



THE EFFECT OF OMEPRAZOLE ADMINISTRATION TO THE QUALITY OF LIFE OF GASTRO ESOPHAGEAL REFLUX DISEASE PATIENTS

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ABSTRACT

Background: The quality of life of Gastro Esophageal Reflux Disease (GERD) patients will consistently decline both physically and psychologically compared to the general population. WHOQOL-BREF is a questionnaire to evaluate the quality of life with high validity and reliability. One of GERD therapy is a proton pump inhibitor (PPI). There are studies on PPI administration in GERD patients worldwide, however in Indonesia there is limited research evaluating how PPI especially Omeprazole influences the quality of life in GERD. We determined the effect of omeprazole to the quality of life of patients with GERD.

Methods: GERD questionnaires (GERDQ) was used to determine life quality of GERD patients and interpretation was performed based on score obtained. The comparison between the perception of the quality of life and perception of health satisfaction in GERD patients before and after Omeprazole administration was analyzed using Wilcoxon signed rank test. While, the comparison of the quality of life based on WHOQOL-BREF before and after administration of omeprazole was analyzed using Wilcoxon signed rank test and t-test.

Results: We included 43 GERD patients with the mean age of 39.50±5.71 years. The most complaints were nausea, pain in the upper middle part of the stomach and heartburn (88.4%; 81.4% and 79.1%, respectively). There was a significant difference in the perception of quality of life ($p=0.000$) and the perception of health satisfaction ($p=0.001$) but, there was no significant difference in WHOQOL-BREF scores before and after Omeprazole administration (each domains of physical, social, psychological, environmental was $p=0.275$; $p=0.380$; $p=0.199$; $p=0.810$ respectively).

Conclusion: Omeprazole did not improve the quality of life of GERD patients.

KEYWORDS: WHOQOL-BREF, quality of life, gastroesophageal-reflux disease

INTRODUCTION

Gastroesophageal reflux disease (GERD) is a disorder in which the contents of the stomach are repeatedly refluxed into the esophagus causing symptoms and/or complications (1). GERD is often experienced by people and can cause serious problems ranging from discomfort to deterioration in the quality of life. The prevalence of GERD in

the last period increased both in children and adults thus became a worldwide problem (2). Symptoms of GERD that can decrease the quality of life are sleeping disturbances, chest pain, wheezing, day and night cough, difficulty of swallowing and nausea (3, 4). GERD can also cause depression and anxiety (2, 4, 5). Most GERD patients (80-90%) often buy their own medicine at pharmacies. One of the drugs they buy is a proton pump inhibitor (6). The use of proton pump inhibitors such as Omeprazole is expected to reduce patient complaints (7). However, there are no studies that have evaluated the effect of Omeprazole on the quality of life of GERD patients in Indonesia. The author's

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interest in selecting a population of GERD patients was due to a large number of young adult female patients with dyspepsia complaints accompanied by anxiety that comes to the health facility level I or private doctor.

Among GERD patients, 15% have daily complaints, 73% with weekly complaints and more frequent of work leave giving an impact on the quality of life of patients (8, 9, 10). GERD can give an impact on the economy status (11, 12) with the largest expenditure by GERD patients is the cost of doctor consultation and hospital care (13). The number of GERD patients to be hospitalized increased by 216% from 1998 to 2005 (14). Medical expenses in the UK is about 342 pound sterling or approximately IDR 5,882,950,09 rupiah each person per year (15). This suggests that the GERD problem is something that cannot be underestimated.

In this study we measured influence of Omeprazole administration to improve the quality of life of GERD patients. We determined how potent Omeprazole in improving the quality of life of GERD patients by minimizing the involvement of psychological, socioeconomic, and environmental factors. We utilized the WHOQOL-BREF questionnaire which consisted of four domains including physical, psychological, social, and environmental was used to evaluate the quality of life with high validity and reliability. WHOQOL is available in over 40 languages that can be applied in a very strong cross-cultural, making it easy and suitable for diverse cultural contexts (16, 17).

METHODS

Population: The study population was all adult GERD patients who came to the gastroentero-hepatology outpatient unit of Dr. Soetomo Teaching Hospital Surabaya in March-June 2016. Inclusion criteria were male or female outpatients with GERD complaints lasting at least 3 months without alarm symptoms, age range 21-60 years old with GERDQ score of > 8 and SRRS score of < 150 . Exclusion criteria were using hormonal such as progesterone, secretin, glucagon, prokinetics, anti-psychotic, antihistamine, cholinesterase inhibitor, neuromuscular blocking drug, beta-adrenergic blocking, alpha and beta adrenergic stimulant, antimuscarinic anticholinergic, vasopressor, nitric oxide vasodilator, nicotinic antagonist, anti-con-

vulsant, tricyclic antidepressant and inhalation anesthetics, neuropsychiatric drugs, or patients undergoing psychotherapy, or in the past year experiencing severe psychosocial stressors. Patients who experienced severe drug side effects, do not adhere to the study procedure or are unable to continue the study will be declared dropped out. The sample size used in this study was 43.

Preparation of the patient: Eligible patients were provided with an explanation of the purposes and benefits of the examination and were asked to agree to participate in the study by signing informed consent. Furthermore, the patient's general data were recorded, such as name, age, gender, ethnicity, and residential address. Other data were recorded according to the data collection form.

Omeprazole administration: Patients fulfilled the GERDQ, SRRS and WHOQOL-BREF scores were treated with Omeprazole for 4 weeks. Patients who had previously received Omeprazole will be neutralized for 1 week and replaced with Ranitidine and or Antacids prior to given Omeprazole. Four weeks after Omeprazole administration, we evaluated the quality of life of patients using WHOQOL-BREF.

RESULTS

Characteristics of Research Subjects: The samples in this study were 56 GERD patients, but 13 patients (23.3%) declared as drop out, so the number of patients analyzed were as much as 43 people. In this study, male was more likely to drop out than female because of unpredictable dropped out, loss of communication and consumption of tranquilizer group (amitriptyline).

The number of female patients were 2.3 times much more than male. The number of patients with GERD aged 31-50 years were twice than the number of patients aged < 30 years or > 50 years (table 1). Meanwhile, mean of BMI was $21.85 \text{ kg/cm} \pm 4.30 \text{ kg/cm}$ indicating that BMI diversity was low in 43 samples. 27 patients among them have a BMI in the normal category (62.8%). Table 2 showed that the majority of complaints of GERD patients were nausea, followed by pain in the upper middle part of the stomach, heartburn, regurgitation and sleep disorders at night, while table 3 showed GERD Patient's Perception of their Quality of Life.

GERD Patient's Perception of the Quality of

TABLE 1.

Characteristics of GERD Patients		
Characteristics	Mean ± SD	Frequency
Sex		
Male		13(30.2%)
Female		30(69.8%)*
Age		
	43,02± 13,89	
18-30 years old	25.11±2.85	9(20.0%)
31-50 years old	39.50±5.71	20(46.5%)*
> 50 years old	59.57±5.95	14(32.6%)
BMI		
	21,85±4, 03	
Very thin		6(14.0%)
Thin		2(4.7%)
Normal		27(62.8%)
Fat		7(16.3%)
Obesity I		1(2.3%)
Obesity II		-
Obesity III		-

NOTE: *The most common frequency

TABLE 2

Complaints of subjects		
Complaints	Frequency	
	n	%
Nausea	38	88.4*
Pain in the middle of the upper abdomen	35	81.4
Heartburn	34	79.1
Regurgitation	30	69.8
Night sleep disturbance due to pain	15	34.9

NOTE: * The most common frequency

TABLE 3

GERD patient's perception of the quality of life				
The Quality of Life	Before Omeprazole		After Omeprazole	
	f	%	f	%
Very poor	0	0.0	0	0.0
Poor	7	16.3	5	11.6
Ordinary	28	65.1	22	51.2
Good	8	18.6	13	30.2
Very good	0	0.0	3	7.0

TABLE 4

GERD patient's perception of health satisfaction				
Health satisfaction	Before Omeprazole		After Omeprazole	
	f	%	f	%
Very Unsatisfactory	2	4.7	0	0.0
Not satisfactory	23	53.5	15	34.9
Ordinary	12	27.9	14	32.6
Satisfactory	6	14.0	14	32.6
Very satisfactory	0	0.0	0	0.0

Life and Health Satisfaction Before and After Omeprazole Administration: Before Omeprazole administration, the majority of patients (65.1%) had an ordinary life quality category. After Omeprazole administration, there was a decrease in the category of poor quality of life from 16.3% to 11.6%, a decrease in the category of normal quality of life from 65.1% to 51.2%, however, there was an increase in the categories of good and excellent quality of life. Prior to Omeprazole administration, the majority of patients belonged to the health satisfactory category, but after Omeprazole administration, the number of patients with the health unsatisfactory category decreased from 53.5% to 34.9%. In addition, the health satisfactory category increased from 14% to 32.6% (Table 4). Wilcoxon sign rank test results showed that there was a significant difference between the quality of life and health satisfaction in 43 GERD patients before and after Omeprazole administration.

Mean value of WHOQOL-BREF Transformed score before and after administration of Omeprazole

The differences of mean value of domain score before and after Omeprazole were shown in table 5. The increase in each of the WHOQOL-BREF domains was still relatively low whereas the increase in scores was the psychological domain. Data distribution obtained from WHOQOL-BREF scores in 43 GERD patients using Shapiro Wilks method was shown in table 6. WHOQOL-BREF scores of physical and social domains before and after Omeprazole administration had no significant difference, meaning that Omeprazole administration was still unable to improve the quality of

TABLE 5

Mean value of WHOQOL-BREF transformed score before and after administration of Omeprazole					
Domains	Min	Max	Med	Mean	Difference
Physical					
Before	31	69	44	47.7± 10.2	0.9
After	31	69	50	48.6± 9.5	
Psychological					
Before	19	88	50	51.9± 14.9	1.9*
After	19	88	56	53.8± 14.1	
Social					
Before	19	100	56	55.5± 15.8	0.8
After	19	100	56	56.3± 15.4	
Environment					
Before	25	81	56	55.5± 11.3	0.2
After	25	81	56	55.5± 11.5	

* The largest difference of psychological factors

life of GERD patients (table 7). WHOQOL-BREF score of psychological and environmental domains before and after Omeprazole administration showed no significant difference (Table 8), suggesting that the administration of Omeprazole in this study was not yet able to improve the quality of life of GERD patients. Based on Wilcoxon rank test, there was no significant difference on WHOQO-BREF score (p value of 0.476). From Wilcoxon rank test on WHOQOL-BREF total score p value of 0.317 was obtained, suggesting that there was no significant difference.

DISCUSSION

In this study, there were significant differences in the perception of quality of life and health satisfaction even though the WHOQOL-BREF transformed score was not significant. Because the perception of quality of life and health satisfaction was the general perception of the patient (GERD) on quality of life and health satisfaction while the WHOQOL-BREF transformed score was a score based on (the formula count) of the domains.

Patients with GERD symptoms will generally have trouble sleeping at night 1.5 times greater than those during the day resulting in decreased work productivity and disruption of daily activities. According to pathophysiology, the relationship between GERD and sleep disturbance can be caused by the length of contact with acid during sleep, comorbidity of obstructive sleep apnea (OSA), sleep sensory disorders, medications used in sleep disorders, comorbidity of a chronic cough or asthma, and sleep disorders caused by an autonomic nervous system disorder (ANS) and a CNS disorder in processing (18).

PPI administration to individuals with low BMI does not accelerate the healing process (19). In other words, a low BMI is a risk factor for the non-responsiveness of PPI in GERD patients (20). In this study we found that the majority of BMI patients were normal; therefore, the response to Omeprazole administration was not very good.

In this study we found that prior to Omeprazole administration most of the subjects had the quality of life in the ordinary category. Meanwhile, after the administration of Omeprazole, the number of research subjects having the poor quality of life and ordinary quality of life decreased and the num-

TABLE 6

Testing of the data distribution of WHOQOL-BREF domain score before and after Omeprazole administration

Domains	Statistic	p Value	Description
Physical			
Before	0.934	0.016	Abnormal
After	0.934	0.015	Abnormal
Psychological			
Before	0.966	0.230	Normal
After	0.956	0.095	Normal
Social			
Before	0.940	0.025	Abnormal
After	0.943	0.034	Abnormal
Environment			
Before	0.959	0.128	Normal
After	0.954	0.087	Normal
Total			
Before	0.981	0.686	Normal
After	0.975	0.453	Normal

TABLE 7

Wilcoxon sign rank test results on WHOQOL-BREF physical and social domain before and after Omeprazole administration

Domains	Median	Z	p value	Description
Physical				
Before	44	-1.091	0.275	Not significantly different
After	50			
Social				
Before	56	-0.878	0.380	Not significantly different
After	56			

TABLE 8

Paired sample t test results on WHOQOL-BREF psychological and social domain before and after Omeprazole administration

Domains	Mean	t	P Value	Description
Psychological				
Before	51.98	-1.304	0.199	Not significantly different
After	53.84			
Environment				
Before	55.51	-0.243	0.810	Not significantly different
After	55.74			
Total				
Before	210.74	-0.999	0.323	Not significantly different
After	214.40			

ber of subjects with the good and excellent category in the quality of life increased. This is very different from the results of Arihiro et al.'s study (2012) (20) which reported that patients in Asia responded less to the PPI than patients in Western countries, suggesting an influence of easier detection of the erosion and the less severe gastrointestinal symptoms (21).

The success of PPI therapy to improve the quality of life of GERD patients is influenced by many factors including patient compliance, *H. pylori* infection, bioavailability, acid breakdown at night, rapid metabolism, peripheral resistance, duodenogastroesophageal reflux, non-acidic gastroesophageal reflux, delayed stomach emptying, visceral hypersensitivity, psychological comorbidity and emotional stress (22).

Patients with anxiety or depression respond poorly to PPIs (23). Patients with sleep disturbances related to lack of quality and duration will associate with more severe GERD symptoms, also may decrease the therapeutic response. Fujiwara et al. (2010) and Kusano et al. (2008) (24, 25) stated that GERD patients experienced sleep disturbance as many as 56.5% and 52.2%, respectively. Patients with a history of psychotherapy and neuropsychiatric treatment were prediction factors for poor response to PPIs (19).

Yoshida et al. (2011) showed that Omeprazole administration relieved complaints with an average satisfaction rate of 61.7% for 4 weeks by using The Quality of Life in Reflux and Dyspepsia Questionnaire (QOLRAD). Kim et al. (2015) showed that GERD patients with PPI have a satisfaction rate of 30.2% so that the health satisfaction will also increase after PPI therapy. Bate et al. (1997) (26), Lind et al. (1997) (27), and Mulder et al. (2002) (28), stated that the satisfaction level of Omeprazole therapy for 4 weeks was 94%, 66%, and 79%, respectively, which increased the satisfaction of health on GERD patients.

Bregtagne et.al (29) compared patient satisfaction with frequent or occasional reflux symptoms, suggesting that patients with frequent reflux showed a satisfactory rate of 64% compared to those who only experienced occasionally reflux (75% satisfaction level) with $p < 0.001$. Patient satisfaction and subjective quality of life (QOL) is an important evaluation in assessing the quality of care from a patient per-

spective. Measurement of satisfaction and quality of life aims to provide a comprehensive level of individual satisfaction with medical care. There is no definitive definition to express patient satisfaction and that of the quality of life (30). Patient satisfaction is correlated with general care needs and the specific needs of the encountered conditions (31).

However, patient satisfaction and the quality of life involve cognition that is subjectively affected by the emotional, social, and physical components associated with the experience of disease and treatment outcomes. The perceived quality of life is a prediction of the perception of satisfaction to health services. Knowledge of the relationship between service satisfaction and the quality of life can help to improve the quality of care in the treatment and management of patients in our environment (30).

In this study, physical domain was obtained with a not-so-high difference of average, it means that most patients experienced pain and/or discomfort due to GERD symptoms, regular drug consumption, lack of energy, sleep, activity, and mobility that ultimately impacts on their ability to work. The difference of score average in social domain was almost similar to that in physical domain, due to the limited number of the questions and varying interpretation of the questions. The environmental domain with the lowest transformed score difference of average can be explained by the poor financial source of the patient, the lack of information and recreation (32).

The difference in the average of transformed score was highest in the psychological domain because GERD is strongly associated with psychological factors. Psychological aspects are stress, emotion, and personality that affect the severity of GERD symptoms (2). Stress causes an exacerbation of 64% symptoms in GERD patients although it does not appear to increase exposure to esophageal acid (33). Psychological stress causes a major disturbance in gastric function and barrier function in the digestive mucosa. GERD patients with psychological comorbidities demonstrate treatment failure with PPI (34). The low response rates of patients with heartburn and normal endoscopic outcomes to PPI may be due to psychological comorbidities (33). The mean duration of GERD symptoms was significantly ($p < 0.001$) greater in patients with psychological comorbidities (34).

Psychological stress may not be associated with GERD but it was produced during the period of symptoms (35). Anxiety and depression affect secondary to GERD; the patient becomes more sensitive to symptoms of reflux. Symptoms of reflux increased 2.8 times in GERD patients who experienced anxiety and depression. The degree of anxiety and depression was higher along with a worse quality of life perception in GERD patients. Research by Oh et al. (2009) (2) showed that GERD patients with anxiety resulted in a lower quality of life score than those with GERD without anxiety ($p < 0.0001$). There was a positive correlation between anxiety levels and GERD patients. Omeprazole administration cures the symptoms of reflux and decreases anxiety (26). Effective treatments heal and relieve GERD symptoms and improve patient wellbeing. Welfare improvements in GERD patients psychologically enable the patient to do activities and participate in a social life (36). The Omeprazole's mechanisms to resolve the psychological domain have not been clear. In addition, the large difference in the psychological domain could be due to relieving the complaints with the treatment of interviews for 30-45 minutes; the patients received more attention in the form of empathy longer than the doctor.

In this study, we found two GERD patients with

liver cirrhosis comorbidities. However, the results of this study found no significant difference between WHOQOL-BREF in GERD patients without comorbidity of liver cirrhosis (before and after Omeprazole administration) with WHOQOL-BREF in GERD patients with comorbidity of liver cirrhosis (before and after Omeprazole administration). This was probably because the number of GERD patients with liver cirrhosis was small when compared with the study sample.

In this study there were no complications using PPI (Omeprazole) such as diarrhea, abdominal pain, constipation, headache, fundic gland polyps, hypochlorhydria, achlorhydria, incidence of Community Acquired Pneumonia (CAP) and *C. difficile* infection.

Some limitations of the study that may affect the results of the study were: no double-blind study performed, difficulty in monitoring the intervention and the provision of Omeprazole in outpatient unit, and many confounding variables.

CONCLUSION

Omeprazole administration of 2x20 mg for 4 weeks could improve the perception of quality of life, but it showed no significant difference in each WHOQOL-BREF domain and overall, it did not improve the quality of life of GERD patients.

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