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Original Research Article

Effect of omeprazole on patient-reported outcome measures in uninvestigated heartburn: a multi-country, multi-center observational study

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ABSTRACT

Background: Heartburn occurs predominantly in the upper gastrointestinal tract and is associated with gastroesophageal reflux disease (GERD) and gastritis. Omeprazole is the most prescribed proton pump inhibitor class of medication to treat heartburn related clinical conditions. To compare the efficacy of omeprazole 40 mg (as a total daily dose) and 20 mg using patient-reported outcome measures (PROMs) in patients with heartburn due to various aetiologies like non-erosive reflux disease, GERD, gastritis, dyspepsia, functional heartburn, gastro-duodenal ulcer.
Methods: Naïve patients presenting heartburn symptoms were treated with omeprazole. PROMs were assessed based on short-form-leeds dyspepsia questionnaires (SF-LDQ), work productivity activity impairment (WPAI), relief obtained using medication and, treatment satisfactory questionnaires (TSQ).
Results: A total of 18,724 patients with heartburn (GERD and gastritis; n=10,509) were treated with omeprazole (Dr. Reddy's omeprazole [DO]/generic omeprazole [GO]/branded omeprazole [BO]) 40 mg (as a total daily dose) and 20 mg. Statistical comparative analysis showed significant improvement with omeprazole 40 mg (as a total daily dose) compared to omeprazole 20 mg in SF-LDQ, relief obtained using medication among patients with heartburn. DO 20 mg showed a greater improvement under the 'a lot' and 'complete' relief category.
Conclusions: Omeprazole 40 mg (as a total daily dose) presented better efficacy as compared to omeprazole 20 mg in patient reported outcomes. This study highlights omeprazole 40 mg as the preferred intervention for improving PROMs and quality of life in the treatment of heartburn related clinical conditions.

Keywords: Heartburn, Gastroesophageal reflux disease, Gastritis, Omeprazole, Patient-reported outcome measures

INTRODUCTION

Heartburn is typically a burning sensation extending from the sternal manubrium to the base of the neck, throat, face, and angle of the arm. Heartburn occurs predominantly in the upper gastrointestinal tract (GIT) and is a key presentation in gastroesophageal reflux disease (GERD) and gastritis.[1,2] GERD and gastritis, the most common debilitating conditions of the GIT, are characterized by an orderly occurrence of injury or inflammation in the innermost layer of the oesophagus and stomach.[3,4] Several risk factors increase the frequency and severity of the condition including, smoking, high body mass index, limited physical activity, and certain medications (such as anti-inflammatory and cytotoxic drugs).[5] Many individuals with heartburn have reported significant impairment in health-related quality of life (HRQoL), psychological well-being, and social functioning.[6] Over the last decade, there has been a substantial rise in the proportion of younger patients with GERD, especially those within the age range of 30–39 years.[7] On average, over the last decade, more than half of world's population has had gastritis at some point in their lifetime.[8]

Currently, various therapeutic classes of drugs are available in the form of generic and branded for treating heartburn. Each of these therapeutic classes have demonstrated their action at different levels by blocking or altering different physiological activities of the GIT.[9] Proton pump inhibitors (PPIs) have remained the cornerstone for GERD and gastritis treatment, which act by irreversibly impeding the release of gastric acid from gastric parietal cells. Many PPIs are now available in generic and branded forms.[10] However, some studies have stated that the use of generic drugs could be related to an increased time to relapse the condition or might lead to therapeutic failure.[11]

In this study, we have focused on omeprazole, which is one of the most prescribed PPIs to treat heartburn associated with non-erosive reflux disease (NERD), GERD, gastritis, dyspepsia, functional heartburn, and gastro-duodenal ulcer. According to the National Health Service business statistics, more than 2 million omeprazole items were prescribed in the UK in 2018 due to an exponential increase in the incidences of GERD and gastritis. The global hospital pharmacy segment dominated the market due to the easy availability of omeprazole in hospitals and the omeprazole segment is expected to continue dominating the market from 2018 to 2026.[12]

This study compared the effectiveness of omeprazole 40 mg (as a total daily dose) and 20 mg using patient-reported outcome measures (PROMs) in heartburn patients (including NERD, dyspepsia, functional heartburn, gastro-duodenal ulcer) as well as GERD and gastritis patients. PROMs were assessed based on the short-form-Leeds dyspepsia questionnaires (SF-LDQ), work productivity activity impairment (WPAI), amount of relief obtained in heartburn using medication, and treatment satisfactory questionnaires (TSQ). Further, the study evaluated the efficacy of Dr. Reddy's omeprazole (DO) 20 mg in patients with heartburn, and in subjects suffering from GERD and gastritis.

METHODS

Study design and study setting

This multi-center, prospective, pre- and post-comparative study was carried out from 1st October 2016 to 31st January 2017 and enrolled naïve patients who presented with heartburn considered as a predominant symptom. Patients were treated with omeprazole 40 mg (as a total daily dose) (DO 40 mg/generic omeprazole [GO] 40 mg/branded omeprazole [BO] 40 mg) and 20 mg (DO 20 mg/GO 20 mg/BO 20 mg). The study was conducted at various hospitals, polyclinics, secondary and tertiary care centers in Russia, Ukraine, Kazakhstan, Belarus, Myanmar, and Romania.

Study population

The present study enrolled naïve patients ≥18 years of age with predominant symptom of frequent (>2 times a week in the last one week) heartburn and complaint of difficulty in swallowing, nausea, or vomiting for the past month.

Inclusion criteria

Patients were included based on the following inclusion criteria: patients with predominant symptoms of heartburn with or without regurgitation for the last 30 days with an increased frequency of ≥2 days in the last 7 days before their baseline visit; treatment of naïve patients; male or female adult patients ≥18-75 years of age; patients who present to the clinic with predominant symptoms of frequent (>2 times a week in the last one week) heartburn such as burning pain in the chest that may extend to the neck or base of the throat, which may occur after eating and at night; patients may also complain of difficulty in swallowing, nausea, or vomiting; patients who have been prescribed omeprazole 40 mg (as a total daily dose) or 20 mg; and patients who had provided written informed consent to participate in the study, which indicated that the patients were informed of all the pertinent aspects of the study before participation.

Exclusion criteria

Patients were excluded: if they participated in an investigational drug or investigational device within 30 days before start of the study; prior treatment for heartburn symptoms with omeprazole or other PPIs or any other over the counter medications of >3 doses during the week immediately before the study; previous history of hypersensitivity to any PPIs including omeprazole in the past; a history of other gastrointestinal conditions such as Barret's oesophagus (>3 cm), Zollinger-Ellison syndrome, scleroderma in the past 12 months; history of cancer (other

than non-melanoma skin cancers) present within the last 5 years, cardiac diseases, alcohol or drug abuse and any other psychiatric disorders, which in the opinion of the investigator, could interfere with the patient's participation in the study.

Subject information and informed consent

The informed consent form (ICF) was signed and dated by the patients personally and the authoritative persons obtained the informed consent individually. All patients provided informed consent before the participation in the study, although they may withdraw from the study at any time point as per their request, or they may be withdrawn at any time at the discretion of the investigator or sponsor for safety, behavioural, or administrative reasons.

Patients' characteristics at baseline

Data including demographic variables (age, gender, body weight, symptoms duration, lifestyle habits, education, employment, and marital status) and clinical variables (medical history with comorbid conditions, surgical history of past one month, and prior medications relevant to heartburn, prior infection, and risk behaviours) were recorded in a de-identified electronic case report form during baseline visit. Individual patients were provided with unique identifying study number, and their data was kept confidential. As per the study protocol, treating physicians diagnosed patients based on the initial heartburn symptoms. Patients were advised laboratory and diagnostic tests (endoscopy) post their baseline visit and before their next follow-up visit to ascertain the presence of gastrointestinal conditions such as GERD, NERD, functional dyspepsia, *Helicobacter pylori* which may cause heartburn symptoms. Treatment of patients were completely at the discretion of the physician who diagnosed the patient and the gastroenterologists who further treated those patients to improve their condition and elevate their quality of life from heartburn related disease conditions.

Patient-reported outcome measures

PROMs were assessed based on SF-LDQ, WPAI, amount of relief obtained in heartburn using medication, and TSQ. SF-LDQ includes five different categories such as 'not at all', 'less than once a month', 'between once a month and once a week', 'between once a week and once a day', and 'once a day or more' to evaluate the frequency and severity of heartburn, indigestion, regurgitation, and nausea. The present study focuses only on the 'not at all' (no symptoms) category in patients with heartburn symptoms, GERD, and gastritis. WPAI measures absenteeism, presentism, work productivity loss and activity impairment. WPAI has demonstrated a high level of convergent and discriminant validity, and has been used to calculate the working hours of employed subjects and evaluate the effectiveness of different dosages of drugs post-treatment.[13,14] Patients were instructed to complete SF-LDQ and WPAI at visit 1 (baseline) and visit 2 (two weeks post-omeprazole treatment); TSQ score was obtained only at visit 2.[15]

The study was approved by the ethics committee (where ever required) of each country/study site, and all research work was carried out in compliance with the Helsinki declaration with ICH topic E6 (R1) guideline for good clinical practice and related local regulations.

Statistical methods and data analysis

As this study was not based on a hypothesized effect size, a formal estimation of sample size and statistical power was not undertaken. The study was conducted across multiple centers in each country. Each investigator enrolled a maximum of 100 patients with heartburn symptoms considering an attrition rate of 50% over the study period.

Subjective data was collected by using PROMs. Collected data were anonymized before analysis and then analyzed using STATA version 13 (based on the form of data availability we were used independent t-test/Mann-Whitney U-test, Chi-square test).[16] Descriptive statistics were used for description of the demographic data, which was mainly presented as a number (percentage) for binary data. Relative percentage change from baseline to endpoint was computed to determine the treatment effect within each intervention. However, to compare the effect between the dosages of the drug, absolute percentage change proportions were compared using the test for two proportions with a significance level of <0.05.

RESULTS

A total of 18,724 patients with symptoms of heartburn were enrolled in the study across various centers. Patients were prescribed with omeprazole 40 mg (as a total daily dose) and omeprazole 20 mg based upon the study protocol to assessed the efficacy by using PROMs. Out of 18,724 patients, a total of 10,509 patients had heartburn with GERD and gastritis. Baseline characteristics of included patients with heartburn have been given in Table 1. Baseline characteristics of heartburn patients suffering from GERD and gastritis is depicted in Table 2.

Short-form-leeds dyspepsia questionnaires

Details on the comparative (between omeprazole 40 mg [as a total daily dose] and 20 mg) statistical analysis of frequency and severity symptoms of patients with heartburn suffering from gastritis, GERD, NERD, dyspepsia, functional heartburn, and gastroduodenal ulcers have been given in Table 3. For both dosages, frequency and severity symptoms were assessed based on heartburn, indigestion, regurgitation, and nausea. Patients with symptoms of heartburn had statistically significant results ($p=0.001$) in the 'not at all' category when compared from visit 1 to visit 2. However, on further comparison, patients

with heartburn symptoms administered with omeprazole 40 mg (as a total daily dose) had a higher incidence of symptoms falling under the 'not at all' category compared to patients with omeprazole 20 mg.

Treatment in heartburn patients due to various etiologies including GERD and gastritis with DO 20 mg showed favourable results (Table 3) in the outcome of SF-LDQ under the 'not at all' category from visit 1 to visit 2. Numerically, a greater number of patients with heartburn who were administered DO 20 mg had not experienced any symptoms post-treatment.

In GERD and gastritis condition, considerable change from visit 1 to visit 2 in the 'not at all' category was observed in patients treated with both dosages of omeprazole (40 mg [as a total daily dose] and 20 mg).

Frequency and severity symptoms in patients with GERD and gastritis related to DO 20 mg, showed better improvement in number of patients from visit 1 to visit 2 (Table 4).

Work productivity activity impairment

Patients with heartburn symptoms who were treated with both dosages of omeprazole (40 mg [as a total daily dose] and 20 mg) had a significant change (p=0.001 and p=0.040) in absenteeism (work time was missed due to health) and presentism respectively. Equal distribution of patients was observed in absenteeism, presentism, overall work impairment, and daily activity impairment (Table 5). Treatment with DO 20 mg reduced the number of patients who had work impairments.

Patients with GERD and gastritis treated with omeprazole 40 mg (as a total daily dose) and 20 mg had a considerable change in presentism (work impairment due to health), overall work impairment, and daily activity impairment. Patients treated with DO 20 mg had a better work improvement (presentism, overall work impairment, and daily activity impairment) among employed patients (Table 6).

Amount of relief obtained in heartburn using medication

Both dosages of omeprazole (40 mg [as a total of daily dose] and 20 mg) showed statistically significant (p<0.001) results in patients who have obtained relief from heartburn. Similarly, treatment with DO 20 mg also provided significant relief from heartburn symptoms.

In GERD and gastritis conditions, similar distribution of patients who were taking omeprazole 40 mg and 20 mg were observed for amount of relief obtained from heartburn categories (none, a little, a moderate amount, a lot and complete relief).

Out of 2572 patients treated with DO 20 mg, 77.53% of patients had a lot (46.5%) and complete (31.03%) relief obtained from heartburn (Table 7).

Table 1: Baseline characteristics of patients with heartburn related disease.

Characteristics	Omeprazole 40 mg (n=11035)	Omeprazole 20 mg (n=7689)
Gender N (%)*		
Male	4399 (43)	2761 (37)
Female	5880 (57)	4759 (63)
Number of patients' N (%) [male/female]		
Belarus	376 (3.66) [153/223]	1538 (20.45) [521/1017]
Kazakhstan	664 (6.46) [253/411]	181 (2.41) [61/120]
Myanmar	1875 (18.24) [735/1140]	290 (3.86) [97/193]
Romania	986 (9.59) [439/547]	1962 (26.09) [727/1235]
Russia	2767 (26.92) [1206/1561]	2406 (31.99) [892/1514]
Ukraine	3611 (35.13) [1613/1998]	942 (12.53) [326/616]
Demographic variables, mean (standard deviation)		
Age	44.29 (12.62)	43.87 (13.02)
Height	167.72 (7.79)	168.03(7.93)
Weight	70.39 (10.97)	70.71 (10.92)
BMI	25.02 (3.62)	25.07 (3.7)
Clinical variables N (%)		
Comorbidities		
Yes	584 (7.75)	1400 (13.43)
No	6954 (92.25)	9021 (86.57)
Concomitant medication		
Yes	368 (4.92)	668 (6.47)
No	7119 (95.08)	9654 (93.53)

Continued.

Characteristics	Omeprazole 40 mg (n=11035)	Omeprazole 20 mg (n=7689)
***H. pylori* infection**		
Yes	626 (8.35)	1706 (16.49)
No	6867 (91.65)	8637 (83.51)
Alcohol/smoking		
Yes	455 (6.07)	1170 (11.35)
No	7043 (93.93)	9138 (88.65)

*756 patients for omeprazole 40 mg and 169 patients for omeprazole 20 mg did not report the gender in the case report form

Table 2: Baseline characteristics of GERD and gastritis patients.

Characteristics	Omeprazole 40 mg (n=7156)	Omeprazole 20 mg (n=3533)
Gender N (%)[#]		
Male	2719 (38)	1179 (35)
Female	3825 (53)	2109 (63)
Number of patients' N (%) [M/F]		
Belarus	201 (3) [75/126]	462 (14) [157/305]
Kazakhstan	492 (8) [169/323]	119 (4) [36/83]
Myanmar	507 (8) [217/290]	85 (3) [21/64]
Romania	586 (9) [258/328]	870 (26) [337/533]
Russia	2051 (31) [836/1215]	1116 (34) [405/711]
Ukraine	2707 (41) [1164/1543]	636 (19) [223/413]
Demographic variables, mean (SD)		
Age	45.01 (12.51)	45.30 (12.91)
Height	168.42 (7.49)	168.11 (7.71)
Weight	71.73 (10.42)	71.89 (10.81)
BMI	25.31 (3.52)	25.47 (3.77)
Clinical variables N (%)		
Comorbidities		
Yes	997 (14.84)	299 (9.09)
No	5722 (85.16)	2991 (90.91)
Concomitant medication		
Yes	407 (6.13)	163 (5.01)
No	6228 (93.87)	3089 (94.99)
***H. pylori* infection**		
Yes	1049 (15.79)	222 (6.82)
No	5595 (84.21)	3033 (93.18)
Alcohol/smoking		
Yes	790 (11.92)	260 (7.97)
No	5838 (88.08)	3001 (92.03)

#612 patients for omeprazole 40 mg and 245 patients for omeprazole 20 mg did not report the gender in the case report form

Table 3: Frequency and severity of symptoms in heartburn related disease conditions with omeprazole 40 mg (as a total daily dose) vs. omeprazole 20 mg, and Dr. Reddy's omeprazole (DO) 20 mg analyzed by SF-LDQ.

Outcome	Visit	Heartburn		Indigestion		Regurgitation		Nausea		Total
		Frequency	Severity	Frequency	Severity	Frequency	Severity	Frequency	Severity	
Omepr-azole 40 mg	Visit 1 N (%)	586 (5)	761 (7)	1263 (11)	1653 (15)	1859 (17)	2348 (21)	3936 (36)	4370 (40)	11035
	Visit 2 N (%)	3376 (31)	3917 (35)	4308 (39)	4820 (44)	4926 (45)	5541 (50)	6674 (60)	7091 (64)	11035

Continued.

Outcome	Visit	Heartburn		Indigestion		Regurgitation		Nausea		Total
		Frequency	Severity	Frequency	Severity	Frequency	Severity	Frequency	Severity	
	Change from baseline (%)	26	28	28	29	28	29	24	24	-
Omepr-azole 20 mg	Visit 1 N (%)	221 (3)	593 (8)	1964 (26)	2573 (33)	1610 (21)	2431 (32)	3565 (46)	4145 (54)	7689
	Visit 2 N (%)	1461 (19)	2019 (26)	3230 (42)	3805 (49)	3016 (39)	3699 (48)	4822 (63)	5183 (67)	7689
	Change from baseline (%)	16	18	16	16	18	16	17	13	-
P value		0.001	0.001	0.001	0.001	0.001	0.001	0.001	0.001	-
DO 20 mg	Visit 1 N (%)	192 (2.95)	374 (5.75)	1649 (25.36)	2093 (32.19)	1344 (20.67)	1975 (30.37)	2930 (45.06)	3386 (52.07)	6503
	Visit 2 N (%)	1115 (17.15)	1481 (22.77)	2643 (40.64)	3065 (47.13)	2422 (37.24)	2972 (45.70)	3987 (61.31)	4284 (65.88)	6503
	Change from baseline (%)	14.20	17.02	15.28	14.94	16.57	15.33	16.25	13.81	-

Table 4: Frequency and severity of symptoms in GERD and gastritis conditions with omeprazole 40 mg (as a total daily dose) vs. omeprazole 20 mg, and Dr. Reddy's omeprazole (DO) 20 mg analyzed by SF-LDQ.

Outcome	Visit	Heartburn		Indigestion		Regurgitation		Nausea		Total
		Frequency	Severity	Frequency	Severity	Frequency	Severity	Frequency	Severity	
Omepr-azole 40 mg	Visit 1 N (%)	262 (3.7)	2450 (34.2)	802 (11.2)	3102 (43.3)	1130 (15.8)	3417 (47.8)	2593 (36.2)	4616 (64.5)	7156 (100)
	Visit 2 N (%)	416 (5.8)	2810 (39.3)	1139 (15.9)	3504 (49.0)	1523 (21.3)	3867 (54.0)	2923 (40.8)	4902 (68.5)	7156 (100)
	Change from baseline (%)	2.1	5.1	4.7	5.7	5.5	6.2	4.6	4	-
Omepr-azole 20 mg	Visit 1 N (%)	95 (2.8)	694 (20.7)	745 (22.2)	1364 (40.7)	556 (16.6)	1263 (37.7)	1470 (43.8)	2089 (62.3)	3353 (100)
	Visit 2 N (%)	263 (7.8)	953 (28.4)	1006 (30.0)	1656 (49.4)	911 (27.2)	1555 (46.4)	1735 (51.7)	2234 (66.6)	3353 (100)
	Change from baseline (%)	5	7.7	7.8	8.7	10.6	8.7	7.9	4.3	-
DO 20 mg	Visit 1 N (%)	76 (2.95)	457 (17.77)	416 (16.17)	875 (34.02)	558 (21.7)	973 (37.83)	1041 (40.47)	1502 (58.4)	2572
	Visit 2 N (%)	145 (5.64)	587 (22.82)	627 (24.38)	1059 (41.17)	691 (26.87)	1131 (43.97)	1205 (46.85)	1595 (62.01)	2572
	Change from baseline (%)	2.69	5.05	8.21	7.15	5.17	6.14	6.38	3.61	-

Table 5: Heartburn related disease conditions with omeprazole 40 mg (as a total daily dose) versus omeprazole 20 mg, and Dr. Reddy's omeprazole (DO) 20 mg analyzed by WPAI.

Outcome	Omeprazole 40 mg			Omeprazole 20 mg			P value	DO 20 mg		
	Subjects (N)	Mean	SD	Subjects (N)	Mean	SD		Subjects (N)	Mean	SD
Absenteeism	6221	3.40	13.05	5532	2.68	10.99	=0.001	4872	2.62	11.11
Presentism	6211	22.15	21.36	5520	22.96	21.44	=0.040	4862	21.43	19.90

Continued.

Outcome	Omeprazole 40 mg			Omeprazole 20 mg			P value	DO 20 mg		
	Subjects (N)	Mean	SD	Subjects (N)	Mean	SD		Subjects (N)	Mean	SD
Overall work impairment	6221	23.67	23.07	5532	24.01	22.48	=0.415	4872	22.56	21.22
Daily activity impair-ment	6425	21.31	21.66	5644	21.73	21.13	=0.284	4972	20.24	19.55
Total	11035	-	-	7689	-	-	-	6503	-	-

Table 6: GERD and gastritis conditions with omeprazole 40 mg (as a total daily dose) versus omeprazole 20 mg, and Dr. Reddy's omeprazole (DO) 20 mg analyzed by WPAI.

Outcome	Omeprazole 40 mg			Omeprazole 20 mg			DO 20 mg		
	Subjects (N)	Mean	SD	Subjects (N)	Mean	SD	Subjects (N)	Mean	SD
Absenteeism	3723	3.32	12.84	2300	2.97	12.13	1871	3.24	12.55
Presentism	3724	25.88	21.40	2295	23.00	21.85	1867	21.19	19.89
Overall work impairent	3723	27.35	22.93	2300	24.24	23.13	1871	22.57	21.55
Daily activity impair-ent	3889	24.85	21.59	2351	21.09	20.56	1914	19.22	18.00
Total	7156	-	-	3353	-	-	2572	-	-

Table 7: Amount of relief obtained in heartburn by use of omeprazole 40 mg (as a total daily dose) versus omeprazole 20 mg, and Dr. Reddy's omeprazole (DO) 20 mg in heartburn related disease conditions, GERD and gastritis.

Condition	Outcome	None	A little	A moderate amount	A lot	Complete	Total
Heartburn related disease condition	Omeprazole 40 mg N (%)	1824 (16.5)	752 (6.8)	824 (7.5)	4332 (39.3)	3303 (29.9)	11035
	Omeprazole 20 mg N (%)	718 (9.3)	198 (2.6)	728 (9.5)	3398 (44.2)	2647 (34.4)	7689
	P-value	<0.001					
	DO 20 mg N (%)	539 (8.29)	183 (2.81)	658 (10.12)	2875 (44.21)	2248 (34.57)	6503
GERD and gastritis	Omeprazole 40 mg N (%)	1352 (18.9)	216 (3.0)	533 (7.4)	2812 (39.3)	2243 (31.3)	7156
	Omeprazole 20 mg N (%)	419 (12.5)	78 (2.3)	280 (8.4)	1532 (45.7)	1044 (31.1)	3353
	DO 20 mg N (%)	280 (10.89)	69 (2.68)	229 (8.9)	1196 (46.5)	798 (31.03)	2572

Table 8: Heartburn related disease conditions with omeprazole 40 mg (as a total daily dose), omeprazole 20 mg, and Dr. Reddy's omeprazole (DO) 20 mg analyzed by TSQ.

Outcome	Agree	Neither agree nor disagree	Strongly disagree	Strongly disagree	Total
Question 1: I am satisfied with how quickly my medication works (N)					
Omeprazole 40 mg N (%)	9051 (96.6)	205 (2.2)	62 (0.7)	51 (0.5)	9369
Omeprazole 20 mg N (%)	6961 (96.8)	146 (2.0)	35 (0.5)	46 (0.6)	7188
DO 20 mg n (%)	5978 (96.81)	139 (2.25)	30 (0.49)	28 (0.45)	6175
Question 2: overall, I am satisfied with how well this medication has controlled my heartburn (N)					
Omeprazole 40 mg N (%)	8925 (95.3)	333 (3.6)	58 (0.6)	54 (0.6)	9370
Omeprazole 20 mg N (%)	6930 (96.4)	167 (2.3)	47 (0.7)	45 (0.6)	7189
DO 20 mg N (%)	5954 (96.41)	156 (2.53)	42 (0.68)	24 (0.39)	6176

Continued.

Outcome	Agree	Neither agree nor disagree	Strongly disagree	Strongly disagree	Total
Question 3: I am confident that this medication will make me feel better (N)					
Omeprazole 40 mg N (%)	9167 (97.9)	100 (1.1)	53 (0.6)	47 (0.5)	9367
Omeprazole 20 mg N (%)	7021 (97.7)	93 (1.3)	37 (0.5)	36 (0.5)	7187
DO 20 mg N (%)	6037 (97.75)	87 (1.41)	32 (0.52)	20 (0.32)	6176
Question 4: I am confident that this medication will continue to work (N)					
Omeprazole 40 mg N (%)	8807 (94.0)	473 (5.0)	50 (0.5)	38 (0.4)	9368
Omeprazole 20 mg N (%)	6776 (94.3)	349 (4.9)	25 (0.3)	35 (0.5)	7185
DO 20 mg N (%)	5824 (94.30)	315 (5.10)	18 (0.29)	19 (0.31)	6176
Question 5: this medication is easy to take (N)					
Omeprazole 40 mg N (%)	9173 (97.9)	108 (1.2)	56 (0.6)	34 (0.4)	9371
Omeprazole 20 mg N (%)	7085 (98.6)	57 (0.8)	10 (0.1)	35 (0.5)	7187
DO 20 mg N (%)	6092 (98.64)	56 (0.91)	9 (0.15)	19 (0.31)	6176
Question 6: taking this medication is convenient (N)					
Omeprazole 40 mg N (%)	9175 (97.9)	111 (1.2)	56 (0.6)	30 (0.3)	9372
Omeprazole 20 mg N (%)	7081 (98.5)	57 (0.8)	22 (0.3)	26 (0.4)	7186
DO 20 mg N (%)	6091 (98.62)	53 (0.86)	19 (0.31)	13 (0.21)	6176
Question 7: I will continue to use this medication for controlling my heartburn (N)					
Omeprazole 40 mg N (%)	8921 (95.2)	334 (3.6)	67 (0.7)	48 (0.5)	9370
Omeprazole 20 mg N (%)	6844 (95.2)	268 (3.7)	43 (0.6)	32 (0.4)	7187
DO 20 mg N (%)	5875 (95.13)	247 (4.00)	39 (0.63)	15 (0.24)	6176

Table 9: Heartburn symptoms exclusively related to GERD and gastritis with omeprazole 40 mg (as a total daily dose), omeprazole 20 mg, and Dr. Reddy's omeprazole (DO) 20 mg analyzed by TSQ.

Outcome	Agree	Neither agree nor disagree	Disagree	Strongly disagree	Total
Question 1: I am satisfied with how quickly my medication works (n)					
Omeprazole 40 mg N (%)	5713 (97.16)	114 (1.94)	22 (0.37)	31 (0.53)	5880
Omeprazole 20 mg N (%)	2960 (96.4)	65 (2.1)	22 (0.7)	22 (0.7)	3069
DO 20 mg N (%)	2333 (96.29)	0 (0)	1 (1.47)	1 (1.47)	2423
Question 2: Overall, I am satisfied with how well this medication has controlled my heartburn (n)					
Omeprazole 40 mg N (%)	5606 (95.32)	220 (3.74)	23 (0.39)	32 (0.54)	5881
Omeprazole 20 mg N (%)	2925 (95.3)	92 (3.0)	28 (0.9)	25 (0.8)	3070
DO 20 mg N (%)	2304 (95.05)	86 (3.55)	24 (0.99)	10 (0.41)	2424
Question 3: I am confident that this medication will make me feel better (n)					
Omeprazole 40 mg N (%)	5786 (98.43)	52 (0.88)	16 (0.27)	24 (0.41)	5878
Omeprazole 20 mg N (%)	2994 (97.6)	42 (1.4)	17 (0.6)	15 (0.5)	3068
DO 20 mg N (%)	2367 (97.65)	37 (1.53)	15 (0.62)	5 (0.21)	2424
Question 4: I am confident that this medication will continue to work (n)					
Omeprazole 40 mg N (%)	5525 (93.98)	318 (5.41)	16 (0.27)	20 (0.34)	5879
Omeprazole 20 mg N (%)	2864 (93.4)	178 (5.8)	12 (0.4)	14 (0.5)	3068
DO 20 mg N (%)	2261 (93.28)	152 (6.27)	7 (0.29)	4 (0.17)	2424
Question 5: This medication is easy to take (n)					
Omeprazole 40 mg N (%)	5777 (98.25)	68 (1.16)	16 (0.27)	19 (0.32)	5880
Omeprazole 20 mg N (%)	3032 (98.8)	20 (0.7)	3 (0.1)	15 (0.5)	3070
DO 20 mg N (%)	2397 (98.89)	20 (0.83)	2 (0.08)	5 (0.21)	2424
Question 6: Taking this medication is convenient (n)					
Omeprazole 40 mg N (%)	5775 (98.20)	66 (1.12)	24 (0.41)	16 (0.27)	5881
Omeprazole 20 mg N (%)	3021 (98.5)	25 (0.8)	9 (0.3)	13 (90.4)	3068
DO 20 mg N (%)	2390 (98.64)	22 (0.91)	6 (0.25)	5 (0.21)	2423
Question 7: I will continue to use this medication for controlling my heartburn (n)					
Omeprazole 40 mg N (%)	5606 (95.36)	230 (3.91)	19 (0.32)	24 (0.41)	5879
Omeprazole 20 mg N (%)	2885 (94.0)	144 (4.7)	24 (0.8)	16 (0.5)	3069
DO 20 mg N (%)	2270 (93.69)	128 (5.28)	21 (0.87)	4 (0.17)	2423

Treatment satisfactory questionnaires

Almost 95% of heartburn patients who were prescribed with both dosages of omeprazole (40 mg [as a total daily dose] and 20 mg) marked 'agree' on all questionnaires. Similarly, heartburn patients who were administered with DO 20 mg also agreed with all seven questionnaires on treatment satisfaction (Table 8).

In GERD and gastritis conditions, nearly 96% of patients who were on omeprazole 40 mg (as a total daily dose) and 20 mg checked the 'agree' category. Numerically, a higher number of patients who were treated with omeprazole 40 mg (as a total daily dose) agreed with all the questionnaires. Likewise, higher number of patients treated with DO 20 mg agreed with the questionnaires (Table 9).

Overall, the results demonstrate that patients who were prescribed omeprazole 40 mg (as a total daily dose) and DO 20 mg were highly satisfied with the treatment and had a positive response to the medication.

DISCUSSION

Success of a treatment has been measured in various ways, based on disease-induced areas of dysfunctions that include HRQoL, loss of work productivity, and other areas of employment.[17] Although many studies have been conducted individually to investigate the effectiveness of omeprazole by using different pharmacokinetic and pharmacodynamic parameters, this is the first study conducted to evaluate the efficacy and compare the different dosages (40 mg [as a total daily dose] and 20 mg) of omeprazole using PROMs.[18,19] Patient-reported outcome instruments are fast emerging as important tools in clinical studies.[20] Two omeprazole regimens (40 mg [as a total daily dose] and 20 mg) have comparable effectiveness in achieving relief from symptoms, work productivity impairment, and treatment satisfaction. In terms of statistics, omeprazole 40 mg (as a total daily dose) has statistically high significance compared with omeprazole 20 mg.

SF-LDQ is a highly reliable, valid, and responsive self-completed outcome measure to quantify the frequency and severity of heartburn, indigestion, regurgitation, and nausea.[21] It is shorter and more convenient than other generic methods.[16] The sensitivity of SF-LDQ was measured using independent t-test/Man-Whitney U test. The results of SF-LDQ related to omeprazole 40 mg (as a total daily dose) and 20 mg in patients with heartburn, omeprazole 40 mg (as a total daily dose) showed significant (p=0.001) findings in frequency and severity of heartburn, indigestion, regurgitation, and nausea. Further, omeprazole 40 mg (as a total daily dose) considerably increased the number of patients (percentage of baseline changes) under the 'not at all' category from visit 1 to visit 2. Treatment with DO 20 mg decreased the frequency and severity of symptoms among heartburn patients.

In GERD and gastritis, results of SF-LDQ associated with both the dosages of omeprazole (40 mg [as a total daily dose] and 20 mg) showed decrease in the frequency and severity of heartburn, indigestion, regurgitation, and nausea. Both dosages of omeprazole greatly increased the number of patients (percentage of baseline changes) under the 'not at all' category from visit 1 to visit 2 (Table 4). Further, DO 20 mg increased the number of patients who had GERD and gastritis at visit 2 under the 'not at all' category. In terms of frequency and severity, changes in heartburn have been assessed using the SF-LDQ scale. However, heartburn had a strong correlation with work productivity impairment. Hence, assessment of work productivity impairment is an important factor in chronic diseases to determine drug effectiveness. It is a self-administered, well-validated method to measure work impairments before and after treatment. It exerts a strong connection between work productivity impairments and disease severity.[13]

In this study, WPAI related data were collected in clinics during visit 1 and visit 2 in the form of absenteeism, presentism, overall work impairment, and daily activity impairment. In heartburn related disease conditions, the sensitivity of WPAI for omeprazole 40 mg (as a total daily dose) was found to be statistically significant in terms of absenteeism (p=0.001) and presentism (p=0.040) among both dosages. As from visit 1 to visit 2 the number of patients has decreased with percent of work time missed and percent of work impairment while working. The remaining outcomes of WPAI (overall work impairment and daily activity impairment) were statistically insignificant since there was no decrease in number of patients with percent of overall work impairment and percent of daily activity impairment from visit 1 to visit 2. Treatment with DO 20 mg has shown better improvement in presentism, overall work impairment, and daily activity impairment as there was significant decrease in the number of patients with percent of work impairment while working, percent of overall work impairment, and percent of daily activity impairment in visit 2 (Table 5).

In GERD and gastritis, omeprazole 40 mg (as a total daily dose) and 20 mg showed favourable improvement in terms of presentism, overall work impairment, and daily activity impairment evident from significant decrease in the number of patients with the percent of work impairment while working, percent of overall work impairment, and percent of daily activity impairment from visit 1 to visit 2. Considerable enhancement in presentism, overall work impairment, and daily activity impairment was achieved with DO 20 mg since there was reduction in number of patients with work impairment while working, overall work impairment, and daily activity impairment in visit 2 (Table 6).

The amount of relief obtained using both omeprazole 40 mg (as a total daily dose) and 20 mg in heartburn, omeprazole 40 mg (as a total daily dose) was statistically significant (p<0.001). An increased number of patients

treated with omeprazole 40 mg (as a total daily dose) was observed under the category of 'a lot of relief and complete relief'. Treatment with DO 20 mg considerably increased the number of patients under the category of 'a lot of relief and complete relief' obtained from heartburn symptoms. In GERD and gastritis conditions, patients who were prescribed with omeprazole 40 mg (as a total daily dose) and 20 mg have obtained 'a lot of relief and complete relief' from heartburn. Likewise, DO 20 mg remarkably increased the number of patients under the category of 'a lot of relief' in heartburn symptoms post-treatment.

TSQ is a reliable and highly useful outcome measure in clinical studies to provide an insight into the patient's outlook towards treatment.[22] This is particularly important when other comparative treatments may have equal efficacy, as satisfaction is likely to lead to patient preferences for one treatment over another. Increased patient satisfaction with treatment has also been shown to be linked to adherence to prescription regimens.[16,17] It is directly correlated to continue or stop taking medication.[23]

In heartburn related diseases, treatment with omeprazole 40 mg (as a total daily dose) and 20 mg greatly increased the percentage of patients under the category of 'agree'. Patients agreed with all the questionnaires as they were satisfied with the given treatment. Likewise, more than 90% of patients treated with DO 20 mg agreed with all questionnaires (Table 8). Patients treated with omeprazole 40 mg and 20 mg for GERD and gastritis were satisfied with the treatment and agreed with all the questionnaires. DO 20 mg treatment showed patient satisfaction with the medication and positive response to the treatment (Table 9).

Limitations

The current study is the first of its kind in assessing the efficacy of omeprazole using PROMs in a large number of patients (n=18,724) from different geographic locations. Besides this, the study has few limitations such as the observational nature of the study which lacks randomization in the design. However, observational studies with a control group will provide considerable evidence on efficacy if the sample size is large enough as in the current study. Additionally, heartburn and indigestion are common in pregnant women who were not included in the present study. Heartburn associated with diseases such as NERD, dyspepsia, functional heartburn, and gastro-duodenal ulcer were not analyzed separately. Since the sample size was not of normal distribution between DO 20 mg and GO 20 mg, no statistical analysis was conducted to compare the results. Similarly, in GERD and gastritis conditions, the results were not statistically compared between the dosages.

CONCLUSION

In conclusion, omeprazole 40 mg (as a total daily dose versus omeprazole 20 mg) reported statistical significance in improving the PROMs in patients suffering from heartburn due to various aetiologies including, GERD and gastritis. Further, DO 20 mg, showed considerable improvements in patients with heartburn symptoms, GERD, and gastritis in terms of PROMs. Based on these clinical outcomes, it can be concluded that omeprazole 40 mg (as a total daily dose) significantly improved the quality of life of patients suffering from heartburn related disease conditions.

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