

# **Efficacy of Rabeprazole versus Omeprazole in Preventing Relapse of Erosive Reflux Oesophagitis**

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## **Abstract**

*Background: Reflux oesophagitis is caused by excessive exposure of the distal oesophagus to gastric juice; in the majority of patients the escape of liquid gastric contents into the distal esophagus is abnormally frequent. Objective: To determine the efficacy of Rabeprazole versus Omeprazole in preventing gastroesophageal complaints associated with reflux oesophagitis recurrence within one year and the quality of life benefits of treatment with these agents. Study Design and Methods: Comparative clinical study was conducted to study efficacy of Rabeprazole versus Omeprazole in prevention of relapse reflux oesophagitis. Eighty patients with reflux oesophagitis from grade (A-D) were admitted to upper gastro-intestinal endoscopic clinic at Al-Thawra hospital-Sana'a-Yemen. Out of 80 participants 20 patients were assigned to use Rabeprazole (10 mg), 30 patients to use Rabeprazole (20mg) and 30 patients to use Omeprazole (20mg) twice a day. Data were analyzed by SPSS, version 12.0 used (x2-test-2-sided) and significance was considered when  $p < 0.05$ . Results: Significantly more patients were healed with Rabeprazole (20mg) versus Omeprazole (20mg) and Rabeprazole (10 mg) for 12 month ( $p < 0.001$ ) and also Rabeprazole (20mg) had a significant efficacy on reduction of day-time and night-time heartburn than Omeprazole (20mg) ( $p < 0.05$ ). Conclusion: From the study findings, Rabeprazole (20mg) appears to be significantly more efficient than Rabeprazole (10mg) and Omeprazole (20mg) in preventing relapse reflux oesophagitis for long-periods and also has a significantly greater efficacy on relieving day-time and night heartburn.*

**Key words:** Reflux oesophagitis, Rabeprazole, Omeprazole, and Heartburn.

## **Introduction:**

Reflux oesophagitis is characterized by heartburn and epigastric pain<sup>1,2&3</sup> The condition is relatively common, with an estimated prevalence of 15%-20% in USA and western countries.<sup>4</sup> In the Middle East, 10% in Egypt and more than 15% in Yemen.<sup>5</sup> Reflux oesophagitis is typically chronic and has a high rate of recurrence, with 50%-80% of patients experience a relapse within the first 6-12 months after stopping drug treatment. Chronic reflux oesophagitis has been associated with ulceration and bleeding, and up to 20% of patients in western countries develop complications, such as esophageal stricture or Barrett's esophagus. In

the Middle East countries a smaller number of patients develop such complications, 2%-8% in Yemen<sup>5</sup> and 10%-15% in Egypt. Rabeprazole, substituted benzimidazol derivative, is the newest member of the PPI class and is structurally related to Omeprazole and Lansoprazole. In preclinical experiments, Rabeprazole demonstrated greater potency than Omeprazole in inhibiting  $H^+, K^+-ATPase$  and reducing acid output<sup>6,7,8,9&10</sup>. In vitro, rapidly than did Rabeprazole inhibited proteins pump activity more rapidly than did Omeprazole or other PPIs<sup>11</sup>. A recent study in healthy volunteers found significantly greater anti-secretion effect after the first dose of Rabeprazole

than with Omeprazole.<sup>11</sup> In moderate to severe reflux oesophagitis, Rabeprazole has been shown to normalize total esophageal acid exposure time as assessed by 24 hrs. PH monitoring.<sup>12</sup> Rabeprazole has also been shown to heal erosions and ulceration in patients with reflux oesophagitis relapse.<sup>12</sup> Rabeprazole (20mg) twice a day produced healing rate comparable to that of Omeprazole (20mg) and was also better in resolving findings and improvement symptoms as well as being better in promoting healing of erosive reflux oesophagitis within one year.

### Objective of the study

The objective of the study is to determine the efficacy of Rabeprazole versus Omeprazole in preventing gastroesophageal complaints associated with reflux oesophagitis recurrence within one year and the quality of life benefits of treatment with these agents.

### Study design and Methods

#### Study Setting

The study was conducted at Al-Thawra modern general hospital, upper gastro-intestinal endoscopic clinic. The hospital provides primary, secondary and tertiary health care and it is a referral hospital for the whole Yemen.

#### Study Design and Patients

A comparative clinical study was conducted to compare the efficacy of Rabeprazole (10mg and 20mg) and Omeprazole (20mg) in prevention of erosive reflux oesophagitis. A total of 80 male and female patients aged 16 to 75 years with reflux oesophagitis grade (A-D) were invited to participate in this study. Patients were recruited from upper G.I. endoscope clinic. One week after signing an informed consent, those who met entry criteria were randomized to receive either the Rabeprazole (10mg) (20 patients), Rabeprazole (20mg) (30 patients) or Omeprazole (20mg) (30 patients). Patients were instructed to take tablets twice a day for 12 months. Clinic visits were scheduled in the morning during months 1, 3, 6 and 12. All baseline measures and endoscopic findings were

obtained from all participants. The researcher instructed the patients to record number of tablets taken and any adverse events in patient diaries. Compliance with study tablet was 99.8% in the Rabeprazole group and 99.9% in the Omeprazole group. No patients in either group had tablet intake of less than 98%.

#### Statistical analysis

A sample size of 80 patients (20 Rabeprazole (10mg), 30 Rabeprazole (20mg) and 30 Omeprazole (20mg)) was calculated. Statistical analysis of the efficacy of the intervention was performed on all randomized patients who had baseline evaluation and no deviation from the study protocol by using SPSS software for windows (version 12.0. SPSS Inc). The efficacy endpoint of complete healing of reflux oesophagitis at month 12 including data carried forward from patients exhibiting complete healing at months 1,3,6 and 12 based on the assumption that if such patients continued treatment, they would remain healed at month 12. Analysis of reflux oesophagitis symptoms were performed at month 12. Baseline characteristics of the study sample were compared using (x<sup>2</sup>) test, 2-sided. Comparisons of endoscopic findings between groups were analyzed by using (x<sup>2</sup>) test, 2-sided. The comparison between groups (Rabeprazole (20mg) and Omeprazole (20mg) regarding day-time heartburn and night-time heartburn were analyzed used chi-square test, 2-sided. All statistical analysis on endoscopic findings and reflux oesophagitis symptoms were performed using 2-sided test of significance and significance was considered when  $p < 0.05$ . Descriptive statistics {(Mean $\pm$ SD), range, frequency and percents with confidence interval 95% were used.

### Results

This study involved 80 patients with reflux oesophagitis from grade (A-D). The characteristics of the study patients were as follows: -

Age distribution: Age distribution of 80 participants aged 16 to 75 years ( $44.8 \pm 12.5$ ) is presented in Table 1. Differences between groups were not significant by age ( $\chi^2=1.23$ ;  $df=2$ ;  $p<0.05$ ).

Sex distribution: Table 2. Presents the distribution of sex among the participants. The data showed that there were 47 (58.8%) males and 33 (41.3%) females. There were no statistically significant differences between the groups by sex ( $\chi^2=4.487$ ;  $df=2$ ;  $p<0.05$ ).

Tobacco habits: Distribution of tobacco among groups is presented in Table 3. The results showed that 27 (33.8%) used tobacco and 53 (66.3%) didn't use tobacco. The difference was not statistically significant among groups regarding tobacco used ( $\chi^2=2.106$ ;  $df=2$ ;  $p<0.05$ ).

Khat habits: the total numbers of Khat chewers in all the groups was 30 (37.5%) and the total numbers of non-Khat chewers in all groups was 50 (62.5%). In Table 4. no difference was noticed between the groups ( $\chi^2=3.556$ ;  $df=2$ ;  $p<0.05$ ).

#### Endoscopic Findings:

In this comparative clinical study 80 patients with reflux oesophagitis were treated with Rabeprazole (10 mg or 20 mg) and Omeprazole (20mg). The endoscopic findings at 12 months are presented in Table 5. The results of the endoscopic findings for reflux oesophagitis at 12 month showed that, healing took place in 10 (50%) patients who received Rabeprazole (10mg) and failed in the rest of the group (10 = 50%). While in patients who received Rabeprazole (20mg) the healing took place in 25 (83.3%) patients and did not take place in 5 (16.7%) patients. In patients who received Omeprazole (20mg) the healing took place in 12 (40%) patients and in 18 (60%) did not disappear reflux oesophagitis. The differences between the groups were statistically significant regarding healing rate of reflux oesophagitis ( $\chi^2=12.465$ ;  $df=2$ ;  $p<0.002$ ). Our findings showed that Rabeprazole (20mg) significantly

had more efficacy than Rabeprazole (10mg) and Omeprazole (20mg) in healing of patients with reflux oesophagitis.

#### Assessment of heartburn:

Day-time heartburn: Results of day-time heartburn is presented in Table 6. The data showed that in Rabeprazole (20mg) group 3 (10%) had day-time heartburn and 27 (90%) were heartburn-free, while in Omeprazole (20mg) group 9 (30%) had day-time heartburn and 21 (70%) were heartburn-free. Efficacy of Rabeprazole (20mg) was greater than Omeprazole (20mg) regarding reduction of day-time heartburn ( $\chi^2=3.98$ ;  $df=1$ ;  $p<0.05$ ).

Night-time heartburn: Results of night-time heartburn is presented in Table 7. In Rabeprazole (20 mg) two patients (6.7%) had night-time heartburn and 27 (93.3%) were heartburn-free while in Omeprazole (20mg) 9 (30%) had night-time heartburn and 21 (70%) had heartburn-free nights. A statistically significant efficacy of Rabeprazole (20mg) is also high as compared to Omeprazole (20mg) regarding reduction of night-time heartburn ( $\chi^2=5.455$ ;  $df=1$ ;  $p<0.05$ ).

#### Discussion

The results of this study in 80 patients with reflux oesophagitis indicated that Rabeprazole (20mg) has several advantages compared with Omeprazole (20mg) and Rabeprazole (10mg). Most important is that healing rate at 12 month with Rabeprazole (20mg) 83.3% represents a greater significant efficacy compared with that of Omeprazole (20mg) 40% and Rabeprazole (10mg) 50%. Heartburn-free days and nights rate at 12 month also significantly greater in Rabeprazole (20mg) 93.3% heartburn-free days and 90% heartburn-free nights than Omeprazole (20mg) 70% heartburn-free days and 70% heartburn-free nights. Rabeprazole demonstrated greater consistency of efficacy across patients groups when baseline severity of reflux oesophagitis was considered. In addition, differences in

healing rates were consistently greater with Rabeprazole (20mg) across all grades of baseline severity (LA Classification) of reflux oesophagitis at 12 month. This study is similar to a study conducted by Dent J. et al<sup>13</sup>. Free-heartburn, the predominant symptoms of reflux oesophagitis, was predictive of healing of reflux oesophagitis 85.2% of patients with resolution of heartburn at 4 weeks also had healing of reflux oesophagitis. Thus, a treatment effect of esomeprazole sustained resolution of heartburn in patients with reflux oesophagitis can be used as a strong indicator of healing of oesophagitis erosions. The result of the current study is consistent with the findings of the earlier 8-weeks study by Kahrilas et al that compared Rabeprazole 20mg and 40 mg with Omeprazole 20mg in patients with reflux esophagitis<sup>14</sup>. Their results indicated that both Rabeprazole 20mg and 40mg were significantly ( $p<0.05$ ) more effective than Omeprazole 20mg for healing erosive oesophagitis. Thus, for the first time, Rabeprazole (20mg) has been shown to offer significant advantages over Omeprazole (20mg) in term of healing of erosive oesophagitis. Resolution of heartburn also occurred faster and in greater percentage of patients with Rabeprazole compared with Omeprazole related to the pharmacodynamic profile of the drugs.<sup>15</sup> and <sup>16</sup> Omeprazole is more slowly cleared and therefore has

greater bioavailability than Omeprazole. Rabeprazole also appears to have more consistent pharmacokinetic properties than Omeprazole, with less inter-patients variability in term of AUC, plasma concentrations, and gastric acid inhibition. Rabeprazole maintained intra-gastric pH above 4.0 for 6 hours longer than Omeprazole and produced a higher median 24 hour intra-gastric pH than did Omeprazole in patients with reflux oesophagitis. The difference was most apparent between 12 to 20 hours after a morning dose, which properly accounts for the greater reduction of night-time heartburn achieved with Omeprazole in both trails. At present, clinical management guidelines for reflux oesophagitis recommended that the most effective treatment should be instituted as early as possible. Currently marked PPIs offer similar healing rates to the standards and usually recommended, dosage of Omeprazole (20mg) at 4 and 8 week.<sup>17,18,19&20</sup>.

### Conclusion

The results of the study indicate that Rabeprazole (20mg) provides more significant advantages than Omeprazole (20mg) and Rabeprazole (10mg) for healing of erosive reflux oesophagitis and reduction of day-time and nights heartburn.

**Table 1. Distribution of age among groups**

Age range	Rabeprazole (10mg)		Rabeprazole (20mg)		Omeprazole (20mg)		Mean± SD
	no	%	no	%	no	%	
16-40	6	30.0	11	36.7	11	36.7	46.2±12.1
41-60	11	55.0	16	53.3	17	56.7	44.7±13.7
>61	3	15.0	3	10	2	6.7	44±11.8
Total	20	100	30	100	30	100	44.8±12.5

**Table 2. Distribution of sex among groups**

		SEX		Total
		Male	Female	
GROUP	Rabeprazole (10mg)	8 40.0%	12 60.0%	20 100.0%
	Rabeprazole (20mg)	18 60.0%	12 40.0%	30 100.0%
	Omeprazole (20mg)	21 70.0%	9 30.0%	30 100.0%
Total		47 58.8%	33 41.3%	80 100.0%

**Table 3. Distribution of tobacco among groups**

		TOBACCO		Total
		No	Yes	
GROUP	Rabeprazole (10mg)	5 25.0%	15 75.0%	20 100.0%
	Rabeprazole (20mg)	13 43.3%	17 56.7%	30 100.0%
	Omeprazole (20mg)	9 30.0%	21 70.0%	30 100.0%
Total		27 33.8%	53 66.3%	80 100.0%

**Table 4. Distribution of Khat chewers among groups**

		KHAT		Total
		No	Yes	
GROUP	Rabeprazole (10mg)	11 55.0%	9 45.0%	20 100.0%
	Rabeprazole (20mg)	9 30.0%	21 70.0%	30 100.0%
	Omeprazole (20mg)	10 33.3%	20 66.7%	30 100.0%
Total		30 37.5%	50 62.5%	80 100.0%

**Table 5. Distribution of endoscopic finding among groups**

	Endoscopic Findings at 12 Month		Total
	Non-Healed	Healed	
GROUP Rabeprazole (10mg)	10	10	20
	50.0%	50.0%	100.0%
Rabeprazole (20mg)	5	25	30
	16.7%	83.3%	100.0%
Omeprazole (20mg)	18	12	30
	60.0%	40.0%	100.0%
Total	33	47	80
	41.3%	58.8%	100.0%

**Table 6. Distribution of heartburn at day among Rabeprazole (20mg) and Omeprazole (20mg) groups**

	Symptoms At 12 Month		Total
	Heartburn during day	Heartburn -free days	
DRUGS Rabeprazole (20mg)	3	27	30
	10.0%	90.0%	100.0%
Omeprazole (20mg)	9	21	30
	30.0%	70.0%	100.0%
Total	12	48	60
	20.0%	80.0%	100.0%

**Table 7. Distribution of heartburn at night among Rabeprazole (20mg) and Omeprazole (20mg) groups**

	Symptoms At 12 Month		Total
	Heartburn during night	Heartburn-free nights	
Drugs Rabeprazole (20mg)	2	28	30
	6.7%	93.3%	100.0%
Omeprazole (20mg)	9	21	30
	30.0%	70.0%	100.0%
Total	11	49	60
	18.3%	81.7%	100.0%

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