Original Article

J Nepal Health Res Counc 2019 Oct-Dec;17(45): 479-84

DOI https://doi.org/10.33314/jnhrc.v17i4.1961

Comparative Study on Effect of Rabeprazole Versus Omeprazole in Acid-peptic Disorder with *Helicobacter pylori* Infection

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ABSTRACT

Background: Gastritis is one of the common diseases, which is frequently caused by *Helicobacter pylori*. Triple therapy has resulted significant decrease in morbidity and complications. Newer proton pump inhibitor drug rabeprazole has been introduced in the market. The aim of this study is to compare its efficacy with omeprazole in triple therapy regimen.

Methods: A total of 100 patients who were positive for *Helicobacter pylori* and gave consent in participating in the study were included. Fifty patients were prescribed omeprazole-based triple therapy and other 50 were prescribed with rabeprazole-based triple therapy. After 2 weeks of triple therapy and 4 weeks of proton pump inhibitor treatment, *Helicobacter pylori* antigen was tested in faecal material.

Results: Out of 100 patients, there was significant correlation between epigastric pain, nausea and water brash with p value, 0.001. Similarly P-value was < 0.001 among hiatus hernia and reflux whereas p value was < 0.05 between bile reflux, hiatus hernia and reflux. In follow up study, after triple therapy, *Helicobacter pylori* antigen tests were negative in 94% of the study population, who were prescribed rabeprazole which was similar who were prescribed omeprazole (92%).

Conclusions: Rabeprazole (20 mg) has proved similar *Helicobacter pylori* eradication rates compared with omeprazole (40 mg) when co-administered with of antibiotics (amoxicillin and clarithromycin) for two weeks.

Keywords: Gastritis; heart burn; hyperchlorhydria; proton pump inhibitors; triple therapy.

INTRODUCTION

Acid Peptic Disorders (APD) include spectrum of maladies that range in importance from simple discomfort to life-threatening illness and include dyspepsia, peptic ulcer disease, gastritis and upper gastrointestinal bleeding. Most of the disorders are acid-related diseases in which gastric acid plays an important role in their development, progression, and treatment.[1] *Helicobacter pylori* (*H. pylori*) infection appears to be a necessary co-factor for majority of gastritis.[1]

The standard triple therapy, widely used for the eradication of *H. pylori*, ncludes proton pump inhibitor (PPI), clarithromycin and amoxicillin for 14 days.[1-4]

Rabeprazole, a recently developed PPI, is known to have similar efficacy to that of omeprazole, when used in combination with clarithromycin and amoxicillin.[1,5-8] However similar findings for Nepalese patients is yet to be fully established. Pharmacodynamic data show rabeprazole can achieve optimal acid suppression from the first administration and can maintain this advantage in the following days of therapy.[9] Moreover, rabeprazole has the highest pKa (~5.0, the pH at which a drug becomes 50% protonated), and hence the molecule can be activated at higher pH levels much faster than other PPIs. Due to its peculiar catabolic pathway, i.e. a prevalent metabolism through a non-enzymatic pathway, rabeprazole is less susceptible to influence genetic polymorphisms for CYP2C19, resulting in minor influences on its pharmacokinetics and phartmacodynamics.[9,10]

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This study aims to compare the effect of prototype Proton-pump inhibitor (omeprazole) with newer Proton-pump inhibitor (rabeprazole) for treatment of peptic ulcer with H.pylori infection.

METHODS

This study was cross-sectional study where two groups of drugs were compared in gastroenterology out-patient department, GRP Polyclinic Pvt, Ltd., Kathmandu, from 15th January 2018 to 15th April 2018. Prior to the conduction of study, permission was obtained from Nepal Health Research Council.

All the patients diagnosed having APD with *H. pylori* infection and consented for this study were included. Patients with features of APD requiring upper gastrointestinal endoscopy with positive *H. pylori* infection were explained regarding on-going study. Patients with history of alcohol or NSAIDs intake, smoking, any gastrointestinal neoplasm and patient not giving consent to participate were excluded from the study.

A proforma was filled, for each patient,which included demographic data, presenting symptoms and signs, endoscopic findings, gastric biopsy findings and stool results for *H. pylori* antigen test using one step *H. pylori* antigen test device (ABON). It is a lateral flow chromatographic immunoassay for detection of *H. pylori* antigen. Those who consented to participate in the study were alternatively enrolled into either group A or group B. Group A patients were treated with omeprazole-based triple therapy. Group B patients were treated with rabeprazole-based triple therapy (Figure 1).

Group A was prescribed omeprazole - 40 mg, clarithromycin- 500 mg and amoxicillin-1 g twice daily for 14 days. Group B was prescribed rabeprazole- 20 mg, clarithromycin-500 mg and amoxicillin-1 g twice daily for 14 days. After completion of triple therapy the proton pump inhibitor of same drug was continued twice daily for a total of 2 weeks followed by once daily for next 2 weeks to ensure complete ulcer healing. After 6 weeks H. pylori antigen test was performed in faecal sample and data were recorded.

Sample size was calculated based on a non-inferiority margin of 20 %, a successful eradication rate in control group (patient receiving omeprazole) of at least 74 %, successful eradication rate in experimental group of at least 80%, a two-sided test at the 5% level, and a power of 90%. Based on this, a sample size of 45 patients per therapy group was calculated to be sufficient. Additional 5 patients were added per therapy group to compensate for approximate loss of 10 % at follow-up.

Statistical package for software analysis (SPSS) version 16 and independent t-test and a value of $p< 0.05$ was considered significant.

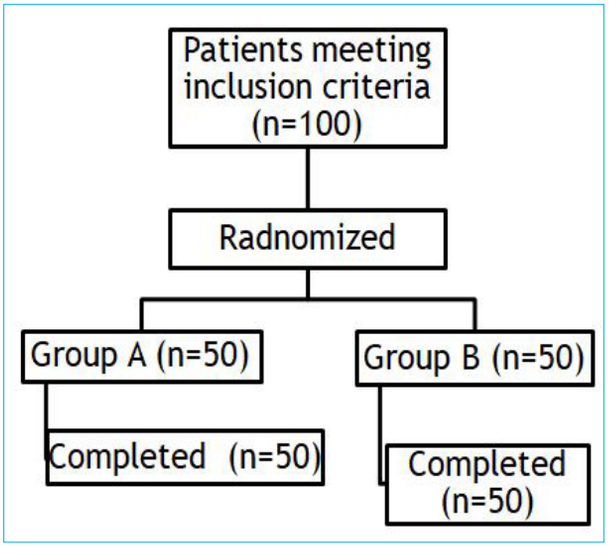

Figure 1. Flow chart. Patients were randomly assigned to Group A (n=50) or Group B (n=50). Group A received Omeprazole based triple therapy (Omeprazole, amoxicillin and clarithromycin); Group B received Rabeprazole based triple therapy (Rabeprazole, amoxicillin and clarithromycin).

RESULTS

A total of 100 patients evaluated at GRP polyclinic were enrolled. Among the study population, mean age was found to be 37.4 years of age with minimum being 12 years of age and maximum 75 years of age. There was slight female preponderance with female to male ratio of 1.38:1 among patients who visited OPD for APD.

In both groups epigastric pain was the major complain among both males (39/42, 92.8%)and females (52/58, 89.6%). Similarly 47 females (81.03%) and 37 males (88.09%) had nausea (Table 1).

Various signs were evaluated during upper gastrointestinal endoscopy out of which most common findings was erythema which was seen in 99 (99%) cases. Erythema was observed in 57 females (98.27%) and 42 (100%) males. Hypercholorhydria and erosion were 2nd most common finding observed in 94 (94%) cases (Table 2).

Table 1. Frequency of presenting complaints in both sex of the patients among both groups (n=100).

Presenting complaints		Group A (n=50)		Group B (n=50)		Total n
		Female n (%)	Male n (%)	Female n (%)	Male n (%)	
Epigastric pain	Yes	20/24 (83.33)	24/26 (92.3)	32/34 (94.1)	15/16 (93.75)	91
	No	4	2	2	1	9
Nausea	Yes	18/24 (75.0)	23/26 (88.5)	29/34 (85.3)	14/16 (87.5)	64
	No	6	3	5	2	16
Waterbrash	Yes	14/24 (58.3)	16/26 (61.5)	17/34 (50.0)	12/14 (85.7)	59
	No	10/24 (41.6)	10	17/34	4	41
Loss of appetite	Yes	10/24 (41.6)	9/26 (34.6)	8/34 (23.5)	5/14 (35.7)	32
	No	14	17	26	11	68

Table 2.UGI endoscopic finding in both sex of the patients among both groups (n=100).

Endoscopic findings		Group A (n=50)		Group B (n=50)		Total n
		Female n (%)	male n (%)	Female n (%)	Male n (%)	
Erythema	Yes	24/24 (100)	26/26 (100)	33/34 (97.0)	16/16 (100)	99
		0	0	1	0	1
Hyperchlorhydria	Yes	24/24 (100)	26 /26 (100)	30/34 (88.2)	14/16 (87.5)	94
	No	0	0	4	2	6
Erosion	Yes	23/24 (95.8)	25/26 (96.1)	31/34(91.7)	15/16 (93.7)	94
	No	1	1	3	1	6
Reflux in Oesophagus	Yes	19/24 (79.1)	22/26 (84.6)	26/34 (76.4)	12/16 (75.0)	79
	No	5	4	8	4	21
Ulcer	Yes	3/24 (12.5)	5/26 (19.2)	2/34 (5.8)	0/16 (0.0)	10
	No	21	21	32	16	90
Bilereflux	Yes	3/24 (12.5)	3/26 (11.5)	0/34 (0.0)	2/16 (12.5)	8
	No	21	23	34	14	92

Table 3. Histopathological diagnosis in both sex of the patients among both groups (n=100).

Histopathological diagnosis	Group A (n=50)		Group B (n=50)		Total n
	Female n (%)	Male n (%)	Female n (%)	Malen (%)	
Chronic active gastritis, mild	9/24 (37.5)	10/26 (38.4)	13/34 (38.2)	7/16 (43.7)	39
Chronic active gastritis, moderate	6/24 (25.0)	3/26 (11.5)	3/34 (8.8)	4/16 (25.0)	16
Chronic active gastritis, severe	1/24 (4.1)	1/26 (3.8)	2/34 (5.8)	0/16 (0.0)	4
Chronic follicular gastritis	7/24 (29.1)	11/26 (42.3)	16/34 (47.0)	5/16 (31.2)	39
Chronic active gastritis, mild with intestinal metaplasia	1/24 (4.1)	0/26 (0.0)	0/34 (0.00	0/16 (0.0)	1
Chronic active gastritis, moderate with intestinal metaplasia	0/24 (0.0)	1/26 (3.8)	0/34 (0.0)	0/16 (0.0)	1

Table 4. Comparison of Omeprazolevs. Rabeprazole and stool antigen test for *H. Pylori*.

H. Pylori pylori SAT test	Medication		p value
	Omeprazole	Rabeprazole	
Positive	4	3	0.69 (>0.05)
Negative	46	47	
Total	50	50	

Endoscopic biopsies were classified into various groups. Among these study groups most common was chronic active gastritis with mild severity and chronic follicular gastritis (n-39; 39%) followed by chronic active gastritis with moderate severity (Table 3). Least common was chronic gastritis with intestinal metaplasia which was observed in 2 % of the study population. There was no significant sex wise variation in this histopathological diagnosis.After one and half month of treatment, stool antigen test for *H. pylori* was done. Among 50 patients, 46 (92%) patients from group A had negative stool antigen test for *H. pylori*. Among group B study population 47/50 (94%) patients were found to be free from H. Pylori in stool antigen test for *H. pylori*. Both proton pump inhibitors were found equally efficient as a component of triple therapy regimen for anti-Helicobacter pylori treatment. However, the findings are not statistically significant (p>0.05) (Table 4).

DISCUSSION

Acid peptic disorder is a common entity presenting in daily clinical practice andis a significant burden to the society, due to chronicity. Since prime cause of this inflammation is *H. pylori*, key element in the success of its treatment is tripleor quadruple treatment regimen which includes PPI, amoxicillin, and clarithromycin in triple therapy and addition of Bismuth salt in quadruple regimen.[11] The use of proton-pump inhibitor (PPIs) revolutionized the therapeutic advance due to more potent inhibition of acid secretion.[12] Ample data from clinical trials and observational experience have confirmed the utility of these agents in the treatment of acid-peptic diseases with differential efficacy and safety characteristics between and within drug classes.[11-14] In this study, most common symptoms was epigastric pain (90%) followed by nausea (84%). Similar finding was found in other study in which heartburn and acid regurgitation was the most common findings.[15] In this study, there was increased incidence of these symptoms in male than in female (92.8 vs. 89.6%) which was in concordance with study done by Kim et al.[16]

During upper oesophago-gastro-duodenoscopy observations like presence or absence of erythema, erosion, increased or diminished acid secretion, erosion, ulcer and bile reflux along with presence or absence of hiatus hernia were documented. Among these, erythema was the most common finding followed by hyperchlorhydria, erosion. The ulcer was observed only in 10% and bile reflux in 8% of the total study population. Erythematous-exudate was the most common finding in a study done by Piatek-Guziewicz et al.[17] In a study, 17.56% patients had peptic ulcer, which is higher than of our study.[18] Reflux was seen in 79% of cases which is similar to the study done by Nobakht et al.[19] Histopathological diagnosis revealed that most common diagnosis was chronic active gastritis with mild severity (39%) followed by chronic follicular gastritis, moderately active chronic gastritis. A study done by KC et al found 45% of patients with mildly active chronic gastritis, however only 19% patients had chronic follicular gastritis.[20] This result is in concordance with other study done by Shrestha R et al.[21] The variation in the frequency of histological type of gastritis may be due to sample selection. Since only *H. pylori* positive patients were included in this study, this may have altered in the outcome in the frequency of different histological subtypes.

In follow-up study, after triple therapy which included omeprazole in group A and rabeprazole in group B, *H. pylori* antigen tests were negative in 92% and 94% patients from group A and group B respectively. However, the findings were not statistically significant. Efficacy of rabeprazole has been found similar in other study. In a study done by Bosques-Padilla et al[22] found 92.3% eradication rate of *H. pylori* in rabeprazole based triple therapy for 2 weeks. In a study done by Miwa et al[23] found 88% (95% CI, 78-94) of eradication rate of *H. pylori*, which was 85% (95% CI, 75-92) among omeprazole based triple therapy. Similar to our study, no significant difference was noted in either manners of analysis, suggesting that the efficacy of these proton pump inhibitors was comparable. Both omeprazole and rabeprazole had similar outcome when included in triple therapy However, this study used 7 days triple therapy regimen which might be the cause for slight decrease in eradiation rate that this study.

Despite having different rate of signs, symptoms and endoscopic findings similar outcome was observed in the both study population. A study done by Arama et al showed 84.6% positive response with 14 days triple therapy regimen.[24] A study done in Japan 83.9% vs. 76.6% eradication rates in the omeprazole- and rabeprazole-based triple regimen groups.[25] In the study, omeprazole, lansoprazole and rabeprazole based triple therapy was studied for eradication of *H. pylori* CYP2C19 genotypes. As in our study, the difference was not statistically significant.[25] Although, rabeprazole as a component of triple therapy was equally efficient in eradicating *H. pylori*, it was not statistically significant. Small sample size may be the cause for this.

Rabeprazole has been proven for its effectiveness in decreasing heartburn and other signs and symptoms.[9] In

this study both group of population, taking rabeprazole-based triple therapy or omeprazole-based triple therapy had similar outcome. The similar findings were observed in the study done by Pace et al.[9]

The study was conducted in a single centre and included only 100 patients with H. pylori infection. Further study involving more patients and at multiple centres may further enlighten the role of this PPI in eradicating H. pylori.

CONCLUSIONS

Fourteen days regimen of triple therapy is quite effective in eradicating *H. pylori*. Rabeprazole (20 mg) has proved similar *H. pylori* eradication rates compared with omeprazole (40 mg) when co-administered with of antibiotics (amoxicillin and clarithromycin) for two weeks.

ACKNOWLEDMENTS

We acknowledge support and contributions of the patients and technical staffs that have helped us in the completion of the study.

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