Randomized, Comparative Study of Standard Dose of Rabeprazole versus Omeprazole in Gerd/Heartburn Symptom Relief

Ajayi A.O[1], Solomon O.A[2]✎, Solomon O.O[3], Olotu O.S[2]

[1]Gastroenterology unit, Medicine Department, University Teaching Hospital, Ado Ekiti
[2]Family Medicine Department, Ekiti State University Teaching Hospital, Ado Ekiti
[3] Community Medicine Department, Ekiti State University Teaching Hospital, Ado Ekiti

Aim and objective: Gastro-esophageal reflux disease (GERD) is becoming increasingly common in Africa and indeed in Nigeria. Data on the efficacy of proton pump inhibitors in patients with GERD are scanty. In this study, we compared symptom relief rate after first dose treatment with Rabeprazole i.e. 20 mg versus omeprazole 20 mg in GERD/Heart burn patients.

Materials and Methods: A total of 66 consenting consecutive patients attending the General Out- Patient Department (GOPD) Clinic of the Ekiti State University Teaching Hospital (EKSUTH), Ado-Ekiti, Nigeria presenting with symptoms of GERD/ heartburn were enrolled for the study. At enrolment, severity of symptom was graded on a five-point scale from none (0), mild (1), moderate (2), severe (3) and very severe (4). After enrolment, the patients were blindly randomized into two groups of 33 each which received either 20mg of Rabeprazole (Barole) stat; Rab- group or 20mg of Omeprazole stat; Ome- group. Symptom status was recorded in Case Report Form (CRF) at enrolment and 1hr 30 min after the treatment with stat dose of the proton pump inhibitor. Efficacy of proton pump inhibitor in symptom relief for GERD/heartburn was assessed by observing the degree of symptom relief after 1hr 30 minutes in each of treatment groups. Approval for the study was obtained from the Ethical and Research Committee of EKSUTH. Informed consent was equally obtained from each of the participants. Data obtained were analyzed using scale of comparison.

Results: The mean age of the population studied was aged 33.98 ± 9.43 years (age range 18-50 years). 19 (28.8%) were males while 47 (71.2%) were females (M: F of 1:2.5). 25.8% of participants had regurgitation as a symptom in addition to heartburn while 40.9% had other GI symptoms. The mean symptom severity score at baseline were 2.33, 0.36 and 0.52 for heartburn, regurgitation and other symptoms respectively. Two of the Rabeprazole group who had 'Very severe' heartburn was after 1hr 30mins downgraded to 1(50%) 'Mild' and 1 (50%) 'Moderate' while only 1 participant with 'very severe' heartburn was downgraded to 'severe' heartburn, 1hr 30mins after Omeprazole.Ten in the Rabeprazole group who presented with 'severe' heartburn were downgraded 4(40%) to 'moderate' and 6 (60%) 'Mild' heartburn compare with Omeprazole group where 10 of the participants who had 'severe' heartburn were downgraded to 6(60%) and 4(40%) with 'moderate' and 'mild' heartburn respectively. One of the participants in Rabeprazole group who had 'Severe' regurgitation was downgraded to 'Nil' regurgitation, while none of the participants in Omeprazole group had 'severe' regurgitation. Two of the participants in Rabeprazole group had other symptoms of 'moderate' severity that were downgraded to 'No symptoms' compared with 5 participants in Omeprazole group with other symptoms with 'moderate severity' out of which 3(60%) and 2(40%) were downgraded to 'mild' and 'No symptoms respectively'.

Conclusion: Symptomatic relief is one of the primary goals in the management GERD.
In this study Rabeprazole (Barole®) is more effective in downgrading the heartburn and other symptoms in GERD within 90 minutes of treatment compared to treatment with Omeprazole.
Keywords: GERD, Heart burns, Rabeprazole, Omeprazole and Symptom relief

✎　　**Solomon O. A (Correspondence)**
✉　　abide7000@yahoo.co.uk
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Introduction

Gastro-oesophageal reflux disease (GERD) is a common and chronic disorder. Its most common symptom is heartburn, which affects about one-quarter of all adults on a regular basis in Western countries [1, 2]. The disease is not self limiting and pathological reflux in patients with GERD typically persists for years or even decades [3]. GERD is observed to be the most common acid related disorders with prevalence of 20% among adults in North America and 26.3% among medical students in Enugu, Nigeria [4-5]. It is a chronic condition characterized by reflux of gastric content into oesophagus with resultant irritation and inflammation of oesophageal mucosa [5].

GERD is commonly associated with several symptoms, such as heartburn, belching, and regurgitation, which results from oesophageal exposure to gastric acid, these symptoms may occur with or without the presence of endoscopically observed oesophageal mucosal damage and inflammation symptoms [6]. Atypical (extra oesophageal) symptoms such as dysphagia, chest pain, laryngitis, GERD induced respiratory and sleep disorders may be seen. GERD could be considered as a spectrum disease, which has milder, non-erosive cases and longer lasting, worse, erosive or complicated cases with deep oesophageal ulcers, stricture or Barrett's oesophagus [6-7].

When treating GERD, the goal of treatment should include not only the healing of mucosal lesions, but also the relief of heartburn symptoms [8-9]. The most effective drugs in treatment of GERD are proton pump inhibitors which produce more complete remission of heartburn symptoms than H2 receptor antagonists or prokinetic agents [8, 10]. They are also more effective than H2 receptor antagonists in promoting healing of oesophageal lesions [8]. In many of the current practice guidelines Proton pump inhibitors are recommended as reasonable for initial treatment for GERD [9]. Rabeprazole since introduction as a proton pump inhibitor has been documented to be effective in treatment of gastric and duodenal ulcers as well as for GERD [11-14].

In this study, we compared symptom relief rate after first dose treatment with rabeprazole i.e. 20 mg versus omeprazole 20 mg in GERD/Heart burn patients.

Methods

This was a randomized comparative study.

A total of 66 consenting consecutive patients attending the General Out- Patient Departments (GOPD) Clinic of the Ekiti State University Teaching Hospital, Ado-Ekiti, Nigeria presenting with symptoms of GERD/ heartburn were enrolled for the study. At enrolment, severity of symptom was graded on a five-point scale from none (0), mild (1), moderate (2), severe (3) and very severe (4).

After enrolment, the patients were blindly randomized into two groups of 33 each which received either 20mg of Rabeprazole (Barole) stat; Rab- group or 20mg of Omeprazole stat; Ome-group.

Other upper GI symptoms of belching ('eructation'), early satiety ('the sensation of filling up quickly'), bloating ('feeling like I have a lot of gas in my belly'), nausea and vomiting were also graded on the five-point scale explained above.

Symptom status was recorded in Case Report Form (CRF) at enrolment and 1hr 30 min after the treatment with stat dose of the proton pump inhibitor. Efficacy of proton pump in symptom relief for GERD/heartburn was assessed by observing the degree of symptom relief after 1hr 30 minutes in each of treatment groups.

Results

1.0 General Characteristics

Participants enrolled into the study were aged 18 to 50 years with mean age of 33.98 ± 9.43 years. Amongst the participants 19 (28.8%) were males while 47 (71.2%) were females, M: F of 1:2.5. 25.8% of participants had regurgitation as a symptom in addition to heartburn while 40.9% had other GI symptoms like belching, early satiety, bloating, nausea and vomiting. The mean symptom severity score at baseline were 2.33, 0.36 and 0.52 for heartburn, regurgitation and other symptoms respectively. Table 1.

2.0 Efficacy of Rabeprazole Vs Omeprazole
2.1 Efficacy of Rabeprazole Vs Omeprazole on Heartburn Relief

Two of the Rabeprazole group who had 'Very severe' heartburn was after 1hr 30mins downgraded to 1(50%) 'Mild' and 1 (50%) 'Moderate' while only 1 participant with 'very severe' heartburn was downgraded to 'severe' heartburn, 1hr 30mins after Omeprazole. **(Fig. 1)**

Ten of the participants in the Rabeprazole group who presented with 'severe' heartburn were downgraded 4(40%) to 'moderate' and 6 (60%) 'Mild' heartburn compare with Omeprazole group where 10 of the participants who had 'severe' heartburn were downgraded to 6(60%) and 4(40%) with 'moderate' and 'mild' heartburn respectively **(Fig. 2).**

Of the 20 with 'moderate' heartburn in Rabeprazole group, 16(80%) and 4(20%) were downgraded to 'Mild' and 'Nil' (0) heartburn compare to

Omeprazole group where 19 participants with 'Moderate' heartburn were downgraded with 9 (47.4%) and 10 (52.6%) with 'Mild' and 'Nil' heartburn **(Fig. 3).**

One of the participants in Rabeprazole group had 'Mild' heartburn at presentation and was downgraded to 'Nil' heartburn compared with 3 in the Omeprazole group which had only one of the participants downgraded to 'Nil' heartburn and the remaining 2 were unchanged **(Fig. 4).**

2.2 Efficacy of Rabeprazole Vs Omeprazole on Regurgitation

One of the participants in Rabeprazole group had 'Severe' regurgitation which was downgraded to 'Nil' regurgitation, while none of the participants in Omeprazole group had 'severe' regurgitation **(Fig. 5).** 3 of those in Rabeprazole group had 'moderate' regurgitation which was downgraded in 1 (33.3%) and 2 (66.7%) to 'Mild' and 'Nil' regurgitation respectively compare with 2 in Omeprazole group which was downgraded to 1(50%) each for 'Mild' and 'Nil' regurgitation **(Fig. 6).** The 5 participants that had 'Mild' regurgitation were downgraded to 'Nil' regurgitation in Rabeprazole group while all 6 that had 'mild' regurgitation were downgraded to 'Nil' regurgitation in Omeprazole **(Fig. 7).** 24 participants and 25 participants in Rabeprazole and Omeprazole respectively were without regurgitation.

2.3 Efficacy of Rabeprazole Vs Omeprazole on Other Symptoms

Two of the participants in Rabeprazole group had other symptoms of 'moderate' severity that were downgraded to 'No symptoms' compared with 5 participants in Omeprazole group with other symptoms with 'moderate severity' out of which 3(60%) and 2(40%) were downgraded to 'mild' and 'No symptoms respectively' **(Fig. 8).** 11 of those in Rabeprazole group has other symptoms with 'mild' severity with 10 (90.9%) downgraded to 'No symptom' while 1(9.1%) was without improvement and compared with 9 in the Omeprazole group with 'Mild' form of other symptoms, 8 (88.9%) were downgraded to 'No symptom' and 1(11.1%) was without improvement **(Fig. 9).** Twenty and 19 of the participants are without 'other symptoms' of GERD in Rabeprazole and Omeprazole group respectively.

Discussion

Various lifestyle factors are reported to be associated with GERD [15], and reflux symptoms negatively affect health-related quality of life, work productivity, and health resource utilization [16-19]. The severity of GERD is directly correlated with the degree and duration of esophageal acid exposure and is highly pH dependent [20-22] Moreover, reflux oesophagitis is a risk factor for esophageal stricture in 4-20% of patients [20], Barrett's esophagus in up to 15% of patients [21-23] and esophageal adenocarcinoma [24]. Proton pump inhibitors (PPIs) are the most effective treatment for GERD, including endoscopically confirmed reflux oesophagitis [25]. Most individuals experience resolution of their reflux symptoms when taking a PPI [25], with a concomitant overall improvement in health-related quality of life [26-27].

Rabeprazole has been documented to have a faster onset of antisecretory action than Omeprazole. In this study we observed that Rabeprazole achieved a more rapid downgrading of heartburn within the 1st one and half hour of ingestion compared with Omeprazole and other symptoms in GERD within 90 minutes of treatment compared to treatment with Omeprazole this is comparable to the observation by Adachi K e t al where downgrading of severity of heartburn amongst patients with erosive reflux oesophagitis was more rapid in Rabeprazole compared to Omeprazole group [28] similar study of symptomatic relief by Rabeprazole and Omeprazole amongst participants with erosive GERD related heartburn by Xia and Wang favoured Rabeprazole 20 mg over Omeprazole 20 mg for relief of heartburn (RR = 1.133; 95% CI: 1.028-1.249; P = 0.012) [29], while a multicenter study done by Sloan in United states observed significant positive effect of 10 mg of Rabeprazole on heartburn and other GERD symptoms like regurgitation, belching, bloating, early satiety, and nausea within 1 and 2 days compare to 20 mg of Omeprazole, this study observed significant effect using 20 mg of Rabeprazole on heartburn, regurgitation and other symptoms of GERD within 90mins of administration when compared with Omeprazole [30].

PPIs are metabolized via the hepatic enzyme cytochromes P450, 2C19 and CYP2C19. There are three genetic polymorphisms of CYP2C19, resulting in homozygous extensive metabolizer (homoEM), heterozygous extensive metabolizer (heteroEM) and poor metabolizer (PM) phenotypes [31]. These CYP2C19 phenotypes have different effects on the pharmacodynamic and pharmacokinetic profiles of PPIs. Gastric acid secretion is affected such that post-PPI intragastric pH values are highest in the PM group and lowest in the homoEM group following administration of omeprazole or Rabeprazole [32]. The clinical relevance of these differences is especially important for patients in Japan, where the PM phenotype is much more common (prevalence 18.0–22.5 %) than in the USA or Europe (prevalence ≤ 3.7 %) [31].

Results obtained from this study are similar to that obtained in the studies among healthy Japanese volunteers where the different CYP2C19 phenotypes

were taken into consideration [33-35]. Compared with omeprazole 20 mg or lansoprazole 30 mg, rabeprazole 10 mg has been shown to exert a faster and more pronounced inhibition of gastric acid secretion in these healthy Japanese volunteers with the homoEM or heteroEM phenotypes [33]. The findings in this study were in contrast to that obtained in the study of Nagahara et al where omeprazole 20mg was found to be more effective than Rabeprazole 10mg at achieving early, sufficient, sustained reflux symptom relief in individuals with

the CYP2C19 PM phenotype, and is similarly effective to rabeprazole 10 mg in those with heteroEM or homoEM phenotypes [36].

Conclusion: Symptomatic relief is one of the primary goals in the management GERD.

In this study Rabeprazole (Barole®) is more effective in downgrading the heartburn and other symptoms in GERD within 90 minutes of treatment compared to treatment with Omeprazole.

**Table 1:** General characteristics of the population

General Characteristics

|	
Sex	
Male	19 (28.8%)
Female	47 (71.2%)
Age	35.23 ± 12.27 yrs
Weight	65.62 ± 12.8 Kg
Mean Symptom Score at Presentation	
Heart Burns	2.33 ± 0.66
Regurgitation	0.36 ± 0.69
Other symptoms	0.52 ± 0.69
Duration of symptoms prior presentation	19.5 ± 28.2 months
Associated mobility	
Diabetes	
Yes	0 (0%)
No	66(100%)
Hypertension	
Yes	7 (10.6%)
No	59 (89.4%)

Fig. 1 Effectiveness of Rabeprazole vs. Omeprazole in Very Severe Heartburn
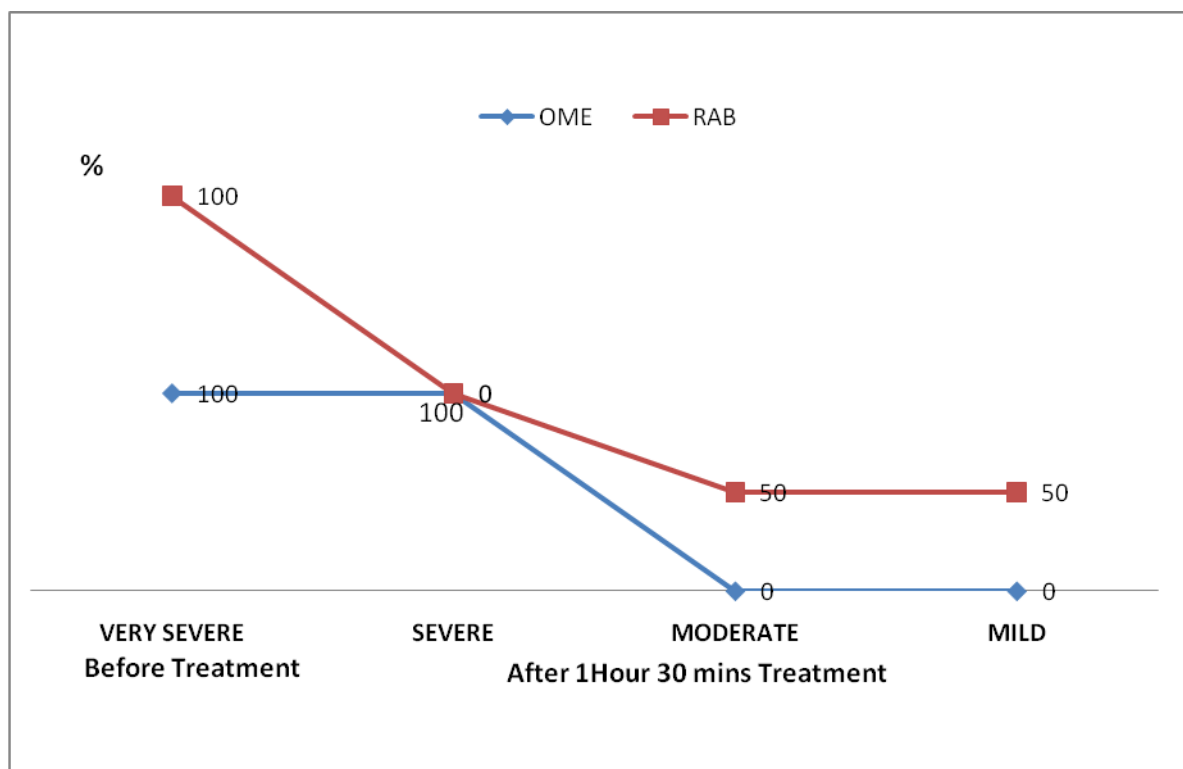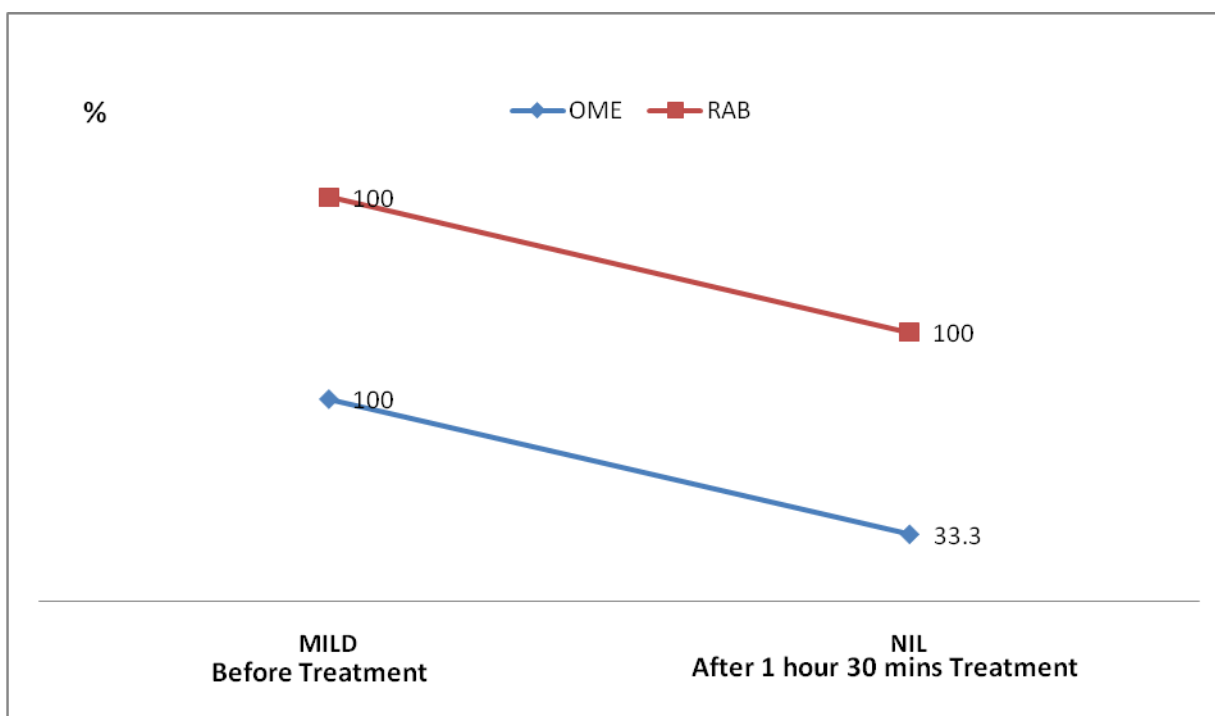

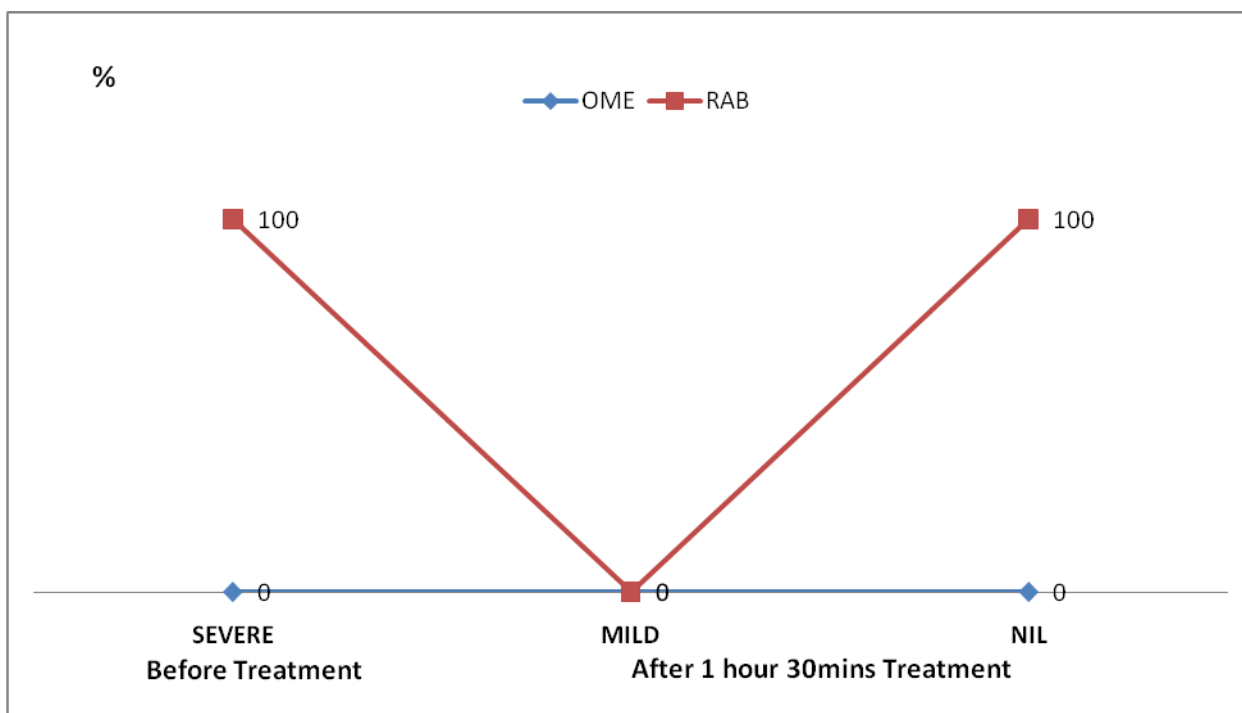**Fig.2** Effect of Rabeprazole Vs. Omeprazole in Severe Heartburn
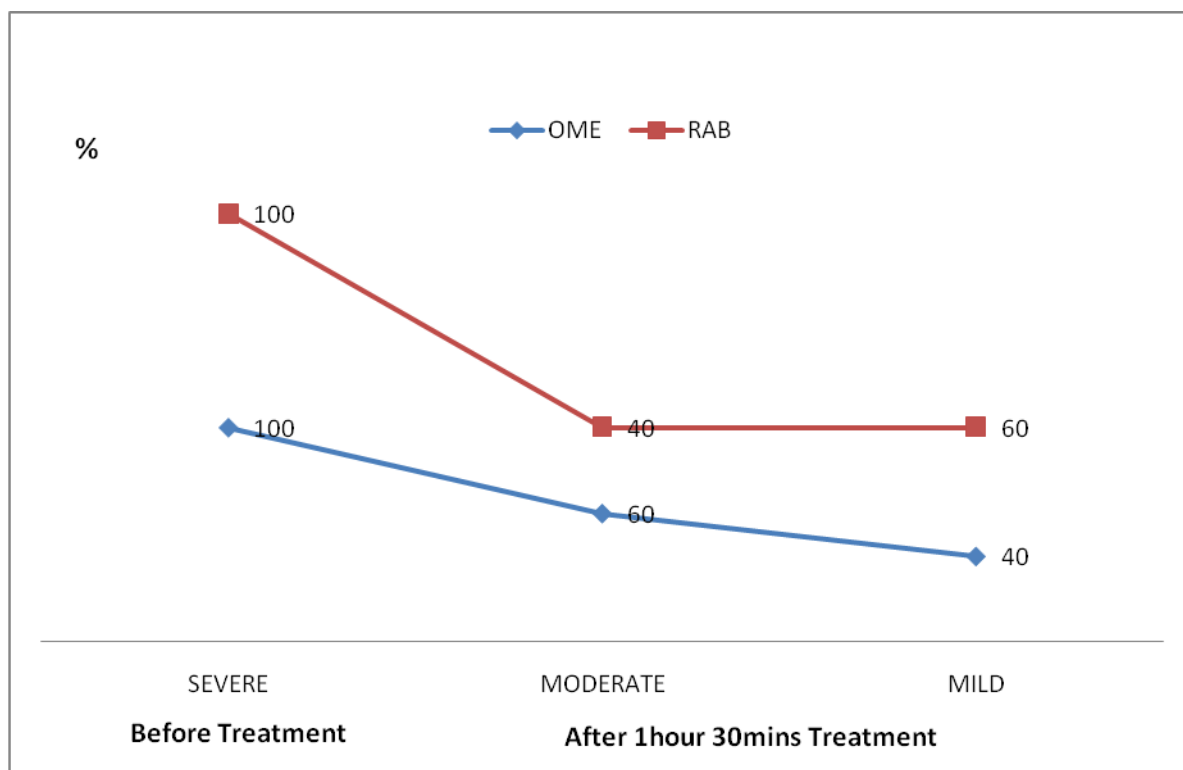
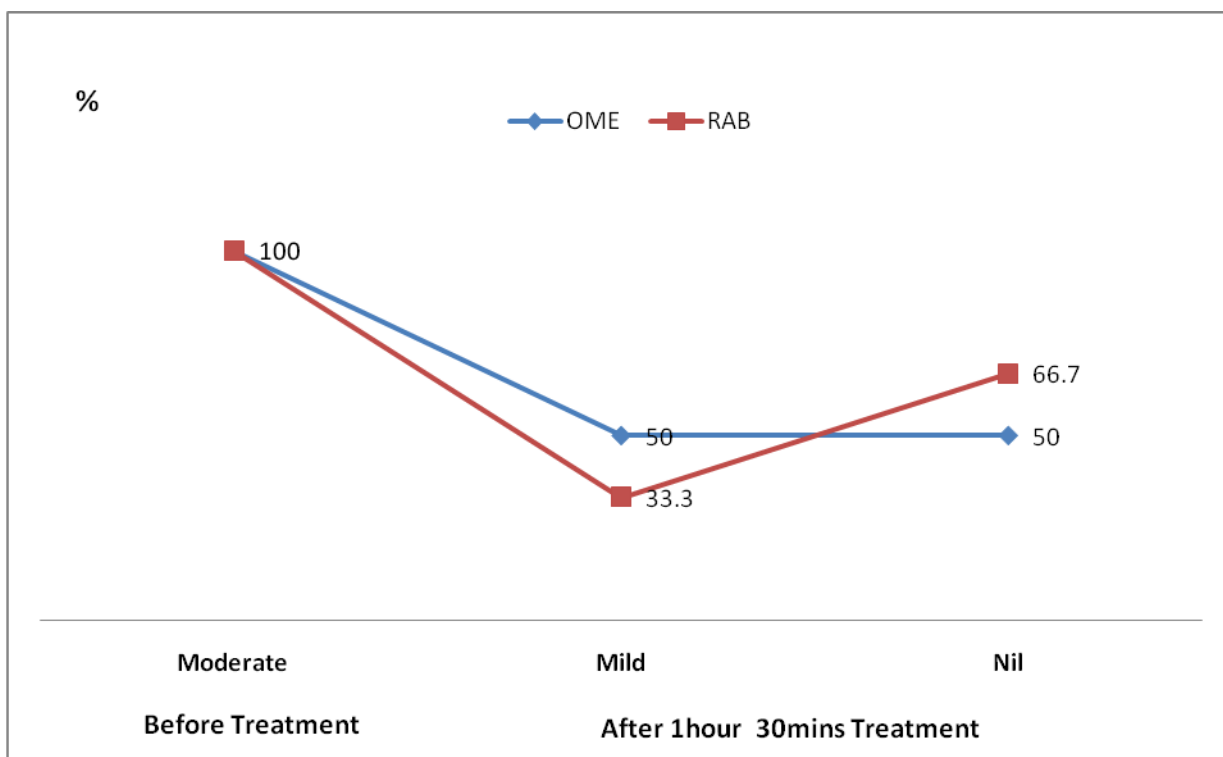**Fig. 3** Effectiveness of Rabeprazole Vs. Omeprazole in Moderate Heartburn
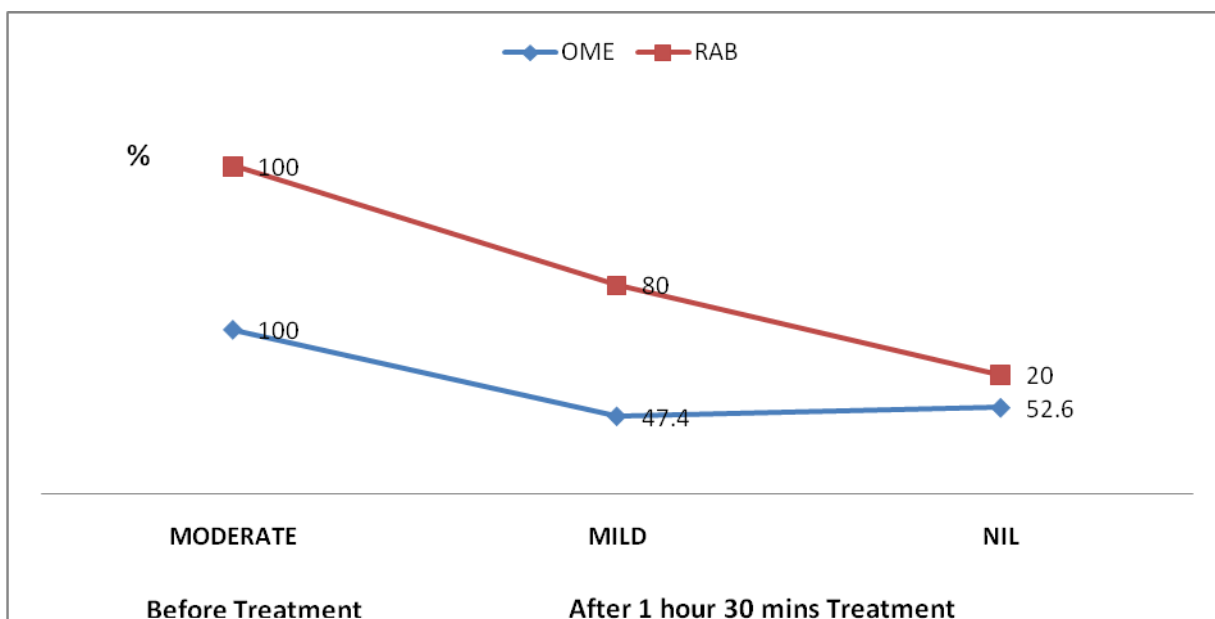
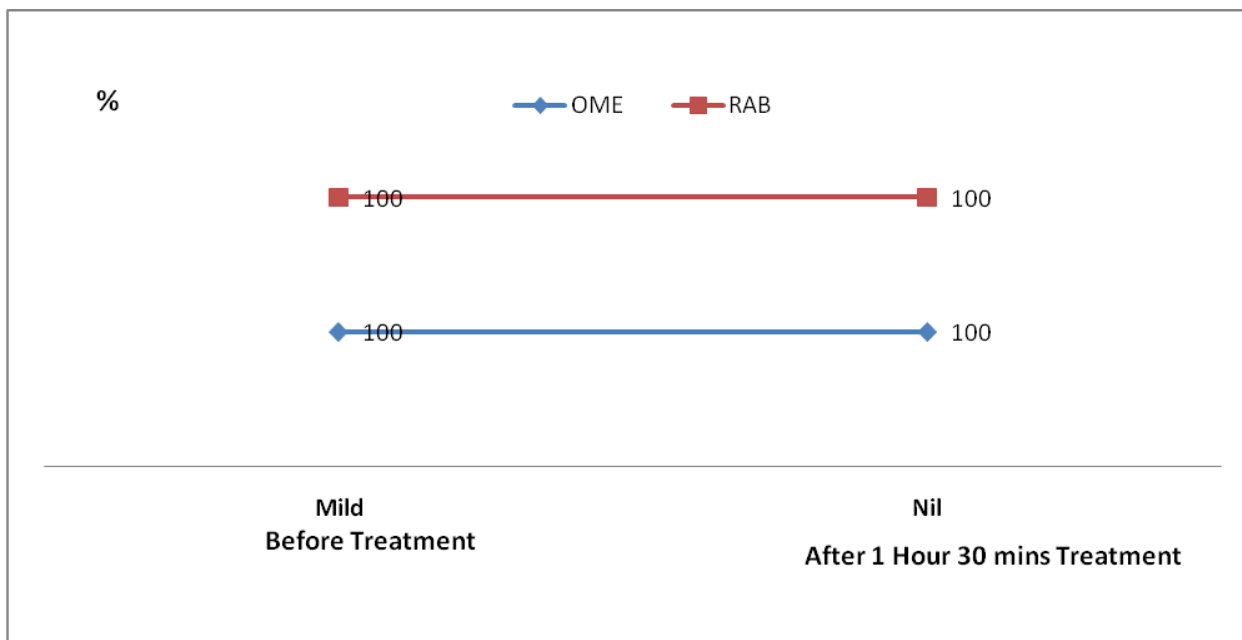**Fig. 4** Effectiveness of Rabeprazole Vs Omeprazole in Mild Heartburn

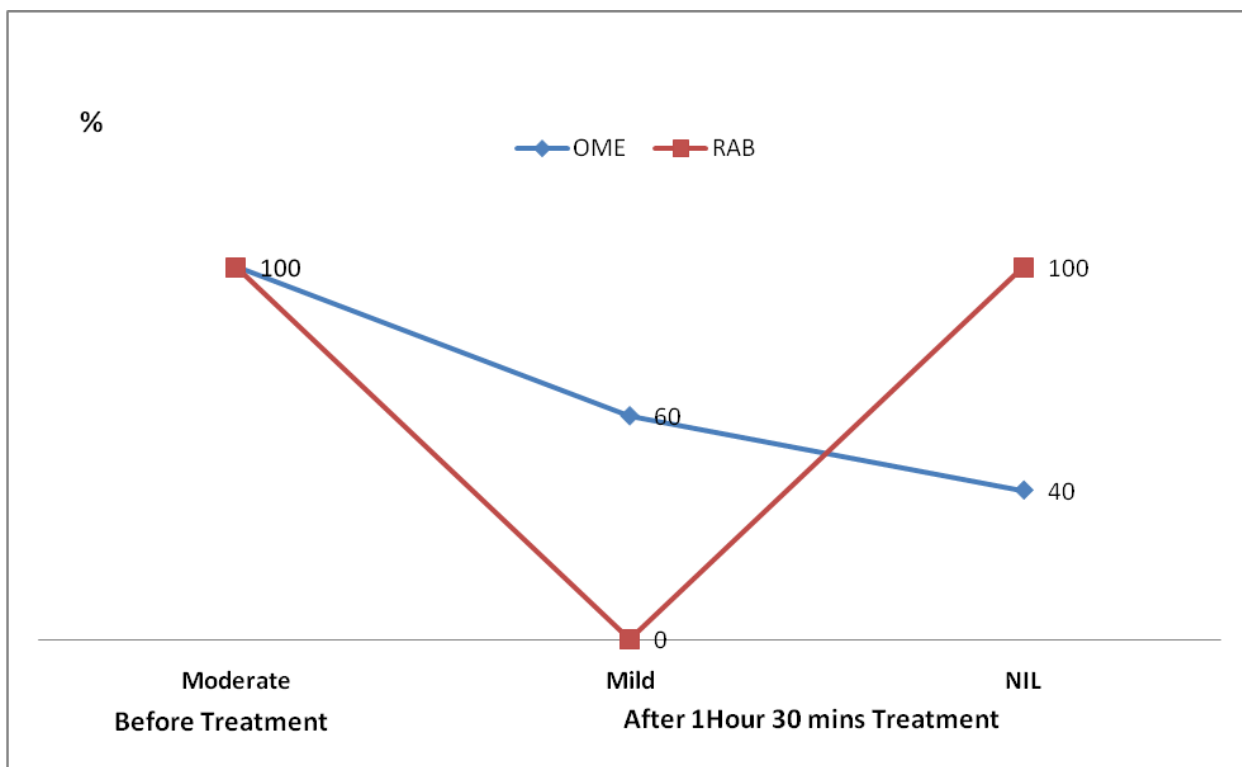**Fig. 5** Effectiveness of Rabeprazole Vs Omeprazole in Severe Regurgitation

Fig 6. Effectiveness of Rabeprazole Vs Omeprazole in Moderate Regurgitation

Fig. 7 Effectiveness of Rabeprazole Vs Omeprazole in Mild Regurgitation
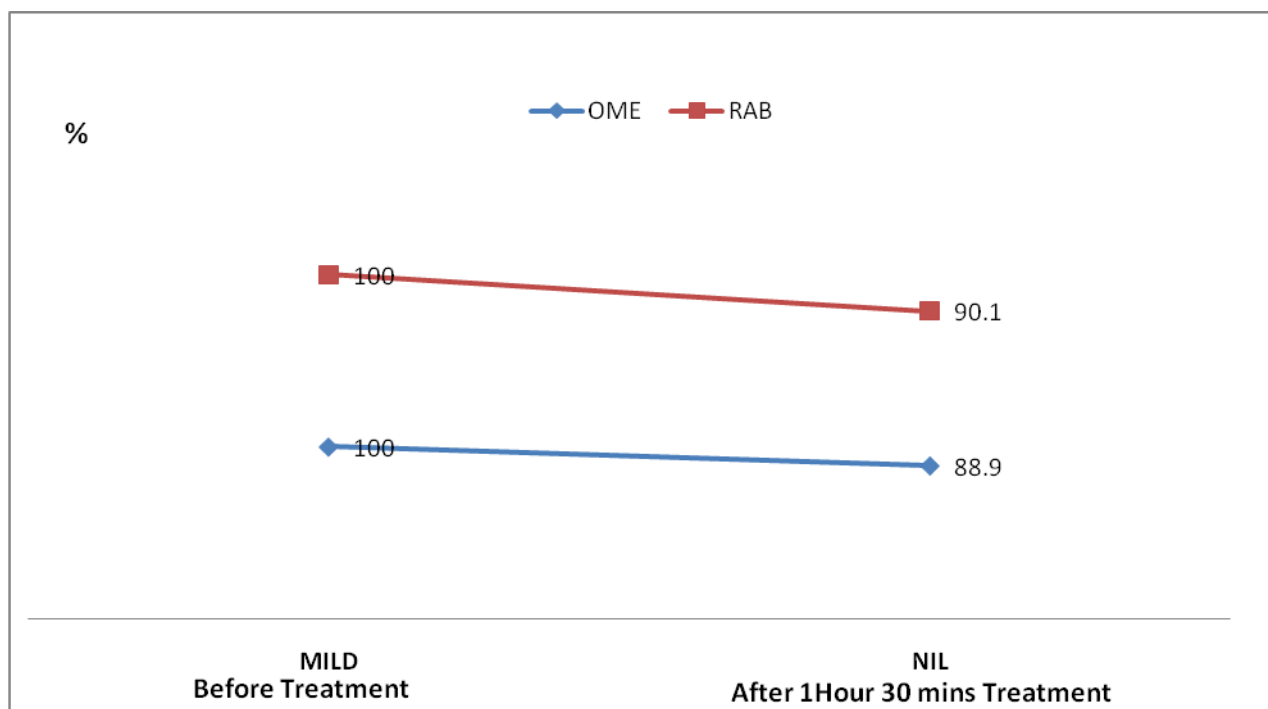

Fig. 8 Effectiveness of Rabeprazole Vs. Omeprazole in Moderate Other GERD Symptoms

Fig. 9 Effectiveness of Rabeprazole Vs. Omeprazole in Mild Other GERD Symptoms

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