

Differences In quality of life between patients with functional dyspepsia after esophagogastroduodenoscopy with empiric treatment and placebo

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Abstract:

Functional dyspepsia is a common health problem found in society. Few of multifactorial aspects which become the underlying cause of functional dyspepsia are anxiety and psychosocial problem. Esophagogastroduodenoscopy (EGD) examination can display exact information to patient with functional dyspepsia and expected to increase patient's quality of life. It is still necessary to evaluate the advantages of EGD examination in improving patient's quality of life. A Randomized double blind controlled trial was conducted to compare between group of patients who have been given an empiric treatment (Proton pump inhibitor and prokinetic agents) and other who have been given a placebo for 2 weeks after underwent EGD examination in patients with functional dyspepsia. The primary outcome of this study is the decrease of NDI-SF score on both of groups at the end of study. A total of 42 patients (22 in EGD+placebo group [Group I] and 20 in EGD + treatment group [Group II]) were enrolled. NDI-SF score decreased significantly in both groups, Group I (26.23 ± 8.43 vs 19.59 ± 7.62 , $P=0.001$) and Group II (27.32 ± 7.57 vs 19.21 ± 5.68 , $P=0.002$), 15 days after underwent EGD examination. NDI-SF score improvement between two groups 15 days after EGD was not significantly different ($P=0.814$). This study showed improvement in quality of life of patients whom diagnosed with functional dyspepsia after EGD examination in both groups. This improvement was not significantly different between two groups and showed the placebo effect of EGD on functional dyspepsia patient.

Keywords: functional dyspepsia, quality of life, NDI-SF score, esophagogastroduodenoscopy.

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Abbreviations: Esophagogastroduodenoscopy (EGD)

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Introduction

Dyspepsia syndrome is a common symptom that is characterized with epigastric pain or discomfort, upper abdomen fullness, early satiety, bloating, belching, nausea and/or vomiting. Functional dyspepsia is diagnosed when there is no significant organic problem of the upper gastrointestinal tract based on upper endoscopy examination that can not be associated with the patient symptoms. Psychosocial disorders are the important background of the functional dyspepsia symptoms and signs. Upper endoscopy examination can inform the anatomical structure of upper gastrointestinal tract in dyspepsia syndrome patients and the normal upper endoscopy result reduced the patients anxiety and afraid of death for 6 months after endoscopy [1]. The quality of life is the appropriate method to asses the therapeutic responses in the disorder that can not be measured with laboratoric examination or other supportive measurement. The quality of life measurement is an important tool to evaluate the role of treatment in dyspepsia syndrome [2]. Upper endoscopy examination in functional dyspepsia patients improved the clinical symptoms and quality of life [3].

Methods

This randomized clinical trial was designed to evaluate the role of esophagogastroduodenoscopy (EGD) examination in the quality of life improvement of patients with functional dyspepsia. This study was performed between January 2018 and June 2018 in Pandan Arang General Hospital, Boyolali Regency, Central Java, Indonesia as one of the principle investigator (Sumardjo) requisites to get his gastroenterohepatology consultant degree in Division of Gastroenterology & Hepatology, Department of Internal Medicine, Faculty of Medicine, Nursing and Public Health, Universitas Gadjah Mada/Dr Sardjito General Hospital, Yogyakarta, Indonesia. The protocol was approved by the Biomedical Research Ethics Commission of the Faculty of Medicine, Nursing and Public Health, Universitas Gadjah Mada, Yogyakarta, Indonesia and Director of Pandan Arang General Hospital, Boyolali Regency, Central Java, Indonesia. Based on a study [7] with $(x1-x2) = 102,1-96,79 = 5,31$ and the standard of deviation was 6,21 we found 23 samples for each group with 10% possibility of lost of follow up. The study involved 50 patients who underwent EGD examinations and 8 patients were excluded because of lesion findings based on the endoscopy results. The EGD examination was performed only with local oropharyngeal sedation with lignocaine 100 mg/mL (Xylocaine® 10% Pump Spray), so that the patient was fully concious. The inclusion criteria: Age > 18 years old, patients with dyspepsia

syndrome and normal EGD examination. Exclusion criteria: patients with dyspepsia syndrome and found abnormality based on esophagogastroduodenoscopy examination. Validated Nepean Dyspepsia Index (NDI)[4] was used to measure the patients quality of life index before EGD examination and two weeks later. Patients in the placebo group (Group 1) were treated with placebo agents (two amylum substance with visually similar design and prescription with treatment group drugs) for 15 days after EGD examination. Patients in the treatment group (Group 2) were treated with proton pump inhibitor (lansoprazole 30 mg capsule b.i.d) and prokinetic agent (domperidone 10 mg tab b.i.d) for 15 days after EGD examination. The patients were positioned so that they could see the live video streaming of their examined upper gastrointestinal tract lumen during the EGD examination. The EGD procedure examined the esophagus, gaster, and descending part of duodenum.

The eligible patients with dyspepsia syndrome filled the informed consent and the NDI-SF questionair before EGD examination on the first day of the study. On the 8th day the research assistant phoned the patients to evaluate the drug side effects. On the 15th day patient came to the hospital and filled the NDI questionair once again. The video endoscope streaming of the patients were evaluated by three experienced endoscopists and included in the study if the two of three endoscopist concluded normal result.

Statistical analysis

The interobserver agreement test (Cohen's Kappa coefficient) was performed before the study was begun. Kolomogorov-smirnov normalioty test was appiled to asses the sample distribution. The NDI score of pre-and post-EGD of one group was evaluated with paired t-test, and the NDI score post-EGD of the two groups was evaluated with unpaired t-test.

Results

The figure 1 showed the CONSORT flow chart of patients considered and enrolled in the study. 42 consecutive patients were randomized to the endoscopy+ placebo group (22 patients) and endoscopy +PPI+ prokinetic group (20 patients). Eight

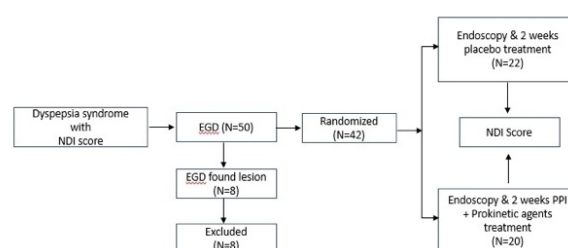


Figure 1. Flow chart of patients

patients were excluded (five patients with erosive gastritis; two patients with esophagitis and lower esophageal sphincter weakness; and one patient with non-cirrhotic esophageal varices). The table 1 showed the good interobserver agreement with the Kappa coefficient 0.737 ($p=0.016$) and the NDI score

normally distributed (table 2). The basic characteristics of the patients were not significantly different (table 3).

This study showed that the NDI score was not statistically different between two groups, however the NDI score showed statistically significant difference before and after endoscopy in each group (table 4).

Table 1. Interobserver agreement in the previous pilot study to measure the Cohen's Kappa coefficient

		Observer 1	
		Functional dyspepsia	Organic dyspepsia
Observer 2	Functional dyspepsia	7	0
	Organic dyspepsia	1	2

Table 2. Kolmogorov-Smirnov normality test of NDI Score between two groups, p values

Table 2: Kolmogorov-Smirnov normality test of NDI Score between two groups, p values		
	Group	NDI Score
Before EGD	Group 1	0.19
	Group 2	0.07
15 days after EGD	Group 1	0.06
	Group 2	0.13

Table 3. Basic characteristics of the patients

Variables	Group		p value
	Group 1 (EGD+Placebo)	Group 2 (EGD +PPI+Prokinetik)	
Sex [†] :			
Male	7	6	0.89
Female	15	14	
Age (y.o.) [‡]	35.22±13.87	36.52±8.80	0.53
Body Mass Index [‡]	22.40±2.92	21.64±4.17	0.43
Education level:			
Low	4	3	1.00
High	18	16	

[†]Chi-square test; [‡]Student t-test

Table 4. The NDI score between the two groups and before versus 15 days after endoscopy in each group.

Variables	Group 1 (EGD+placebo)	Group 2 (EGD+PPI+Prokinetic)	p value
N	22	20	
NDI score before endoscopy (Mean±SD)	26.23±8.43	27.32±7.57	0.396*
NDI score 15 days after endoscopy (Mean ± SD)	19.59±7.62	19.21±5.68	0.814*
NDI score before vs 15 days after endoscopy in each group	0.002 ($p < 0.01$)**	0.001($p < 0.01$)**	

*Mann-Whitney test; **Wilcoxon Signed rank test

Discussion

The mean of NDI-SF score before EGD examination was not significantly different between the two groups and mostly similar with previous study [4]. The significant decrease of NDI-SF before and after EGD in each group showed the benefit of EGD examination in this study. The NDI-SF score at the end of the study showed there was no significant difference between the placebo and treated group. This result support the role of esophagogastroduodenoscopy examination in improving patients quality of life in functional dyspepsia and the added dyspepsia treatment (proton pump inhibitor and prokinetic drugs) did not show better response in this study. A study in Spain [5] showed that the functional dyspepsia patients NDI-SF score mean was 22 and the healthy population was 13, and a study in Asia [6] found the mean of NDI-SF score in functional dyspepsia patients between 26.7 ± 5.73 in group placebo and 28.5 ± 4.73 in group multienzyme complex supplementation.

A study in Sweden with 190 endoscopy examinations in uninvestigated dyspepsia found that dyspepsia symptoms and quality of life improvement in patients group with normal endoscopy examination. This study also supported the treatment effect of endoscopy in patients with functional dyspepsia eventhough it did not eradicate the symptoms completely [7]. Study in China also showed that lansoprazole did not improve functional dyspepsia patients compare with placebo [8], and study in Japan showed that lansoprazole only improved the ulcer-like functional dyspepsia [9].

A meta analysis study about placebo effect in functional dyspepsia patients showed symptoms improvement from 6% to 72% in placebo group, eventhough not all placebo groups showed similar results with the treated groups [10].

Functional gastrointestinal symptoms has long been known its relation with patient psychosocial disorders. Patients with functional gastrointestinal disorders who seek medical treatment had greater anxiety disorders.

In this study, we also found the placebo response of EGD examination based on the NDI-SF score. The NDI-SF score improvement in the placebo group might be associated with the placebo response to the EGD examination.

As we know, this is the first randomized clinical trial to measure the role of EGD examination in improving the quality of life of functional dyspepsia patients. Our study showed that the EGD examination had a role in improving functional dyspepsia patients quality of life. The limitation of the study was the short period of time of evaluation interval (only two weeks).

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