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Improvement of Dyspeptic Symptoms in Non-ulcer Dyspepsia after *Helicobacter pylori* Eradication at Srinagarind Hospital

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ABSTRACT

Background: Non-ulcer dyspepsia (NUD) is a common disorder in clinical practice. The role of *H. pylori* eradication in patients with NUD remains controversial. The aim of this study was to evaluate the effect of omeprazole with antibiotics compared with omeprazole alone on symptom improvement in NUD patients with *H. pylori* infection.

Patients and Methods: This study was a double-blinded, randomized controlled study. Patients with NUD of 12 weeks or longer were randomized to receive omeprazole 20 mg twice daily, clarithromycin 500 mg twice daily and amoxicillin 1 g twice daily for 14 days (treatment group) or omeprazole alone (placebo group). Esophagogastroduodenoscopy was performed in all patients. *H. pylori* infection was confirmed by positive rapid urease test and histopathological exam of antral mucosa. Symptom improvement was evaluated in terms of symptom score before treatment, 2 weeks, and 6 weeks after treatment.

Results: There were 36 patients in treatment group and 33 patients in placebo group. Symptom score after treatment was significantly lower than before treatment in both group (p <0.001) but there was no significant difference between treatment group and placebo group.

Conclusion: Omeprazole with antibiotics significantly reduced the overall symptom scores after 6 weeks of treatment compared to baseline in NUD patients but there was no significantly difference from omeprazole treatment alone.

Key words : Efficacy, non-ulcer dyspepsia, *Helicobacter pylori* infection

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INTRODUCTION

Dyspepsia is defined as pain or discomfort center in the upper abdomen[1]. The other dyspeptic symptoms include bloating, early satiety, nausea, vomiting, and belching. Most patients complained multiple symptoms. Dyspepsia is the most common problem in clinical practice and the prevalence is approximately 30%[2,3].

The most common cause of dyspepsia is non-ulcer dyspepsia (NUD)[4]. The other causes of dyspepsia are peptic ulcer, drug-induced dyspepsia, gastric cancer, biliary disease, psychiatric disease, and diet. Non-ulcer dyspepsia is diagnosed when no evidence of structural disease explanation for a patient's symptom is identified by appropriate investigation including esophagogastroduodenoscopy (EGD)[5].

NUD resulted from multiple mechanisms such as abnormal visceral sensitivity, gastric motor function, psychological distress, genetic and Helicobacter pylori infection[6]. *H. pylori* is spiral-shaped, gram-negative microorganisms in the mucus layer overlying gastric mucosa and is estimated to infect more than 50% of the world's population. *H. pylori* infection is the cause of peptic ulcer, gastric cancer, and mucosal associated lymphoid tissue lymphoma (MALT)[7].

The reported prevalence of *H. pylori* infection in patients with NUD varied from 39%-87%[8]. The prevalence of *H. pylori* was 48.2% with the high prevalence in the Northeastern part of Thailand (67.1%)[9]. However, the relationship between NUD and *H. pylori* is unclear. Several studies have examined the effect of *H. pylori* eradication on dyspeptic symptom in NUD patients but the results were controversial[8,10-16]. In a recent review of Cochrane collaboration, *H. pylori* eradication had a small but significant effect in *H. pylori* positive NUD patients[17]. The aim of this study was to assess the effect of *H. pylori* eradication in NUD patients in Northeast Thailand.

MATERIALS AND METHODS

Patients

Patients presenting dyspepsia for at least 3 months at GI clinic, Srinagarind Hospital, Khon Kaen between March 2010 and February 2011 were enrolled into the study. Patients were included if they were over 18 years old; were diagnosed having NUD from clinical symptom and *H. pylori* positive without peptic ulcer during EGD. Exclusion criteria included history of peptic ulcer disease; gastro-oesophageal reflux symptom; history of gastrointestinal bleeding; recent consumption of antibiotics or NSAIDs; previous gastric surgery; pregnancy; allergic to any study medication or severe illness.

After informed consent was obtained, patients were randomized using the random numbers to be under either treatment group (given omeprazole 20 mg twice daily, clarithromycin 500 mg twice daily and amoxicillin 1 g twice daily for 14 days) or placebo group (omeprazole 20 mg twice daily and placebo for 14 days). The randomization was carried out independently by the Pharmacy Department.

EGD was performed at the time of inclusion, and 6 weeks after inclusion. During endoscopic examination, antral mucosa was taken for histopathological examination and rapid urease test. Patients were considered *H. pylori* positive if both rapid urease test and histology were positive.

Symptom scores were assessed at the time of inclusion, 2 weeks, and 6 weeks after inclusion using symptom questionnaire comprising questions on epigastric pain or discomfort, nausea, vomiting, bloating, early satiety, and belching. The Gastrointestinal Symptom Rating Scale in this questionnaire evaluates the frequency, severity, and duration of symptom. The symptoms were classified into seven grades (3 grades with half steps between each rating as categorical scale); grade 0: absence symptom; grade 1: mild intensity with 1-3 attacks in 1 week; grade 2: mild intensity with more than 4 attacks in 1 week; grade 3: moderate intensity with 1-3 attacks in 1 week; grade 4: moderate intensity with more than 4 attacks in 1 week; grade 5: severe intensity with 1-3 attacks in 1 week; and grade 6: severe intensity with more than 4 attacks in 1 week.

Statistical Analysis

For the main outcomes, student's *t*-test was employed to compare the mean of symptom scores between treatment and placebo groups based on an intention-to-treat principle (ITT). *P*-value less than 0.05 was considered significant. The differences in proportions were compared using a χ^2 test. Data analysis was carried out using STATA for Window version 10.

RESULTS

Baseline characteristics of the patients

Seventy one patients were enrolled in the study

and two patients were excluded from final analysis because of the absence of *H. pylori* in pathological specimens. Thirty six patients were assigned to treatment group and 33 patients were assigned to placebo group.

Table1. Baseline characteristics of patients with non ulcer dyspepsia.

Characteristics	Treatment N = 36	Placebo N = 33
Male sex (%)	47	54
Age (yr)		
mean ± SD	48.72 ± 11.61	50.00 ± 10.34
range	26-81	32-76
Smoking (%)	3	15
Alcohol drinking (%)	9.86	6
Symptom score		
mean ± SD	6.25 ± 3.39	6.63 ± 2.49
range	2-13	2-13

Two groups were well matched with respect to age, sex, pre-treatment symptom scores, prevalence of alcohol drinking and smoking (Table 1). The baseline characteristics did not differ significantly between the two groups.

Changes in symptoms after treatment

There were no statistical difference in symptom scores between the two groups, either at baseline or at 6 weeks after medication except early satiety and belching symptom scores were significantly different between two groups at baseline (Table 2).

The mean (± SD) symptom scores at 6 weeks of treatment group and placebo group were not significantly different (2.08 ± 1.02 VS. 2.09 ± 1.50; $p = 0.98$). In subgroup analysis, the improvement in total symptom scores before treatment and after treatment showed no statistical difference in both groups for all items. After treatment, the total symptom scores were significantly lower than those at baseline in both groups (Table 2). Figure 1 demonstrated the total symptom

Table 2. Change in symptom scores before and after 6 weeks of the treatment (mean ± SD).

	Symptom score		Symptom score after treatment			*p*-value (95%CI)
	before treatment	*p*-value	At 2 week	At 6 week	*p*-value	(before- 6 week)
Total symptom score						
Placebo	6.63 ± 2.49	0.59	2.51 ± 1.46	2.09 ± 1.50	0.98	<0.001 (3.48 to 5.60)
Treatment	6.25 ± 3.39		2.83 ± 1.84	2.08 ± 1.02		<0.001 (3.10 to 5.22)
Epigastrium pain/discomfort						
Placebo	2.69 ± 1.10	0.74	1.18 ± 0.76	1.06 ± 0.82	0.73	<0.001 (1.19 to 2.07)
Treatment	2.61 ± 1.10		1.36 ± 0.99	1.00 ± 0.63		<0.001 (1.24 to 1.97)
Nausea						
Placebo	0.30 ± 0.76	0.61	0.60 ± 0.24	0.06 ± 0.24	0.51	0.07 (-0.23 to 0.50)
Treatment	0.22 ± 0.54		0.05 ± 0.23	0.02 ± 0.16		0.05 (-0.001 to 0.38)
Vomiting						
Placebo	0.30 ± 0.88	0.16	0.00 ± 0.00	0.03 ± 0.17	0.29	0.09 (-0.05 to 0.59)
Treatment	0.08 ± 0.28		0.00 ± 0.00	0.00 ± 0.00		0.08 (-0.01 to 0.17)
Bloating						
Placebo	1.75 ± 1.34	0.71	0.72 ± 0.80	0.51 ± 0.61	0.43	<0.001 (0.76 to 1.72)
Treatment	1.63 ± 1.35		0.77 ± 0.95	0.63 ± 0.68		<0.001 (0.52 to 1.42)
Early satiety						
Placebo	1.00 ± 1.41	0.02	0.27 ± 0.62	0.09 ± 0.29	0.91	<0.001 (0.42 to 1.38)
Treatment	0.38 ± 0.72		0.11 ± 0.31	0.08 ± 0.28		0.01 (0.06 to 0.54)
Belching						
Placebo	0.63 ± 0.78	0.01	0.24 ± 0.45	0.33 ± 0.59	1.00	0.02 (0.04 to 0.56)
Treatment	1.30 ± 1.34		0.52 ± 0.65	0.33 ± 0.47		<0.001 (0.51 to 1.42)

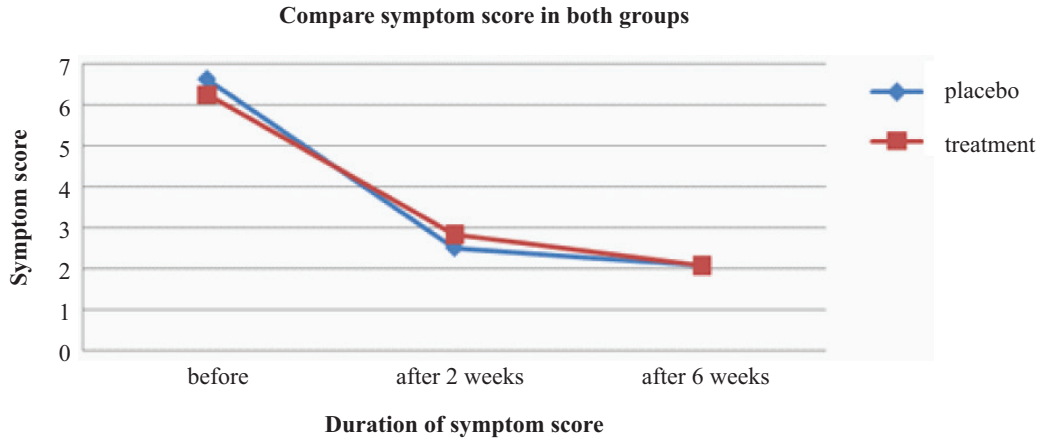

Figure 1. Comparison of total symptom scores between before treatment, after 2 weeks, and 6 weeks treatment and placebo groups.

scores before and after treatment at 2 weeks, and 6 weeks between two groups.

Discussion

The treatment of non-ulcer dyspepsia is difficult. A variety of medications have been employed with varying success because of its complex underlying pathophysiologic mechanism involving a change in gastric motility, visceral hypersensitivity, genetic susceptibility and psychosocial factors, and *H. pylori* infection[18]. The role of *H. pylori* infection in NUD patients is still debated.

This study assessed the effect of *H. pylori* eradication in NUD patients in Northeast Thailand. The result showed that the overall symptoms were improved in both treatment and placebo group at 2 weeks, and 6 weeks after treatment. Specifically, epigastric pain, bloating, early satiety, and belching were significantly improved while nausea and vomiting did not respond to treatment. However, there was no difference in symptoms improvement when compared between treatment group and placebo group. Therefore, the other mechanisms of NUD rather than *H. pylori* are likely to be responsible for NUD because patients in control group who received omeprazole also responded to treatment.

The limitation of the study is a small size population. Although we cannot conclude that *H. pylori* eradication is not better than omeprazole alone in terms of symptom resolution in NUD patients with *H. pylori* infection, we can observe the trends of treatment response which was not different in both groups (Figure 1). In the future, a larger clinical trial or systematic review with meta-analysis is needed to answer this question.

Conclusion

Omeprazole with antibiotics significantly reduced the overall symptom scores after 6 weeks of treatment compared to baseline in Thai NUD patients with *H. pylori* infection but it was not significantly different from omeprazole treatment alone.

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