BRIEF ARTICLE

Age-dependent eradication of *Helicobacter pylori* in Japanese patients

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Abstract

AIM: To determine the general risk factors affecting the failure rate of first-line eradication therapy in Japanese patients with *Helicobacter pylori* (*H. pylori*) infection.

METHODS: The present study enrolled 253 patients who had an *H. pylori* infection, underwent gastroendoscopy, and were treated with *H. pylori* eradication therapy. Eradication therapy consisted of 30 mg lansoprazole plus 750 mg amoxicillin and 400 mg clarithromycin twice daily for 7 d. All of the patients underwent a ^{13}C urea breath test at least 1 mo after the completion of eradication therapy. The current study investigated the independent factors associated with successful *H. pylori* eradication using a multiple logistic regression analysis.

RESULTS: The overall success rate in the patients was 85.8%. Among the general factors examined in the multivariate analyses, only having an age less than 50 years was found to be significantly associated with a poor response to *H. pylori* eradication. Moreover, side effects were the only clinical factors in the patients who were under 50 years of age that significantly influenced the poor response to *H. pylori* eradication.

CONCLUSION: *H. pylori*-positive elderly patients should undergo eradication therapy. In addition, it is necessary to improve *H. pylori* eradication therapy in younger patients.

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INTRODUCTION

Helicobacter pylori (*H. pylori*) infections cause chronic gastritis and are associated with an increased risk of major upper gastrointestinal diseases, such as peptic ulcer disease, gastric adenocarcinoma, and mucosa-associated lymphoid tissue lymphoma[1]. Proton-pump inhibitor (PPI)-based triple therapy, with a PPI, clarithromycin (CAM), and either amoxicillin (AMPC) or metronidazole, is a widely recommended eradication therapy[2]. In addition, this triple therapy has been approved by the medical insurance system in Japan, and the eradication therapy is administered by physicians in general practice.

Consensus conferences have recommended therapeutic regimens that achieve *H. pylori* cure rates of over 80% on an intent-to-treat basis[3-5]. However, several large-scale clinical trials and meta-analyses have demonstrated that the most common first-line therapies fail in up to 20% of patients[6,7], and in the clinical setting, the actual treatment failure rate may be even higher[8]. Few studies have examined the causes of patient failure in these therapies among the general clinical factors in Japan. The aims of the current study were to determine the general risk factors that affect the failure rate of first-line eradication therapy in Japanese patients with *H. pylori* infection using a multivariate analysis.

MATERIALS AND METHODS

The current series included 253 patients who underwent a gastro-endoscopy between January 2006 and September 2007 in the Shinko hospital in Kobe, Japan, and who were diagnosed with an *H. pylori* infection by the presence of the bacterium at endoscopy, detection of the bacteria or an antibody in patient urine, or a positive ^{13}C urea breath test (UBT; with a cut-off value of 2.5‰; Ubit, Otsuka Pharmaceuticals, Tokyo, Japan). All patients were treated with *H. pylori* eradication therapy, consisting of 30 mg lansoprazole, 750 mg amoxicillin, and 400 mg clarithromycin twice daily for 7 d. Patient compliance and treatment-related side effects were assessed at the end of the treatment period. The patients underwent a UBT at least 1 mo after the completion of eradication therapy. Successful *H. pylori* eradication was defined as a negative result on the UBT. Independent factors that may have been associated with successful *H. pylori* eradication were studied using multiple logistic regression analysis. The following variables were evaluated as independent factors: sex, age (generation), diagnosis, and side effects. The StatView system software package (version 5.0) was used for the statistical analysis. A *P*-value of less than 0.05 was considered to be statistically significant.

RESULTS

Demographic and clinical features of the patients who underwent first-line eradication therapy

Table 1 lists the demographic and clinical features of the patients who underwent *H. pylori* eradication therapy. Adverse events were observed in 41 patients within the first week after the initiation of the eradication therapy. The most common adverse events included diarrhea and gustatory dysfunction. None of the patients withdrew from the treatment course due to eradication therapy-related side effects.

Success rate of first-line eradication therapy

The overall success rate in the patients was 85.8%. Figure 1A shows the success rate of the first-line eradication therapy in patients with *H. pylori* infection when correlated with the patients' sex, diagnoses, and side effects. The success rate tended to be higher in patients with peptic ulcers than in

Table 1 Demographic and clinical characteristics of patients undergoing eradication therapy for an *Helicobacter pylori* infection

	n = 253
Sex	
Male	174
Female	79
Generation (s)	
20	10
30	15
40	50
50	92
60	54
70	27
> 80	5
Diagnosis	
Ulcer	165
Non-ulcer	88
Side effect	
No	212
Yes	41

Ulcer: A peptic ulcer was detected by gastroscopy; Non-ulcer: No peptic ulcer was detected by gastroscopy (instead, for example, atrophic gastritis, among others); Side effects: Diarrhea (*n* = 23), gustatory dysfunction (*n* = 10), among others.

those without peptic ulcers (87.9% *vs* 81.8%). Figure 1B shows the success rates according to the patient's age. A good success rate was observed, even among elderly patients.

Multivariate analysis of independent factors for the patient response to first-line eradication therapy

The independent factors associated with the response to first-line *H. pylori* eradication therapy were evaluated by a multivariate analysis. The only factor (among sex, age, diagnosis, and side effects) examined in the multivariate analysis that was found to be significantly associated with a poor response to first eradication therapy was patient age of less than 50 years of age (*P* = 0.015, Table 2). Moreover, side effects were the only independent factor significantly associated with a poor response in patients under 50 years of age (*P* = 0.033, Table 3).

DISCUSSION

The current study showed that first-line eradication treatment failures occurred significantly more frequently in patients aged less than 50 years of age. Elderly patients are frequently infected with *H. pylori* for a longer period of time, present with enlarged atrophic gastritis, and progress to intestinal metaplasia. These patients may experience easier *H. pylori* eradication with first-line eradication treatment. In addition, the gastric mucosa becomes more atrophic in elderly patients in comparison to younger patients, and elderly patients also display gastric acid hyposecretion. This can compromise their ability to inactivate the AMPC and CAM. These conditions may contribute to the current results.

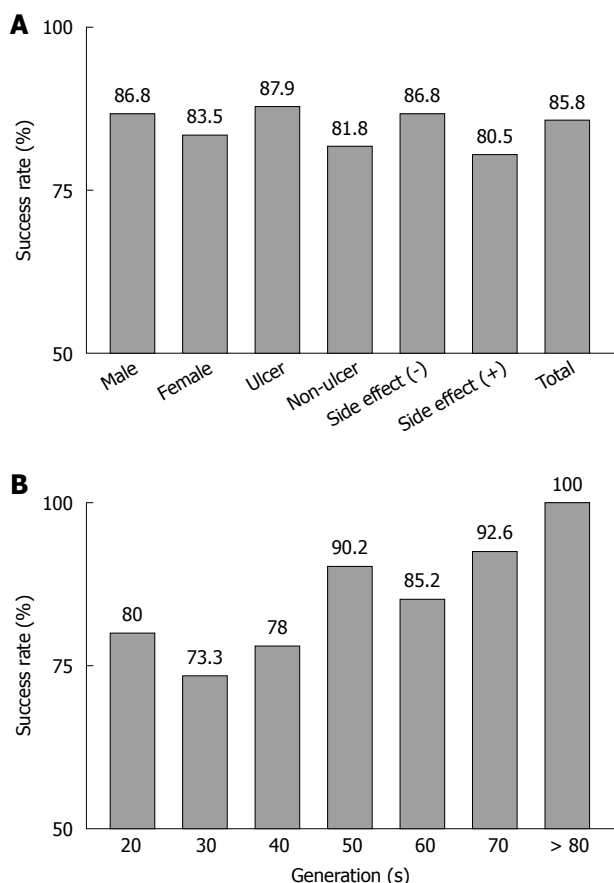Pretreatment antibiotic resistance is the primary rea-

Figure 1 Success rate of first-line eradication therapy. A: Success rates according to sex (male, female), diagnosis (ulcer or non-ulcer), side effects [no (-) or yes (+)], and the total patient success rate of eradication therapy for the treatment of *Helicobacter pylori* (*H. pylori*); B: Success rates according to the patient generation of eradication therapy for *H. pylori*.

Table 2 A multivariate analysis of all patients (*n* = 253)

Variable	Multivariate OR	95% CI	*P*-value
Sex (male *vs* female)	1.29	0.62-2.71	0.50
Age (under 50 yr *vs* over 50 yr)	0.41	0.20-0.84	0.015[a]
Disease (ulcer *vs* non-ulcer)	1.61	0.79-3.30	0.19
Side effect (no *vs* yes)	1.59	0.67-3.80	0.29

[a]Statistically significant. OR: Odds ratio; CI: Confidence interval.

Table 3 Multivariate analysis of under 50-yr-old patients (*n* = 75)

Variable	Multivariate OR	95% CI	*P*-value
Sex (male *vs* female)	1.46	0.49-4.33	0.50
Disease (ulcer *vs* non-ulcer)	0.79	0.24-2.57	0.70
Side effect (no *vs* yes)	3.97	1.12-14.16	0.033[a]

[a]Statistically significant. OR: Odds ratio; CI: Confidence interval.

son some patients do not respond to initial treatment[9-13]. In particular, antibiotic CAM resistance has been identified as a major factor affecting the ability to cure *H. pylori* infection, and the rate of resistance to this antibiotic is increasing in many geographical areas[14,15]. A similar tendency is believed to be occurring in Japan. The efficacy of PPI-based regimens is decreasing, and several studies have reported intention-to-treat eradication rates lower than 75%[16-24]. The overall success rate in patients was greater than 85% in the current series. This high success rate may be due to patients having been diagnosed with an *H. pylori* infection during the medical examination, and the fact that few patients were receiving any medication. Future studies will examine whether patients with *H. pylori* infections display antibiotic resistance.

The only factors that significantly influenced the response to eradication therapy in patients were being under 50 years of age and diarrhea, which was the most common side effect for half of the patients. It is necessary to determine how to increase the treatment success rate among younger patients. A previous study from Japan reported that the use of the probiotic bacterium *Clostridium butyricum* MIYAIRI 588 strain reduced fluctuations in the intestinal flora and decreased the incidence of gastrointestinal side effects[25]. Supplementation with probiotics

may have several beneficial effects on *H. pylori* eradication, especially in younger patients.

Elderly patients also exhibited a good success rate in the current series. A previous report showed that approximately 53%-73% of elderly peptic ulcer patients are *H. pylori*-positive; however, the percentage of *H. pylori*-positive elderly patients who are treated for an *H. pylori* infection remains low. One-week PPI-based triple therapy regimens are highly effective and well tolerated in elderly patients[26]. Therefore, it is recommended that *H. pylori*-positive elderly patients be treated with eradication therapy.

In conclusion, the current study was conducted to determine the general risk factors that affect the failure rate of first-line eradication therapy in Japanese patients with an *H. pylori* infection. The overall success rate in patients was 85.8%. Among the general factors examined in the multivariate analyses, a patient age of less than 50 years significantly influenced the response to *H. pylori* eradication. Moreover, among the other clinical factors in patients under 50 years of age, only the presence of side effects was found to be significantly associated with the response to *H. pylori* eradication. It is necessary to determine how to increase the eradication success rate among younger patients.

COMMENTS

Background
Proton-pump inhibitor (PPI)-based triple therapy with PPI, clarithromycin, and amoxicillin is a widely recommended eradication therapy for *Helicobacter pylori* (*H. pylori*) in Japan.

Research frontiers
Few studies have described the causes of patient failure with these therapies with regard to general clinical factors in Japan.

Innovations and breakthroughs
Among the general factors examined in the multivariate analyses, only a patient age of less than 50 years was significantly related to the response to *H. pylori* eradication treatments. Moreover, among the other clinical factors in patients under 50 years of age, only the presence of treatment side effects was found to be significantly associated with the patient's response to *H. pylori* eradication.

Applications

H. pylori-positive elderly patients should undergo eradication therapy, and it is necessary to determine how to increase the success rate among younger patients in Japan.

Peer review

The subject of this article to examine the results of *H. pylori* eradication is important. There are geographic differences in antibiotic resistance affecting the eradication results and the antimicrobial resistance may vary in time. Also, reports of other factors affecting the clinical treatment results are welcome.

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