

Effect of *N*-Acetyl Cysteine on *Helicobacter pylori*

Ahmet Kemal Gurbuz, MD, A. Melih Ozel, MD, Ramazan Ozturk, MD, Sukru Yildirim, MD, Yusuf Yazgan, MD, and Levent Demirturk, MD

Background: Use of mucolytic agents that result in reduced mucous viscosity of the gastric mucous has been suggested to have an additive effect in curing *Helicobacter pylori* infection.

Methods: Seventy *H pylori*-positive patients were given either eradication treatment consisting of 500 mg clarithromycin bid and 30 mg lansoprazole bid for 10 days plus 10 mL (400 mg) *N*-acetyl cysteine (NAC) liquid tid (AC group) or eradication treatment only (control group). The results were compared 1 month after the completion of the treatment.

Results: Fifty-eight patients were available for statistical analysis. Of the 28 patients in the AC group, 14 (50.0%) eradicated the infection after treatment, whereas only 7 of 30 (23.3%) patients in the control group had negative results. The difference between the AC group and the control group was statistically significant ($P = 0.034$). In both groups, there was no difference in the number of smokers and in the eradication rates between smokers and nonsmokers. Eradication treatment with or without NAC caused no significant side effects in either group.

Conclusions: Our findings suggest that NAC has an additive effect on the eradication rates of *H pylori* obtained with dual therapy with lansoprazole and clarithromycin. NAC does not have any known activity against *H pylori*, but it may improve the delivery of antibiotics at the site of infection due to its ability to reduce the thickness of the mucus.

Key Words: eradication therapy, *Helicobacter pylori*, *N*-acetyl cysteine

Helicobacter pylori plays an important role in the pathogenesis of many gastroduodenal diseases.¹⁻⁴ Eradication of this organism improves gastritis and prevents relapse

of gastroduodenal ulcers.^{5,6} Despite good results with chemotherapy and combination drugs,⁷ an optimal form of treatment for *H pylori* has not yet been established.

In patients who have viscid or thickened airway mucus, *N*-acetyl cysteine (NAC) is sometimes used as a mucolytic agent by opening disulfide bonds and lowering mucous viscosity.^{8,9} A limited number of studies have evaluated whether lowering the viscosity of gastric mucus might affect the treatment outcome of *H pylori* infection.¹⁰⁻¹² The aim of this study was to evaluate whether the addition of NAC to the treatment regimen of *H pylori* infection would affect eradication rates of the disease.

Methods

Patients with dyspeptic symptoms, who were scheduled for upper GI endoscopy between January 2004 and January 2005, were included in the study. Exclusion criteria included recent use of antibiotics, bismuth salts or proton pump inhibitors (PPI), chronic use of nonsteroidal antiinflammatory drugs or corticosteroids, severe comorbid diseases, pregnancy or lactation, prior gastric surgery, history of peptic ulcers, and patient or family history of gastric malignancy.

The *H pylori* detection procedure consisted of four gastric biopsies (two from the antrum and two from the corpus) for histopathological studies and two antral biopsies for rapid urease test (CLOtest, Ballard Medical Products, Draper, UT).

Key Points

- The use of agents that result in reduced mucous viscosity, such as *N*-acetyl cysteine (NAC), might have an additive effect in curing *Helicobacter pylori* infection.
- Eradication treatment with NAC caused no significant side effects.
- Our findings suggest that NAC has an additive effect on the eradication rates of *H pylori* obtained with combination therapy consisting of lansoprazole and clarithromycin.

From the Departments of Gastroenterology and Pathology, Gülhane Military Medical Academy, Haydarpaşa Training Hospital, Istanbul, Turkey.

Reprint requests to A. Melih Ozel, MD, GATA Haydarpaşa Eğitim Hastanesi, Gastroenteroloji Kliniği, Istanbul 81327, Turkey. Email: melihozel@superonline.com

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Table. Results of eradication treatment with and without N-acetyl cysteine^a

	AC group (mean age, 46.0 ± 13.9)					Control group (mean age, 51.2 ± 1.4)				
	n	Posttreatment <i>H pylori</i> status				n	Posttreatment <i>H pylori</i> status			
		(+)	(-)	I/D	N/A		(+)	(-)	I/D	N/A
Female	17 (48.6%)	6	8	1	2	16 (45.7%)	10	4	2	-
Male	18 (51.4%)	8	6	2	2	19 (55.3%)	13	3	2	1
Total	35	14 (50.0%)	14 (50.0%)	3	4	35	23 (76.7%)	7 (23.3%)	4	1

^aAC, N-acetyl cysteine; I/D, indeterminate; N/A, not available for follow-up.

H pylori was diagnosed when both histology and the rapid urease test revealed a positive result.

Patients with positive results were randomly assigned into two groups. The first group (AC group) was given 500 mg clarithromycin bid and 30 mg lansoprazole bid for 10 days plus 10 mL (400 mg) NAC liquid tid. The control group was given 500 mg clarithromycin bid and 30 mg lansoprazole bid for 10 days. One month after completion of the treatment, the diagnostic procedures were repeated in both groups.

Results

Seventy patients were included in the study. Age, sex distribution, and smoking history was not significantly different in either group. At the end of the study period, 65 patients were available for follow up. Because 7 patients had indeterminate results on repeat testing, a total of 58 patients were included in the statistical analysis. At the end of the treatment period, the infection was eradicated in 14 of the 28 patients (50%) in the AC group and in only 7 of the 30 patients in the control group (23.2%). The difference between the AC group and the control group was statistically significant ($P = 0.034$). Neither smoking nor gender affected the outcome. Treatment caused no significant side effects in either group, aside from three patients who complained of altered taste, which may be attributed to clarithromycin.

Discussion

The addition of NAC during eradication therapy for *H pylori* improved the cure rate achieved by the dual therapy with lansoprazole and clarithromycin. Because NAC has no known activity against *H pylori*, we postulated that it might improve the delivery of antibiotics at the site of infection due to its ability to reduce the thickness of the mucus. We chose a Food and Drug Administration (FDA)-approved treatment program that was relatively weak (antibiotic monotherapy plus PPI instead of dual antibiotherapy plus PPI) to clearly evaluate whether NAC was an effective agent in the eradication treatment of *H pylori*.⁷ As studies have shown that the eradication rates with dual antibiotherapy plus PPI treatment

are higher, we thought it would be difficult to measure the true effect of NAC if used in conjunction with dual antibiotherapy.

The mechanism of effect of NAC on *H pylori* is not known, but it is believed that NAC might interfere with the antigenic determinants of the bacterium, presumably by exposing the bacteria to an acidic environment, leading to degradation of the antigen.¹⁰ Another study suggested that NAC decreased the oxidant load on the mucosa preventing the inflammatory response seen during *H pylori* infection.¹³ NAC is known to reduce the thickness of gastric mucus in rats.^{14,15} It is not clear, however, whether NAC or pronase exerts its activity on the mucous layer by decreasing the thickness of the mucus or by degrading the epithelium.¹⁶ It is, however, apparent that the lower the viscosity of the mucus, the higher the eradication rates for *H pylori*.^{11,12,16,17} (Table).

Conclusions

Our findings suggest that combination of NAC with antibiotic therapy appears to be a promising means of eradicating *H pylori* infection.

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Age does not protect you from love. But love, to some extent, protects you from age.

—Anais Nin

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