

Eradication of Helicobacter Pylori Improves Dyspepsia Symptoms in Elderly People

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Abstract

Background

Therapy for eradication of *Helicobacter pylori* (*H. pylori*) improves symptoms of *H. pylori*-associated dyspepsia (HPD), but the effects of eradication in elderly patients are unclear.

Aims

To evaluate the outcomes of eradication therapy and effects of eradication on dyspepsia symptoms in elderly patients.

Methods

This retrospective study included 496 patients who received *H. pylori* eradication therapy. The patients were divided into a group of elderly patients (group E: ≥ 65 years old) and a group of non-elderly patients (group N: < 65 years old). Abdominal symptoms were evaluated using a questionnaire about 12 abdominal symptoms before eradication and after eradication (1-2 months and more than one year). Dyspepsia was defined as a score of 4 points or more score for at least one of 4 items (postprandial fullness, early satiety, epigastric pain, and hunger pain).

Results

Successful *H. pylori* eradication rate in group E was significantly lower than that in group N (74.7 % vs. 84.4 %, $P < 0.05$) and it was remarkable in the 3rd-line therapy (59.7 % vs. 76.5 %, $P < 0.05$). Serious adverse events did not occur in either groups. Successful eradication improved symptoms in patients with dyspepsia in both groups within 2 months (70.3% of the patients in group N, 76.2% of the patients in group E) and decrease of GOS score lasted for more than 1 year.

Conclusions

H. pylori eradication would be recommend for elderly patients with dyspepsia symptoms.

Introduction

Functional dyspepsia (FD) is defined in the ROMA \boxtimes criteria as one or more of the following symptoms persisting for the past 3 months with symptom onset at least 6 months ago: postprandial fullness, early satiation, epigastric pain and epigastric burning [1]. *Helicobacter pylori* (*H. pylori*) infection is often associated with dyspepsia symptoms, and it has been reported that eradication of *H. pylori* improved the symptoms [2- 4]. In the Kyoto Global Consensus Report in 2015, it was stated that **all *H. pylori*-positive individuals worldwide should receive eradication therapy** [5]. *H. pylori*-associated dyspepsia (HPD) is also defined as sustained symptomatic relief for 6 to 12 months after eradication.

In Japan, *H. pylori* infection is one of the major infections, especially in elderly people [6]. Mamori et al. reported that the rate of successful eradication of *H. pylori* in first-line therapy was lower in patients less than 50 years of age than in patients aged over 50 years [7]. However, Kobayashi et al. reported that age did not affect the efficacy or safety of eradication therapy [8]. There has been no report on the effect of eradication of *H. pylori* on dyspepsia symptoms in elderly people. We therefore evaluated the outcomes of *H. pylori* eradication therapy and the effect on dyspepsia symptoms in elderly patients.

Methods

Patients

Consecutive patients who visited our *H. pylori*-specific out-patient unit and received eradication therapy during the period from January 2009 to December 2017 were retrospectively analyzed.

Esophagogastroduodenoscopy revealed no active gastric diseases before eradication in any of the patients. We divided the patients into two groups according to age: an elderly group (group E) of patients who were 65 years of age or older and a non-elderly group (group N) of the patients who were less than 65 years of age. The study was approved by the Ethics Committee of Hokkaido University Hospital (approval number 018-0367).

H. pylori test

Before eradication, both ^{13}C -urea breath test (UBT) (Ubit[®], Otsuka Pharmaceutical, Tokyo, Japan) and one or more other *H. pylori* tests (rapid urease test, serological and urinary anti-*H. pylori* IgG antibody, culture and microscopic examination) were used. Generally, the patients was defined as positive for *H. pylori* when in whom one of those tests was positive. Generally, the patients was defined as positive for *H. pylori* when in whom one of those tests was positive. When the values of UBT were weak positive (2.5 to 5.0‰, cut-off value: 2.5‰), we confirmed that other tests were positive for excluding false positive for UBT tests.

Successful eradication was confirmed using UBT at 1 to 2 months after the completion of eradication treatment.

Eradication regimen

The prescribed regimens during the study period are summarized in Table 1. Vonoprazan (VPZ) has been available since March 2015 in our institution and proton-pump inhibitors (PPIs) were changed to VPZ after it became available.

Evaluation of upper gastrointestinal symptoms

A questionnaire with a scale from 1 (no problem) to 7 (very severe problem) consisting of 17 items covered Global Overall Systems (GOS) and Gastrointestinal Symptom Rating Scale (GSRS) was used [9, 10]. The questionnaire was filled out by each patient before the urea breath test. For evaluation of upper

gastrointestinal (GI) symptoms, that GOS questionnaires are simple and valid outcome measurements to assess the symptoms of FD according to the severity of the following eight symptoms: epigastric pain, heartburn, acid reflux, stomach discomfort, nausea, belching, early satiety and distention [9,11,12]. Patients who had a score of 4 points or more for at least one of 4 items (postprandial fullness, early satiety, epigastric pain, and hunger pain) were defined as patients with dyspepsia. Improvement of dyspepsia was defined as a decrease in the maximum score of abdominal symptoms before eradication by more than 2 points and each GOS item after eradication therapy being less than 3 points.

For evaluation of the long-term effects *H. pylori* eradication on dyspepsia symptoms, a 3rd GOS questionnaire was given to patients for whom more than 1 year had passed after successful eradication. We mailed the questionnaires to the patients who had dyspepsia before eradication. HPD was defined as sustained dyspepsia relief for more than 1 year after successful eradication.

Measured outcome parameters

The primary endpoint was long-term improvement in the GOS score after successful *H. pylori* eradication in elderly patients with dyspepsia. Secondary endpoints were successful eradication rates, adverse events, and short-term and long-term improvements of each GOS item in groups E and N.

Analysis of *H. pylori* eradication efficacy was performed on an intention-to-treat (ITT) basis. Compliance with therapy and adverse events were determined by a questionnaire at the time of judgement of *H. pylori* eradication.

Statistical analysis

Mean values were calculated for continuous variables and percentages were calculated for categorical data. Categorical data were compared using Fisher's exact test and numerical data were compared using Student's *t* test. A *P* value of < .05 in each analysis was considered statistically significant.

Results

Outcomes of H. pylori eradication therapy

A total of 496 patients received *H. pylori* eradication therapy during the study period. Fifty-nine patients were excluded for the reason of not meeting our *H. pylori* diagnosis criteria, finally a total of 437 patients including 275 patients in group N and 162 patients in group E were analyzed. A flow diagram for treatment and characteristics of the patients are shown in Figure 1 and Table 2. Three patients discontinued the eradication therapy due to adverse events (skin eruption) and 6 patients did not visit the hospital for judgement of eradication. According to the questionnaires, compliance with the protocol was 100%. ITT eradication rates were 84.4% (232/ 275) in group N and 74.7% (121/ 162) in group E, and there was a significant difference between the two groups ($P < 0.05$). According to the number of eradications, only the success rate for the 3rd-line eradication in group E was significantly lower than that in group N

(59.7% vs 76.5%, $P < 0.05$) (Table 3). But there were no significant differences in the patients with between 7-days and 14-days regimen in both groups (for 14-days regimen, group E: 19% (12/62), group N: 25% (21/85), $P = 0.55$).

Furthermore, there were no significant differences of adverse events associated with eradication therapy between the two groups.

Upper GI symptoms before and after eradication therapy

Forty-six participants did not fill out the questionnaire, and data for 391 patients including 350 patients in whom eradication was successful and 41 patients in whom eradication therapy failed were analysed.

In the patients in whom eradication therapy failed, there was no significant difference of GOS scores before and after eradication therapy: 1.80 ± 1.11 before and 1.82 ± 0.80 after in group E ($n = 20$) ($P = 0.94$) and 2.13 ± 1.15 before and 1.84 ± 0.94 after in group N ($n = 21$) ($P = 0.06$).

Before eradication, there were no significant differences between the two groups in total GOS score and score of each item. Successful eradication significantly improved all upper GI symptoms regardless of age (supplement 1). According to our definition of dyspepsia, 84 (36.1%) of the patients in group N and 37 (31.6%) of the patients in group E had dyspepsia before eradication. Within 2 months after successful eradication, 76.2% (64/ 84) of the patients in group N and 70.3% (26/ 37) of the patients in group E had improvement in dyspepsia ($P = 0.48$) (Table 4).

Long-term effects of H. pylori eradication on dyspepsia for long term

Responses to questionnaire were obtained from 40 patients in group N and 20 patients in group E (supplement 2). Mean periods from successful eradication were 52.4 months in group N and 54.8 months in group E ($P = 0.51$).

GOS scores at more than 1 year after successful eradication were significantly decreased compared to those before eradication in both groups (Figure 2). 32 patients (80%) in group N and 12 patients (60%) in group E had long-term improvement in HPD after eradication ($P = 0.13$). Short-term and long-term effects of eradication on dyspepsia symptoms were different in 35.0% of the patients in group N and 50.0% of the patients in group E (supplement 3).

Discussion

This is the first report on the effects of *H. pylori* eradication on dyspepsia in elderly patients.

Dyspepsia symptoms often occur in *H. pylori*-positive individuals. Shimatani et al. reported that the prevalence of patients with dyspeptic symptoms was significantly higher in *H. pylori*-positive patients than in *H. pylori*-negative patients (28.7% vs 6.5%) [13]. Kawamura et al. also reported that 46.3% of *H.*

pylori-positive patients had dyspepsia symptoms [14]. Approximately 30% of our patients had dyspepsia symptoms, and the percentage is similar to that in previous studies.

It has been reported that *H. pylori* eradication therapy improved dyspepsia symptoms in 24-53% of patients [2, 15-18]. In our study, dyspepsia symptoms after successful eradication improved in about 73% of the patients in the long term, and the percentage of patients was slightly higher than in the previous studies (supplement 3). Unfortunately, the definitions of improvement of dyspepsia were different in some studies, and further research is needed to compare the symptoms using the same methods at same timing after eradication.

Tsuda et al. reported that a questionnaire within 2 months after *H. pylori* eradication might be useful for diagnosis in 70% of patients with HPD [19]. Similarly, questionnaires in the short term after eradication was predicted HPD in 60% of elderly patients. However, the symptoms in 40% of the patients with dyspepsia changed in the long term and HPD could not be predicted. According to Kyoto Global Consensus Report, it is necessary to follow symptoms for more than 6 months after successful eradication to determine HPD as was indicated by our results [5].

There have been a few studies on outcomes of eradication therapy for the elderly, but the outcomes investigated in those studies were for 1st-line and 2nd-line therapy [7, 8, 20, 21]. In our study, there was a significant difference in eradication rates only in 3rd-line therapy. There were no significant differences in rates of eradication using PPIs and VPZ, and Kusunoki et al. and Nishida et al. reported that the effect of VPZ was unclear in elderly patients [20, 21]. Resistance to clarithromycin (CAM) might be the main reason for failure of 3rd-line therapy, but that was unfortunately not checked in our subjects [22, 23].

Recently, Furuta et al. reported that autoimmune gastritis (AIG) patients were often misdiagnosed as refractory to eradication therapy [24]. Because, AIG causes achlorhydria and non *H. pylori* urease-positive bacteria overgrowth. Although patients with suspected false positive for UBT were excluded from this study, 4 of them were positive for anti-parietal cell antibody (APCA) and/ or anti-intrinsic factor antibody.

Adverse events of eradication therapy are one of the concerns for the elderly. We have not experienced serious adverse events in eradication therapy, but there has been a report of death in an elderly patient [25]. Therefore, it is necessary to pay attention to drug interaction, hepatorenal function and co-morbidities in eradication, especially for the elderly.

The present study has several limitations. This was a retrospective study with a small sample size at a single institution. And antibiotic resistance was not tested.

In conclusion, eradication of *H. pylori* would improve dyspepsia for long term in elderly patients with dyspepsia symptoms.

Declarations

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Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due [secondary use of data was not approved by our IRB] but are available from the corresponding author on reasonable request.

Authors' contributions

All authors read and approved the final version of the manuscript, including the authorship. IT, SO and MK designed the study; IT, SO and MT performed the research; YS, SK, MI, MO, KY and YS analyzed the data; IT and SO wrote the paper; and NS revised the manuscript for final submission.

Ethics approval and consent to participate

This study was performed in accordance with the ethical standards detailed in the Declaration of Helsinki. The study was reviewed and approved by the Hokkaido University Hospital Review Board 018-0367.

Competing interests

The authors declare that have no competing interests.

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Tables

Table 1. Regimens of *Helicobacter pylori* eradication.

Eradication	Antibiotics	Antacids
1st and 2nd lines	AMPC 750mg and CAM 200mg, b.i.d. 7days	RPZ 20mg
	AMPC 750mg and MNZ 250mg, b.i.d. 7days	or LPZ 30mg
3rd line	AMPC 500mg q.i.d. and STFX 100mg, b.i.d. 7 or 14days	or
4th line	STFX 100mg and MINO 250mg b.i.d. 7 days and AMPC 500mg q.i.d. 14 days	VPZ 20mg, b.i.d.
For penicillin allergy	CAM 200mg and MNZ 250mg b.i.d.7 days	
	MNZ 250mg and STFX 100mg b.i.d. 7 days	

RPZ: rabeprazole, LPZ: lansoprazole, VPZ: vonoprazan, AMPC: amoxicillin, CAM: clarithromycin, MNZ: metronidazole, STFX: sitafloxacin, MINO: minomycin, b.i.d: bis in die, q.i.d: quarte in die

Table 2. Characteristics of patients.

	Group N (n = 275)	Group E (n = 162)
Male: female, n	116: 159	61: 101
Mean age at <i>H. pylori</i> eradication, years (range)	51.7 (17-64)	70.6 (65-87)
Gastric disease, n (%)		
Chronic gastritis	164 (59.6)	100 (61.7)
Peptic ulcer scar	43 (15.6)	13 (8.0)
Gastric cancer post treatment	9 (3.3)	13 (8.0)
Eradication therapy, n (%)		
1 st -line	160 (58.1)	80 (49.4)
2 nd -line	25 (9.1)	13 (8.0)
3 rd -line	85 (30.9)	62 (38.3)
4 th -line	5 (1.8)	7 (4.3)
Penicillin allergy, n (%)		
PPI-based regimen	186 (67.6)	104 (64.2)
PCAB-based regimen	89 (32.4)	58 (35.8)

PPI: proton-pump inhibitors, PCAB: potassium competitive acid blocker

Table 3. Outcomes and adverse events of *Helicobacter pylori* eradication therapy.

	Group N (n = 275)	Group E (n = 162)	<i>P</i>
Eradication rates, % (n)	84.4 (232/ 275)	74.7 (121/ 162)	< 0.05
1 st -line	88.8 (142/ 160)	87.5 (70/ 80)	0.83
2 nd -line	90.1 (23/ 25)	84.6 (11 /13)	0.59
3 rd -line	76.5 (65/ 85)	59.7 (37/ 62)	< 0.05
4 th -line	40.0 (2/ 5)	42.9 (3/ 7)	1.00
PPI-based regimen	84.9 (158/ 186)	77.9 (81/ 104)	0.15
PCAB-based regimen	83.1 (74/ 89)	69.0 (40/ 58)	0.07
Adverse events, n (%)	48 (17.5%)	23 (14.2%)	0.42
Diarrhea	25 (9.1%)	10 (6.2%)	0.36
Skin rash	7 (2.5%)	7 (4.3%)	0.40
Others	16 (5.8 %)	6 (3.7 %)	0.37

PPI: proton-pump inhibitors, PCAB: potassium competitive acid blocker

Table 4. Dyspepsia before and after successful eradication.

	Group N (n = 233)	Group E (n = 117)	<i>P</i>
Mean age at <i>H. pylori</i> eradication, years ± SD	51.3 ± 9.9	70.5 ± 4.89	□
Gender (male/ female)	99/ 134	43/ 74	N.S
Patients with dyspepsia before eradication, n (%)	84 (36.1)	37 (31.6)	N.S
Improvement in dyspepsia after eradication, n (%)	64/ 84 (76.2)	26/ 37 (70.3)	N.S

Figures

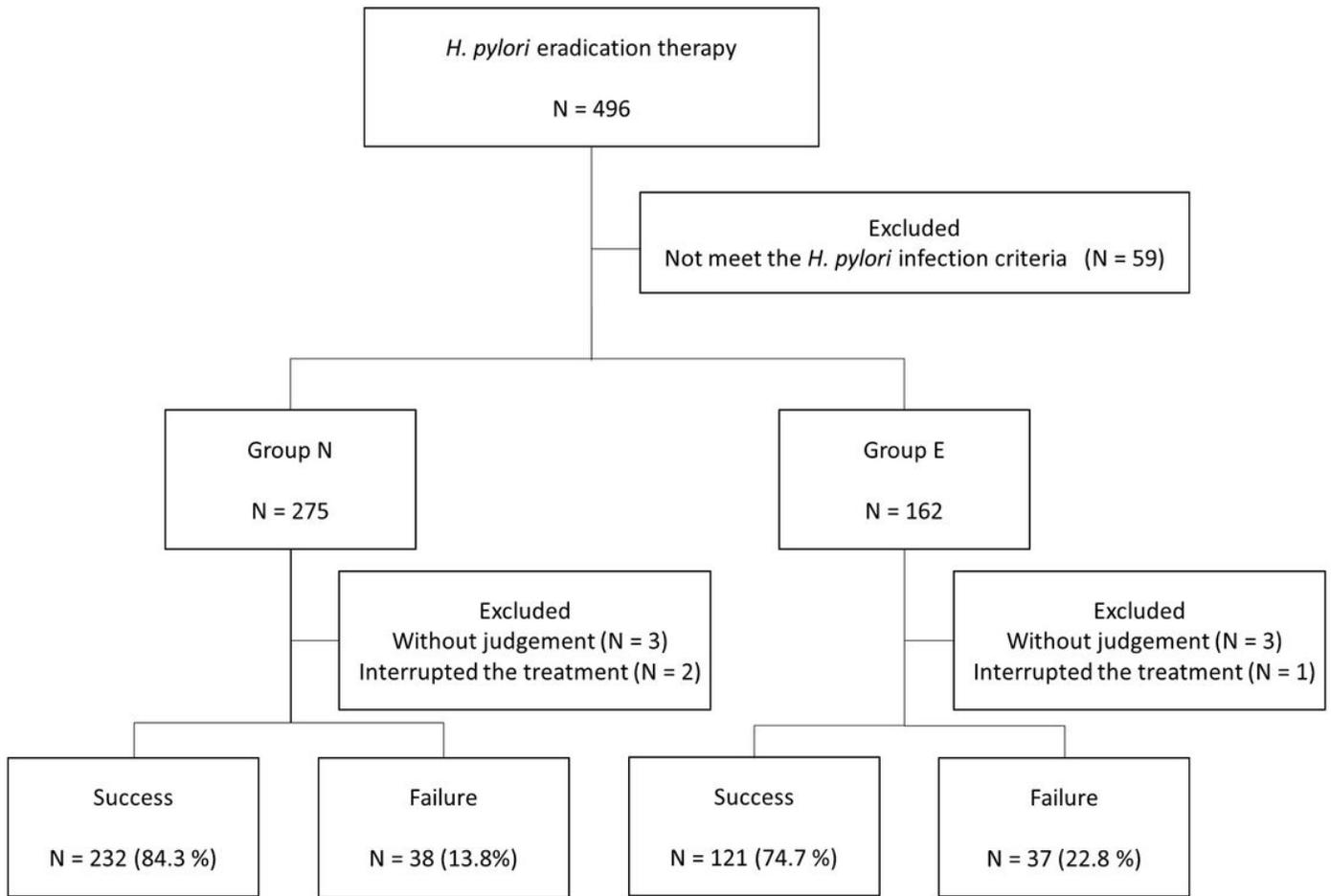


Figure 1

A flow diagram for treatment and characteristics of the patients are shown in Figure 1

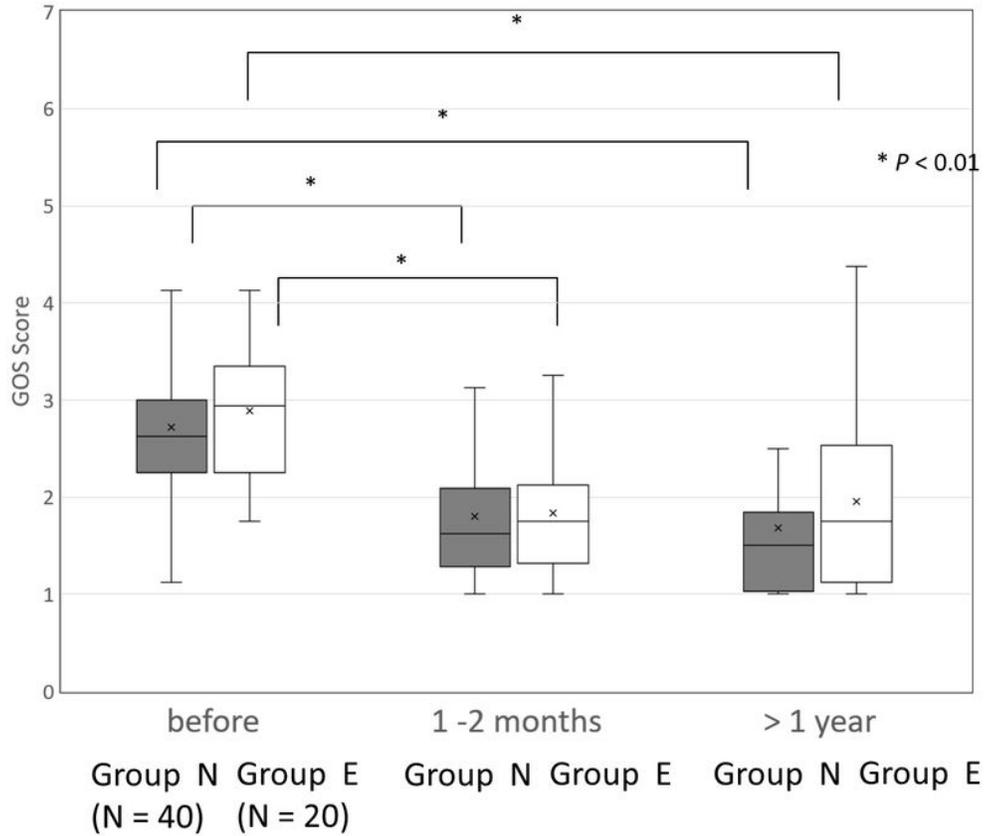


Figure 2

GOS scores at more than 1 year after successful eradication were significantly decreased compared to those before eradication in both groups (Figure 2).

Supplementary Files

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