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ORIGINAL ARTICLE

Observational Study

Effect of *Helicobacter pylori* eradication on elder cases: Observational study in community-based medicine

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Abstract

AIM

To examine the effect of *Helicobacter pylori* (*H. pylori*) eradication therapy on the extra-gastrointestinal factors in elderly patients by a before-after observational study in community medicine.

METHODS

Medical records (1 May 2013-31 January 2014) of 130 patients who underwent *H. pylori* eradication therapy with 2-year after-eradication observation in our institute were reviewed. Data on sex; age; body weight; body mass index (BMI); mean corpuscular volume (MCV); total protein; low-density lipoprotein cholesterol, triglyceride, haemoglobin A1c and haemoglobin levels and gastric hyperplastic polyps (GHPs) at eradication was extracted. Two-year after-eradication change in data was analysed by paired-sample *t*-test; relationship between GHPs and subclinical iron deficiency anaemia (IDA) improvement was evaluated.

RESULTS

The mean patient age (median, interquartile range) at eradication was 69.6 (71.5, 64-77) years. Paired-sample *t*-tests showed that body weight, BMI and MCV increased by 0.52 kg (P = 0.018), 0.25 kg/m^2 (P = 0.006) and 0.83 fL (P < 0.001), respectively. The nonparametric Mann-Whitney test showed no significant difference in the change rate of MCV after eradication between the groups with and without GHPs (P = 0.892).

CONCLUSION

H. pylori eradication therapy prevented weight loss and subclinical IDA in elderly individuals. GHPs were not associated with subclinical IDA.

Key words: *Helicobacter pylori*; Iron deficiency anaemia; Body weight; Elderly; Polyp

Core tip: The effect of *Helicobacter pylori* (*H. pylori*) eradication therapy on the extra-gastrointestinal factors in elderly patients was focused in this study. *H. pylori* eradication therapy prevented weight loss and subclinical iron deficiency anaemia (IDA) in elderly individuals. Gastric hyperplastic polyps were not associated with subclinical IDA. The results obtained in this study will help physician to treat elderly patients in community-based medicine.

Maruyama M, Kamimura K, Hoshiyama A, Hoshiyama K, Hoshiyama M, Hoshiyama Y, Terai S. Effect of *Helicobacter pylori* eradication on elder cases: Observational study in community-based medicine. *World J Clin Cases* 2017; 5(12): 412-418 Available from: URL: http://www.wjgnet.com/2307-8960/full/v5/i12/412.htm DOI: http://dx.doi.org/10.12998/wjcc.v5.i12.412

INTRODUCTION

Helicobacter pylori (*H. pylori*) infection affects many extra-gastrointestinal symptoms and diseases, including iron deficiency anaemia (IDA), obesity, diabetes mellitus and hyperlipidemia[1,2]. Although major population surveys and meta-analysis have revealed an increased risk for IDA in addition to a strong evidence for the efficacy of *H. pylori* eradication for the treatment of unexplained IDA, the relationship between *H. pylori* infection and prevalence of other extra-gastrointestinal tract diseases is unclear. The influence of *H. pylori* pathogenicity is currently unknown, particularly in elderly individuals[1,3-6]. In addition, the underlying mechanism of *H. pylori*-related IDA is still unclear[7,8].

H. pylori eradication therapy for patients with peptic ulcer is associated with gain of body weight[9,10]. The relationship between *H. pylori* infection and overweight is unclear, even in large-scale epidemiological studies[11-14]. However, this increase might related to the recovery of peptic ulcer and chronic inflammation. On the other hand, because of previously reported inconsistent results, the cause-and-effect relationship between *H. pylori* infection and metabolic disease is also ambiguous, and there are few reports on elderly individuals[2,15-19]. Because the development of an aging society may be upcoming event in the near future, the effect of *H. pylori* eradication therapy on the extra-gastrointestinal organs in elderly individuals should be investigated.

Therefore, the purpose of this observational study was to examine the effects of *H. pylori* eradication in elderly individuals on systemic conditions including body weight, biochemical results, and manifestations of clinical or subclinical anaemia comparing data between before-eradication and 2 years after *H. pylori* eradication. We have also compared rates of IDA improvement in chronic gastritis with and without gastric hyperplastic polyp (GHP) to investigate the relationship between GHP and *H. pylori*-related IDA.

MATERIALS AND METHODS

This was an observational before-after study in which the case group included 130 individuals who were continuously treated with medications for chronic diseases, such as essential hypertension, hyperlipidemia and/or diabetes mellitus. They were all diagnosed with *H. pylori*-infected chronic gastritis by routine esophagogastroduodenoscopy (EGD) and the rapid urease test at Kashiwazaki Central Hospital between 1 May 2013 and 31 January 2014.

The patient was considered to be eligible when fulfilled the following inclusion criteria: (1) *H. pylori* eradication therapy was successful and was followed by the urea breath test; and (2) the patient had been measured/tested for body weight; body mass index (BMI); mean corpuscular volume (MCV); total protein (TP) and low-density lipoprotein cholesterol (LDL-C), triglyceride (TG), haemoglobin (Hb) and haemoglobin A1c (HbA1c) levels at two time points: Before and 2 years after *H. pylori* eradication therapy was completed. However, we included patients with some missing measurement values and as elderly if older than 65 years old. We excluded patients with mucosal breaking lesions, such as gastric cancer or peptic ulcers, history of gastrointestinal surgery, and the other diseases might cause anemia. This study was approved by the institutional review board of Kashiwazaki Central Hospital. Written informed consent was obtained from all patients, and the study was conducted in accordance with the ethical guidance of the 1975 Declaration of Helsinki.

To identify differences in a patient between two time points, a paired-sample *t*-test was performed. When there were ⩽ 30 cases, a Wilcoxon signed test was performed. For continuous variables, two-group

Table 1 Comparison of various factors before and after *Helicobacter pylori* eradication therapy in all subjects (*n* = 130)

Variable	Subjects	Missing	Pre-eradication mean (SD)	Post-eradication mean (SD)	Mean difference	95%CI	*P* value
Body weight (kg)	124	6	57.3 (10.4)	58.2 (10.3)	0.52	0.09-0.94	0.018
BMI (kg/m^2)	121	9	23.4 (3.1)	23.7 (3.0)	0.25	0.074-0.42	0.006
Hb (g/dL)	115	15	13.8 (1.4)	13.8 (1.3)	0.018	-0.35	0.84
MCV (fL)	113	17	89.2 (4.9)	90 (4.4)	0.83	0.32-1.34	< 0.001
TP (g/dL)	90	40	7.4 (0.5)	7.5 (0.4)	0.024	-0.168	0.56
LDL-C (mg/dL)	107	23	114.3 (23.9)	116.2 (25.0)	1.20	-8.12	0.55
TG (mg/dL)	107	23	122 (70.5)	126.6 (77.1)	6.81	-22.59	0.23
HbA1c (%)	42	88	6.2 (0.81)	6.3 (0.75)	0.057	-0.305	0.45

BMI: Body mass index; Hb: Haemoglobin; MCV: Mean corpuscular volume; TP: Total protein; LDL-C: Low-density lipoprotein cholesterol; TG: Triglyceride; HbA1c: Haemoglobin A1c.

comparisons, such as Hb and MCV, were performed using the nonparametric Mann-Whitney test because assumptions of normality of the distribution were not verified. We excluded the patients with missing data in each group before analysis. The threshold for significance was $P < 0.05$. In all statistical analysis, we used EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics[20]. The results for changes in variable before and after *H. pylori* eradication are presented as the mean ± SD.

RESULTS

Patient characteristics

Between 1 May 2013 and 31 January 2014, 228 patients were diagnosed as having *H. pylori*-infected chronic gastritis by EGD and the rapid urease test were included. The patients who had been diagnosed as having gastric cancer ($n = 3$), gastric ulcer ($n = 16$), duodenal ulcer ($n = 20$) and gastro-duodenal ulcer ($n = 7$) who could not be followed up for 2 years after *H. pylori* eradication ($n = 52$), a total of 98 patients, were excluded from the initial 228 patients with *H. pylori*-infected chronic gastritis. Finally, a total of 130 patients [mean age, 69.6 years; median age, 71.5 (interquartile range, 64–77 years); 52 (40%) males] were analysed in the study. No patients showed re-infection of *H. pylori* after the eradication.

Effect of H. pylori eradication on various factors

The effect of *H. pylori* eradication therapy on various physiological factors was carefully examined comparing the value before and after the therapy in all 130 elderly patients with the interval of 2 years for each (Table 1). The body weight increased from a mean ± SD of 57.3 ± 10.4 kg before *H. pylori* eradication to 58.2 ± 10.3 kg 2 years after *H. pylori* eradication ($P = 0.018$). In addition, BMI increased from 23.4 ± 3.1 before *H. pylori* eradication to 23.7 ± 3.0 2 years after *H. pylori* eradication ($P = 0.006$). MCV increased from 89.2 ± 4.9 fL before *H. pylori* eradication to 90.0 ± 4.4 fL 2 years after *H. pylori* eradication ($P < 0.001$) whereas no significant changes were seen in the value of Hb ($P = 0.84$). The paired-sample *t*-test showed no significant differences in other measurements including TP, LDL-C, TG, and HbA1c, before and 2 years after *H. pylori* eradication (Table 1).

Subgroup analysis of factors in elderly patients

The patients older than 65 years old were considered to be elderly and the factors affected by the *H. pylori* eradication treatment have been carefully assessed by the subgroup analyses (Table 2). In the group of patients ⩾ 65 years ($n = 97$), BMI increased from 23.6 ± 3.0 before *H. pylori* eradication to 23.8 ± 3.1 2 years after *H. pylori* eradication ($P = 0.045$). MCV increased from 89.2 ± 5.3 fL before *H. pylori* eradication to 90.1 ± 4.7 fL 2 years after *H. pylori* eradication ($P = 0.0017$) whereas no significant changes were seen in the value of Hb ($P = 0.84$). There were no significant differences in other measurements in the group of patients ⩾ 65 years (Table 2).

These results suggest that the *H. pylori* eradication contribute to maintain the BMI avoiding the loss of body weight, and to recovery from subclinical IDA caused by the chronic inflammation in the stomach. In addition, even with the 2 years period of the study, no significant changes were seen in the various nutritional factors, indicating that the better digestion, absorption, after the eradication therapy.

Effect of eradication and the level of Hb

To determine the effect of eradication on anaemia, level of Hb was carefully assessed in the patients (Table 3). Although the patients with Hb levels < 12.5 g/dL before *H. pylori* eradication increased from 11.5 ± 0.86 g/dL to 12.3 ± 0.99 g/dL at 2 years after *H. pylori* eradication ($P = 0.017$), paired-sample t-tests showed no significant difference in Hb levels before and 2 years after *H. pylori* eradication in the group with Hb ⩾ 12.5 g/dL (Table 3). In addition, to examine whether the rates of IDA improvement in chronic gastritis is related to the existence of GHP, the level of improvement of Hb and MCV values before and after the eradication

Table 2 Subgroup analysis of various factors before and after *Helicobacter pylori* eradication therapy in the group of patients > 65 years (*n* = 97)

Variable	Subjects	Missing	Pre-eradication mean (SD)	Post-eradication mean (SD)	Mean difference	95%CI	*P* value
Body weight (kg)	92	5	57.1 (10.4)	57.8 (10.3)	0.41	-1.017	0.12
BMI (kg/m^2)	90	7	23.6 (3.0)	23.8 (3.1)	0.21	-0.4159	0.045
Hb (g/dL)	85	12	13.7 (1.5)	13.7 (1.3)	-0.02	-0.4	0.84
MCV (fL)	85	12	89.2 (5.3)	90.1 (4.7)	0.95	-1.17	0.0017
TP (g/dL)	66	31	7.5 (0.5)	7.5 (0.4)	0.011	-0.216	0.84
LDL-C (mg/dL)	77	20	111.9 (21.2)	114.2 (24.8)	1.25	-9.65	0.61
TG (mg/dL)	77	20	116.7 (56.2)	112.6 (44.8)	-1.68	-20.35	0.74
HbA1c (%)	30	67	6.4 (0.8)	6.4 (0.7)	0.013	-0.35	0.88

BMI: Body mass index; Hb: Haemoglobin; MCV: Mean corpuscular volume; TP: Total protein; LDL-C: Low-density lipoprotein cholesterol; TG: Triglyceride; HbA1c: Haemoglobin A1c.

Table 3 Differences in the eradication effect on the rate of increase in haemoglobin level between groups of patients with < haemoglobin 12.5 g/dL (*n* = 20) and patients with ⩾ haemoglobin 12.5 g/dL (*n* = 96)

Variable	Subjects	Missing	Pre-eradication mean (SD)	Post-eradication mean (SD)	Mean difference	95%CI	*P* value
Less than Hb 12.5 g/dL	19	1	11.5 (0.7)	12.3 (1.0)	0.85	0.22-1.48	0.017
More over Hb 12.5 g/dL	96	11	14.2 (1.1)	14.1 (1.2)	-0.15	-0.1592	0.064

Hb: Haemoglobin.

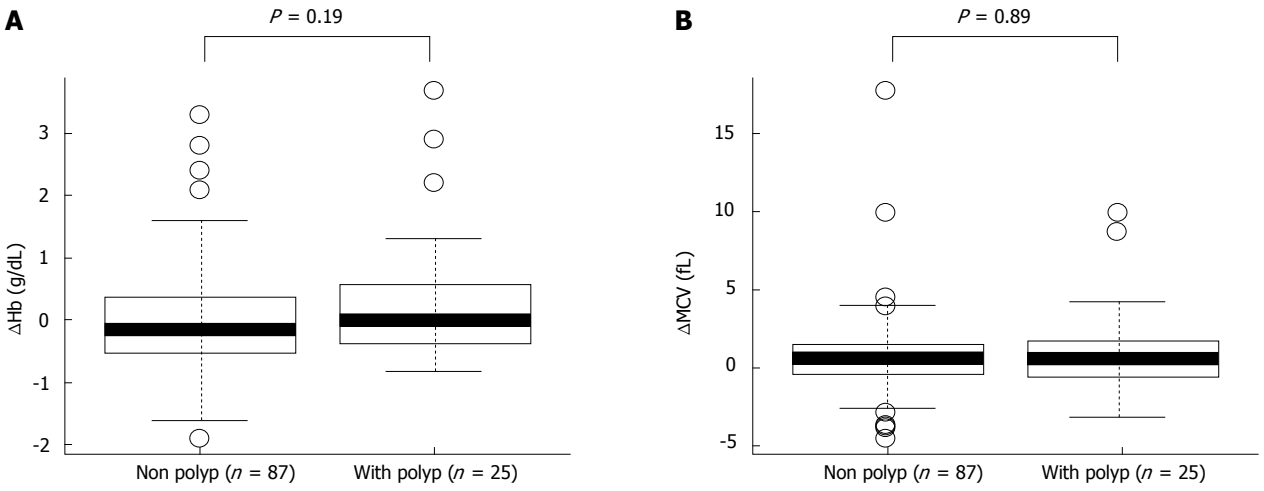

Figure 1 Comparison of haemoglobin and mean corpuscular volume levels before and after *Helicobacter pylori* eradication therapy in patients with or without gastric hyperplastic polyps. A: Change in the haemoglobin level; B: Mean corpuscular volume level. Hb: Haemoglobin; MCV: Mean corpuscular volume.

were compared (Figure 1). The nonparametric Mann-Whitney test showed no significant increase in Hb levels and MCV (P = 0.89) from before to 2 years after *H. pylori* eradication (P = 0.19) between the groups with and without GHP (Figure 1) and its size. These results indicate that the improving tendency of anaemia after *H. pylori* eradication did not correlate with the presence of GHP or its size.

DISCUSSION

Our study showed that *H. pylori* eradication therapy for elderly patients with chronic gastritis increased BMI and MCV, 2 years as a result of successful *H. pylori* eradication. The level of MCV has been considered as one of the marker of subclinical IDA and its recovery reflect the improvement of IDA[21]. Previous studies have shown similar results in patients with anaemia whose Hb significantly improved after *H. pylori* eradication[1,3-6]. There was no difference in the rate of increase in MCV (improvement in IDA) between groups with and without GHP. This finding suggests that GHP is not involved in an anaemic improvement pathway after *H. pylori* eradication.

It is known that the proportion of individuals with BMI > 30 generally increases up to the age of 60 years, and BMI tends to decrease after the age of 61 years[22]. In addition, the body weight loss in elderly individuals

is a predictive factor for death, mildly obese individuals have the lowest mortality rate[23,24]. It might be related to the recently established concept of "Frailty", a risk factor for falls, disability, hospitalization and mortality during old age. It is defined by the following criteria: Unintentional weight loss, self-reported exhaustion, weakness (grip strength), slow walking speed and low physical activity[25] and energy and protein support is recommended to treat the condition[26]. Interestingly, in our study, we found that elderly patients gained weight after *H. pylori* eradication. This result was inconsistent with the general tendency towards body weight loss in the elderly population and suggested that the effect of *H. pylori* eradication on preventing body weight loss or increase. The mechanisms might include, improvement of gastro-duodenal inflammation, ulcerative lesions, *etc*., as well as decrease of serum level of leptin which plays a crucial role to regulate food intake and energy expenditure[11,27]. Thus, we infer that *H. pylori* eradication therapy for elderly patients with *H. pylori*-infected chronic gastritis may be an effective therapy for prevention of weight loss in elderly individuals.

Our results are consistent with those of previous studies showing improvement of anaemia after *H. pylori* eradication therapy in elderly individuals[1,3-6]. Our study also showed that MCV increased after *H. pylori* eradication in the total study population as well as in the elderly patient group. However, presence of GHP was not related to the increase in the MCV rate. An important finding from previous study is that 80% of GHP disappeared after *H. pylori* eradication therapy within an average of 7.1 mo[28]. A recent report suggested that *H. pylori*-related IDA was associated with several factors in patients with GHP and nodular gastritis[29]. Bleeding from GHP is assumed to be the cause of *H. pylori*-related IDA. However, a previous study showed that even faecal occult blood-negative patients may be anaemic[30]. In addition, the mechanism might not be applicable to nodular gastritis. A recent study suggested that the cause of anaemia in patients with GHP is not bleeding from GHP but rather a decrease in iron absorption caused by a low-acid state[26]. Therefore, our results provide some support for the hypothesis that the improvement of *H. pylori*-related IDA is caused by an underlying mechanism other than GHP deletion.

One plausible reason for the finding of no significant changes in TP, TG, LDL-C and HbA1c levels is the presumed administration of statins and/or antidiabetic drugs to the patients. A previous report showed that serum total cholesterol levels did not change after *H. pylori* eradication[11]. Therefore, our results may be consistent with these previous findings.

A limitation of our study, however, is that although previous studies have shown that diabetes was exacerbated by *H. pylori* infection[17-19], our findings suggest no exacerbation or improvement of diabetes by eradication was because of strict management by a diabetologist in our hospital. In addition, the power of this study was limited because of the small number of participants and patients with subclinical IDA, of the single-centre analysis and of the retrospective-observational study design. Therefore, future larger, ad hoc, and better designed prospective studies are essential to confirm the effect of *H. pylori* eradication on systemic conditions by monitoring symptoms, medical history, and laboratory exams comparing with cases failed for the eradication.

In conclusion, our findings suggest that an increase in MCV is associated with body weight gain and improvement of subclinical IDA after *H. pylori* eradication in elderly patients with chronic gastritis. The tendency for subclinical IDA to improve after *H. pylori* eradication did not correlate with the presence of GHP. In addition, even with the 2 years period of the study, no significant changes were seen in the various nutritional factors, indicating that the better digestion, absorption, after the eradication therapy. For the future perspective, as the development of an aging society may be upcoming event in the near future, *H. pylori* eradication therapy may be a useful approach for preventing weight loss and frailty in elderly individuals to keep their quality of life and health.

ARTICLE HIGHLIGHTS

Research background

The relationship between *Helicobacter pylori* (*H. pylori*) infection and various extra-gastrointestinal symptoms, including obesity, diabetes mellitus and hyperlipidemia have been reported.

Research motivation

Although major population surveys and meta-analysis have suggested an increased risk for iron deficiency anaemia (IDA), however the relationship between *H. pylori* infection/its eradication on IDA and other extra-gastrointestinal tract diseases has not been clarified, especially in elderly patients.

Research objectives

This study was aimed to examine the effect of *H. pylori* eradication therapy on the extra-gastrointestinal factors in elderly patients by a before-after observational study in community medicine.

Research methods

Medical records (1 May 2013-31 January 2014) of 130 patients who underwent *H. pylori* eradication therapy with 2-year after-eradication observation in our institute were reviewed. Data on sex; age; body weight; body mass index (BMI); mean corpuscular volume (MCV); total protein; low-density lipoprotein cholesterol, triglyceride, haemoglobin A1c and haemoglobin levels and gastric hyperplastic polyps (GHPs) at eradication was extracted. Two-year after-eradication change in data was analysed by paired-sample *t*-test; relationship between GHPs and subclinical IDA improvement was evaluated.

Research results

The mean patient age (median, interquartile range) at eradication was 69.6 (71.5, 64-77) years. Paired-sample *t*-tests showed that body weight, BMI and MCV increased by 0.52 kg (P = 0.018), 0.25 kg/m^2 (P = 0.006) and 0.83 fL (P < 0.001), respectively. The nonparametric Mann-Whitney test showed no significant difference in the change rate of MCV after eradication between the groups with and without GHPs (P = 0.892).

Research conclusions

H. pylori eradication therapy prevented weight loss and subclinical IDA in elderly individuals, therefore, the eradication should be considered even for

those elder patients.

Research perspectives

For the future perspective, as the development of an aging society may be upcoming event in the near future, *H. pylori* eradication therapy may be a useful approach for preventing weight loss and frailty in elderly individuals to keep their quality of life and health.

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