2 days of treatment; but by the 5th day of treatment, Omeprozole was fount to be just as effective as Esomeprozole in symptom reduction. In light of these findings, it would be beneficial to perform more 7 day trials of PPI treatment to determine if these findings are credible and to determine if Esomeprozole would be a better choice if one was looking for the quickest way to successfully reduce GERD symptoms.

It was mentioned in Lighdale 2006 study that when comparing the healing rate of 4 and 8 weeks, the rate of esophageal healing although, not significant at 8 weeks, was beginning to approach significance. This opens up the possibility that, if given for a longer duration, Esomeprozole could show a significant difference in efficacy with regards to esophageal healing rates compared to Omeprozole. It would be beneficial to "attempt this experiment again for a longer period of time; for about 12 to 16 weeks.

After reviewing the methods section of each article it was noted that certain variable that were not controlled for and may be beneficial in future studies to more definitively confirm the similar efficacy of these two medications. One specific variable is the dietary habits of the participants. There was no mention of control in the patients dietary habits. This could have had an impact on GERD symptom presentation and exacerbations of participants. In order to control for this it would

be beneficial to put all participants on a diet restricting individuals from foods known to exacerbate GERD symptoms.

In conclusion It has been determined by this systematic review that both Esomeprozole and Omeprozole are equally safe and effective in treating GERD symptoms and for improving the rate of EE healing. If patients propose that the cannot afford the more expensive esomeprozole then the physician can offer the alternative of the cheaper Omeprozole to the patient. The Physician should explain to the patient that Omeprozole may not be as effective in the first few days but if given time is just as safe and effective as its more expensive counterpart.

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