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RAPID COMMUNICATION

Effect of drug treatment on hyperplastic gastric polyps infected with *Helicobacter pylori*: A randomized, controlled trial

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Abstract

AIM: To study the effects of drug treatment on hyperplastic gastric polyps infected with *Helicobacter pylori* (*H pylori*).

METHODS: Forty-eight patients with hyperplastic gastric polyps (3-10 mm in diameter) infected with *H pylori* were randomly assigned to a treatment group (n = 24) which received proton-pump inhibitor (omeprazole or lansoprazole), clarithromycin, bismuth citrate and tinidazole, and a control group (n = 24) which received protective agent of gastric mucosa（tepretone）. Patients underwent endoscopy and *H pylori* examination regularly before enrollment and 1-12 mo after treatment.

RESULTS: Twenty-two patients in the treatment group and 21 in the control group completed the entire test protocol. In the treatment group, polyps disappeared 1-12 mo (average, 6.5 ± 1.1 mo) after the treatment in 15 of 22 patients (68.2%) and *H pylori* infection was eradicated in 19 of the 22 patients (86.4%). However, 12 months after the study, no change in polyps or *H pylori* status was seen in any controls ($^bP < 0.01$).

CONCLUSION: Most hyperplastic gastric polyps disappear after eradication of *H pylori*.

Key words: *Helicobacter pylori*; Hyperplastic gastric polyps; Therapy

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INTRODUCTION

The risk of conversion of hyperplastic gastric polyps is very low, only accounting for 1.5%-3% [1]. Patients with gastric polyps may present with bleeding of the upper gastrointestinal tract, abdominal pain, or gastric outlet obstruction. Large gastric polyps or polyps associated with complications can be removed endoscopically or surgically. *Helicobacter pylori* (*H pylori*) infection is closely associated with hyperplastic gastric polyps and *H pylori* is present in 100% of hyperplastic gastric polyps[2-4]. Hyperplastic gastric polyps may disappear in 40-71% patients after eradication of *H pylori*[5, 6]. Since the pathogenicity of *H pylori* is different in various regions, we conducted this randomized, controlled trial to see whether hyperplastic gastric polyps disappear after eradication of *H pylori*.

MATERIALS AND METHODS

Selecting and grouping of patients

Forty-eight patients were from the Gastroenterology Department, First Affiliated Hospital of Zhejiang University and Red Cross Hospital of Hangzhou (26 men, 22 women, age range from 21 to 73 years, average 47 years). All patients did not receive antibiotics, bismuth, steroid and non-steroid drugs before their enrollment in the study. Hyperplastic gastric polyps (3-10 mm in diameter) were diagnosed on the basis of the examination results at least three histological samples. Patients were considered to have multiple gastric polyps (at least 5) when they were easily cut. Our criteria for hyperplastic gastric polyps included hyperplasia of the foveolar epithelium on histologic examination and infiltration of inflammatory cells into the stroma in biopsy specimens [7, 8]. Hyperplastic gastric polyps were diagnosed by two blinded pathologists. Patients with adenomatous gastric polyps, Peutz-Jegher syndrome and juvenile polyps were excluded. The diagnosis of *H pylori* infection was based the positive results of staining with Giemsa and ^{14}C-urea breath test. The patients were randomly assigned to two groups and sequentially numbered. In the treatment group (n = 24), patients received proton-pump inhibitor (omeprazole 20mg/d or lansoprazole 30 mg/d), clarithromycin (1g/d), bismuth citrate (440 mg/d) and tinidazole (1g/d), 2 weeks a course. In the control group (n = 24), patients had endoscopic examination and received protective agent of gastric mucosa (tepretone 150 mg/d). Two patients of the treatment group did not take the drugs for one course. In the control group, 2 patients lost follow-up and 1 patient took both proton-pump in-

hibitor and amoxicillin. These 5 patients exited from our study. If polyps progressed and were accompanied with malignant transformation, the study was stopped and the polyps were removed endoscopically. After completion of our study, endoscopic removal of polyps or eradication of *H pylori* was proposed for those who failed in *H pylori* eradication.

Endoscopy, histologic examination and assessment of H pylori eradication

Patients in the treatment group underwent endoscopy every 3 months after the treatment. On each occasion, biopsy specimens were taken from the same areas (three from the antrum and three from the body) for histologic examination. If patients without eradication of *H pylori* were not adapted to endoscopic examination very well, controls underwent endoscopy every 3 months after enrollment. Biopsy specimens for histologic examination were stained with Giemsa and evaluated for the presence of *H pylori*. Histologic diagnosis of the biopsied mucosa of the antrum and body was made by two blinded pathologists. The severity of activity, inflammation, atrophy, and metaplasia was graded on a scale from 1 to 4 and expressed as the histologic index according to the updated Sydney System: 1: normal, 2: mild, 3: moderate, and 4: marked [9]. Eradication of *H pylori* was confirmed by the negative results of these two tests 1-3 months after the treatment and endoscopic examination. The size and number of polyps were measured at each endoscopic examination using biopsy forceps (GIF XQ240 or GIF140, Olympus) placed near the polyp (open size: 6 mm in diameter; closed size: 2 mm in diameter). The endoscopic data on the disappearance and regression of polyps were reviewed independently by two blinded endoscopists.

Statistical analysis

All data were analyzed by unpaired *t* test (for age), Wilcoxon rank-sum test and Fisher's exact test. $P < 0.05$ was considered statistically significant. All data were coordinated by SPSS RDS and statistical analyses were done by SPSS software.

RESULTS

Comparison of baseline clinico-pathological characteristics between treatment and control groups

Twenty-two patients in the treatment group and 21 patients in the control group completed the entire study. The two groups were similar with respect to the number, age, sex, coexisting disease, as well as the number, size and distribution of polyps, histologic findings (Table 1). The two groups were comparable.

Analysis of curative effects between treatment and control groups

In the treatment group, *H pylori* was eradicated without serious side effects in 19 of 22 patients (86.3% [95% CI, 63%-99%]), and polyps disappeared in 15 of 22 patients (68.2% [95% CI, 54%-91%]) 1-12 months after treatment (Figure 1). Hyperplastic gastric polyps in the other 4 patients with successful *H pylori* eradication regressed to a certain extent, decreasing in size or number. However, in the remaining 3 patients without *H pylori* eradication, no polyps showed regression and no diminution of inflammation in the gastric mucosa 12 months after the treatment. In the control group, all patients showed no change of *H pylori* infection (0% [95% CI, 0%-21%]), no hyperplastic gastric polyp regression or disappearance (0% [95% CI, 0%-21%]) and no significant diminution of inflammation (Table 2). Polyps were enlarged or increased in number in 5 of the 21 patients. The rates of eradication of *H pylori* and disappearance of polyps in the treatment group were significantly higher than those in the control group ($P < 0.01$).

Table 1 Clinico-pathological characteristics of treatment and control groups

Characteristics	Treatment groups (n = 22)	Control groups (n = 21)
Mean age(mean±SD，yr)	49 ± 9	47 ± 8
Men, n(%)	13(59.1)	11(52.4)
Coexisting disease, n(%)		
Chronic atrophic gastritis	10(45.4)	12(57.1)
Duodenal ulcer	2(9.1)	2(9.5)
Gastric ulcer	0(0)	1(4.8)
Mean number of polyps	5.6	4.2
Mean size of polyps(mm)	6.6	7.8
Distribution of polyps, n (%)		
Body	79(64.2)	61(69.3)
Antrum	19(15.4)	15(17.0)
Angle	8(6.5)	5(5.7)
Fundus	9(7.3)	4(4.5)
Cardia	8(6.5)	3(3.4)
Histologic findings		
Inflammation	2.7, 2.4	2.6, 2.4
Activity	2.5, 2.5	2.5, 2.3
Atrophy	2.4, 2.6	2.5, 2.4
Metaplasia	0.9, 0.6	1.0, 0.6

DISCUSSION

In our study, *H pylori* was successfully eradicated in 19 of the 22 patients. The regression or disappearance of hyperplastic gastric polyps was seen in the 19 patients. The polyps disappeared in 15 of the 19 patients 1-12 months (average, 6.5 ± 1.1 mo) after the treatment. However, none of the polyps in any of the controls or in patients without *H pylori* eradication showed regression. These results strongly suggest that eradication of *H pylori* leads to regression and disappearance of hyperplastic gastric polyps. *H pylori* is the main cause of chronic active gastritis and can produce multi-virulence agents, damage the gastric mucosa, stimulate gastric body to release inflammation medium, activate various cytokines and promote inflammation reaction. *H pylori* infection damages the gastric mucosa and glandular cells, stimulates crypt epithelia and muscularis mucosa hyperplasia with eminent mucus. If the damage factors continue their existence, the pathological changes can progress to intestinal metaplasia or atypical hyperplasia and even

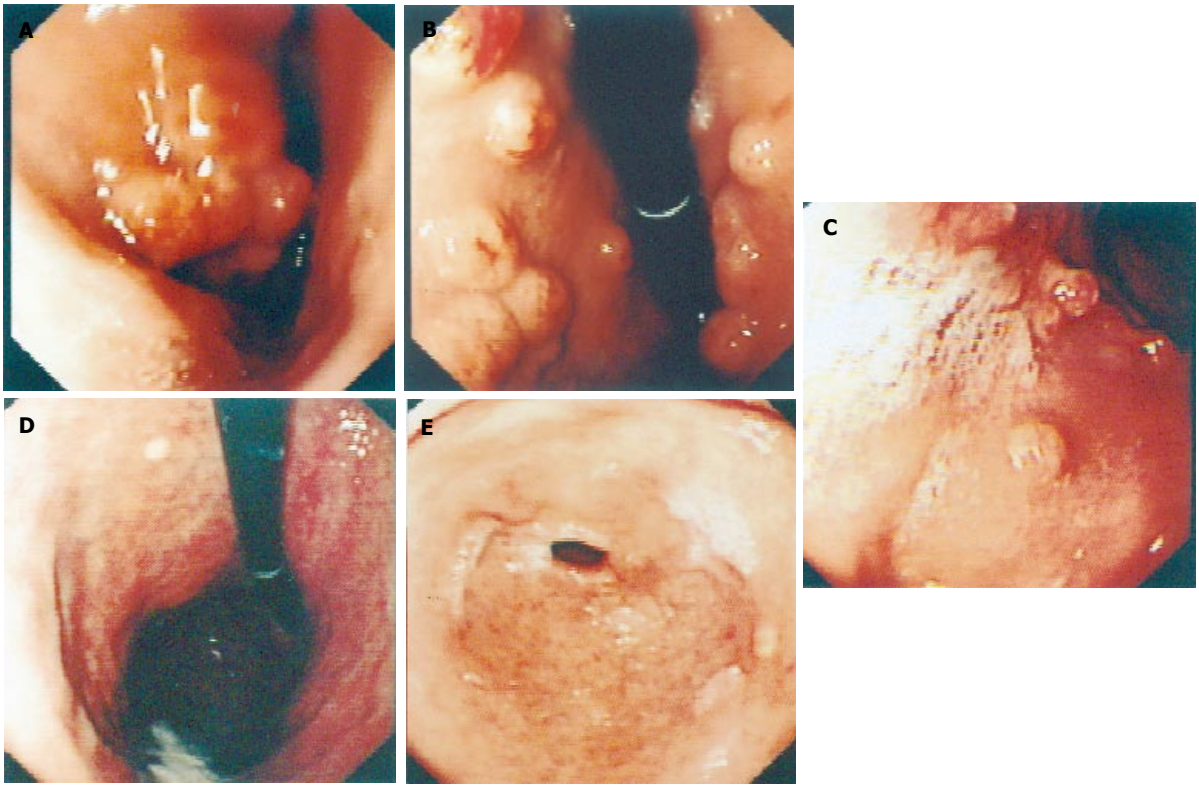

Figure 1 Effect of drug treatment on hyperplastic gastric polyps infected with *H pyori*. **A** and **B**: Multiple gastric polyps of the antrum and body; **C**: Decreased size of gastric polyps 7 mo after treatment; **D** and **E**: Disappearance of gastric polyps 11 mo after treatment.

Table 2 Inflammation status in treatment and control groups

Variable	Treatment groups (n = 22)	Control groups (n = 21)	P
Histologic findings			
Inflammation	1.6, 1.5	2.4, 2.3	<0.01
Activity	1.1, 1.3	2.4, 2.5	<0.01
Atrophy	2.2, 2.1	2.4, 2.4	>0.05
Metaplasia	0.8, 0.6	0.9, 0.7	>0.05

carcinoma. Yasunaga *et al* [10] reported that increased production of interleukin-1 beta and hepatocyte growth factor due to *H pylori* infection may contribute to thickening of the stomach by stimulating epithelial cell proliferation and foveolar hyperplasia in patients with enlarged fold gastritis, leading to formation of hyperplastic polyps.

Although hyperplastic gastric polyps did not accompany malignant transformation during the 9-12 month follow-up period in our study, *H pylori* infection is closely associated with gastric carcinoma. We therefore recommend that when hyperplastic gastric polyps are detected during endoscopy, serologic and pathologic tests should be done to detect and eradicatw *H pylori*.

Though the risk of hyperplastic gastric polyps conversing into cancer is very low, large hyperplastic gastric polyps should be snared and removed completely. Because of the malignant potential, all gastric polyps (0.5 cm or larger in diameter) should be removed. In addition, about 1 year after eradication of *H pylori* (4 patients in this study), any remaining hyperplastic polyps should be removed endoscopically because of the potential for development of cancer.

In conclusion, *H pylori* infection is related with hyperplastic gastric polyps and inflammatory cell infiltration, eradication of *H pylori* can prevent formation of hyperplastic gastric polyps.

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