

Helicobacter pylori

Clinical Characteristics of Patients with Failed Eradication of *Helicobacter pylori* and Antibiotic Resistance

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Background/Aims: The decisive factors influencing the eradication of *H. pylori* still remain unclear. To identify such factors, we investigated the clinical characteristics and antibiotic resistance of patients. **Methods:** Patients with *H. pylori* infection were treated with dual or triple regimens. Eradication rates were analyzed on the basis of clinical factors, endoscopic factors and antibiotic resistance. **Results:** Sixty-three *H. pylori* infected patients were enrolled (mean age 49.4). The eradication rate was significantly higher in compliant patients (71.9%) than in non-compliant patients (20%). Other clinical and endoscopic factors did not significantly influence the outcome of treatment. In 42 isolated strains, metronidazole resistance (MIC>8 µg/mL) was observed in 35.7% of the strains and clarithromycin resistance (MIC>2 µg/mL) was observed in 7.1%. The eradication rate in metronidazole resistant strains was 55.5%, which was lower than that in metronidazole sensitive strains (78.6%). The median value of metronidazole MIC in the group of successful eradication (0.94 µg/mL) was significantly lower than that in the group of failed eradication (64.0 µg/mL). **Conclusions:** Patient's compliance for regimens seems to be the most important factor which affect *H. pylori* eradication. Metronidazole resistance which is highly prevalent in our population may influence the efficacy of anti-*H. pylori* treatment regimen containing metronidazole. (**Kor J Gastroenterol 1999;33:311 - 320**)

Key Words: *Helicobacter pylori*, Failed eradication, Antibiotic resistance

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Helicobacter pylori Warren Marshall

H. pylori

H. pylori

H. pylori

.23 *H. pylori*

bismuth
hibitor

proton-pump in-

(Olympus Q200, XQ200 sys-
tem, Tokyo, Japan)

rapid urease (CLO[®]; Delta West,
Bentley, Western Australia) *H. pylori*

가

가

metronidazole

,410 metronidazole

metronidazole

.211

thromycin

clari-

.10,12-14

BMA, OA, OC 2

4

rapid urease

가

가

H. pylori

25

hematoxylin-eosin (H&E)

H. pylori

rapid

urease

urease

가

가

H. pylori

가

99%

1.

가

1

1997 6

1997 12

(blood agar)

H. pylori

63

gaspak jar (Difco, Detroit, Mi-
chigan, USA) 37 , O2 5%, CO2 10%, N2

85% *H. pylori* .15 Metroni-
dazole clarithromycin epsilometer

test (E test; AB Biodisk, Solna, Sweden)

2

McFarland nephelometer 2 3
 E
 test strip
 3
 oxidase
 metronidazole 가 8 µg/mL
 , clarithromycin 가 2 µ
 g/mL
 3.

Fig. 1. Metronidazole resistance of *H. pylori*. Metronidazole resistance was defined as minimal inhibitory concentration of metronidazole >8 µg/mL in epsilometer test.

SPSS (version 7.5)
 ±
 2-test,
 ANOVA, unpaired t-test, Mann-Whitney test
 p 0.05

1.

63 29 , 34
 1:1.2 . 49.4 ± 11.9 ,
 28 72 .
 29 (46%), 21
 (33%), 13 (21%) .

Fig. 2. Clarithromycin resistance of *H. pylori*. Clarithromycin resistance was defined as minimal inhibitory concentration of clarithromycin >2 µg/mL in epsilometer test.

Fig. 3. Distribution of minimal inhibitory concentrations of metronidazole and clarithromycin to *H. pylori*. Bars showed the cutoff value to antibiotic resistance.

2. *H. pylori* 95.2%, rapid urease 88.7%
H. pylori , 48 가
 가 76.2% *H. pylori*
 .
 3. *H. pylori* 42 me-
 tronidazole 가 15 (35.7%)
 26.3%, 43.5% metronidazole
 . Clarithromycin 3 (7.1%)
 (Fig. 1-3).
 4. Metronidazole
 Metronidazole , , ,
 , , 가 가 5
 5 metroni-
 dazole (p=0.04)(Table 1).
 5. *H. pylori*
H. pylori 가
 36 .
 , ,
 , , ABO , , 가 , , ,
 , ,
 , ,
 (Table 2, 3).
 6. *H. pylori* OA
H. pylori OA
 72.7%, BMA 50.0%, OC
 77.8%
 (Table 4).

7. *H. pylori* 80%
 가 , 가
 71.9% *H. pylori* 가
 (20.0%)
 (p=0.01)(Table 4).
 8. Metronidazole *H. pylori*
 Metronidazole 가 8
 µg/mL metronidazole
 55.5% 78.6%
 가 ,
 metronidazole
 0.94 µg/mL,

Table 1. Metronidazole Resistance according to Various Factors

Factors	Resistant rate (%)	p
Sex		0.25
Male (n=19)	26.3	
Female (n=23)	43.5	
Age		0.58
<50 years (n=22)	40.0	
50 years (n=20)	31.8	
Residence		0.19
Urban (n=35)	31.4	
Rural (n=7)	57.1	
Alcohol		0.67
Present (n=7)	28.6	
Absent (n=20)	30.0	
Smoking		0.60
Present (n=15)	33.3	
Absent (n=19)	42.1	
Family size		0.04
No. <5 (n=12)	33.3	
No. 5 (n=3)	100	
Diagnosis		0.48
Gastric ulcer (n=13)	46.2	
Duodenal ulcer (n=16)	25.0	
Non-ulcer (n=13)	38.5	

Table 2. *H. pylori* Eradication Rate according to Clinical Factors

Factors	Eradication rate (%)	p
Sex		0.46
Male (n=16)	62.5	
Female (n=20)	55.0	
Age		0.68
<50 years (n=15)	60.0	
50 years (n=21)	66.7	
Blood group		0.90
A (n=7)	57.1	
B (n=6)	55.0	
O (n=8)	62.5	
AB (n=6)	66.7	
Symptom duration		-
<6 months (n=15)	66.7	
6 months (n=12)	66.7	
Alcohol		0.86
Alcohol (n=6)	66.7	
Non-alcohol (n=27)	63.0	
Smoking		0.14
Smoking (n=13)	84.6	
Non-smoking (n=22)	54.5	
NSAID		0.63
Used (n=4)	75.0	
Non-used (n=28)	57.1	
Residence		0.46
Urban (n=30)	53.3	
Rural (n=6)	83.3	

Table 3. *H. pylori* Eradication Rate according to Endoscopic Findings

Factors	Eradication rate (%)	p
Endoscopic diagnosis		0.40
Gastric ulcer (n=16)	62.5	
Duodenal ulcer (n=15)	73.3	
Chronic gastritis (n=5)	40.0	
Duodenal bulb		0.59
Deformed (n=7)	85.7	
Non-deformed (n=8)	75.0	
Intestinal metaplasia		0.21
Present (n=6)	33.3	
Absent (n=300)	63.3	

64.0 µg/mL metronidazole
(p=0.05)(Table 5).
9. 가
Metronidazole 23
metronidazole *H. pylori*
28.6% 60.0%
metronidazole
(Mann-Whitney test)
metronidazole 가
(p=0.08). Clarithromycin
1 clarithromycin 6
clarithromycin
H. pylori (Table 6, 7).
H. pylori
, *H. pylori*
.23 *H. pylori*
H. pylori
bismuth proton-pump
inhibitor ,
가 .16
, , , ,
.17,18
bismuth, metronidazole
amoxicillin (BMA) ,
metronidazole
.16,19 omeprazole
가 가
,201 omeprazole
clarithromycin 2 (OC) 75%

Table 4. *H. pylori* Eradication Rate according to Therapeutic Factors

Factors	n	Eradication rate (%)	p
Treating drugs			0.29
OA	11	72.7	
BMA	16	50.0	
OC	9	77.8	
Compliance			0.01
Compliant (≥80%)	31	71.9	
Non-compliant (<80%)	5	20.0	

OA, omeprazole + amoxicillin; BMA, bismuth + metronidazole + amoxicillin; OC, omeprazole + clarithromycin.

Table 5. *H. pylori* Eradication Rate according to Bacteriologic Factors

Factors	n	Eradication rate (%)	p
Clarithromycin			0.30
Resistant (MIC ≥ 2 µg/mL)	1	0.0	
Susceptible (MIC < 2 µg/mL)	23	72.7	
Metronidazole			0.36
Resistant (MIC ≥ 8 µg/mL)	9	55.5	
Susceptible (MIC < 8 µg/mL)	14	78.6	

MIC, minimum inhibitory concentration.

Table 6. Characteristics of patients Treated with Metronidazole

	Treatment success	Eradication rate (%)	p
No. of patients	12	11	
Metronidazole resistance (MIC ≥ 8 µg/mL)	28.6%	60.0%	0.56
Metronidazole MIC (Median µg/mL)	2.0	256.0	0.08*
Compliance	80.0%	63.6%	0.04
Sex (Male:Female)	1:2.4	1:2.8	0.79
Age (≥50 years)	50.0%	36.4%	0.5
Residence (urban:rural)	10:2	11:0	0.36

MIC, minimum inhibitory concentration; *, by Mann-Whitney test.

Table 7. Characteristics of Patients Treated with Clarithromycin

	Treatment success	Treatment failure
No. of patients	6	2
Clarithromycin resistance (MIC ≥ 2 µg/mL)	0%	50%

MIC, minimum inhibitory concentration.

zole 가 .7,12,16,22-24 Omepra-
 85-90% ,7,25,26 가 BMA 28.6% 60.0%
 2.5% dazole , metroni-
 .21 64.0 µg/mL 0.94 µg/mL metroni-
 가 *H. pylori* dazole BMA *H. pylori* me-
 .11 *H. pylori* 가 troniazole
 , 가 , omeprazole, bismuth
 가 clarithromycin metronida-
 , zole *H. pylori* 가
 .13,14,29 *H.*
 가 *pylori* 108 1 bismuth
H. pylori 가
 .4 *H. pylori* peni 가 . Metronidazole
 cillin, erythromycin, tetracyclin, norfloxacin BMA 68-96%
 , trimethoprim-sulfamethoxa- ,5,79 omeprazole BMA
 zole , tinida- 90%
 zole tripotassium dicitratobismuthate 70% 30 metronidazole
 .27
 Metronidazole *H. pylori*
 clarithromycin 가
 clarithromycin
 . *H. pylori* metronidazole 7.0-87.5% metronidazole
 , metronidazole , clarithromycin
 BMA .13 Clarithromycin
 ,410 가 23S rRNA
 BMA metronidazole ,12,31 clarithromycin
 .2 metronidazole 2.0-7.8% , clarithromycin
 metroni-
 dazole 가 20% .10,12-14 Clarithromy-
 .4,28 28 *H. pylori* cin ,32
 metronidazole 32% 54% clarithromycin 25-50%
 ,
 BMA 17% .12,13 clarithromycin
 68% 가 2 µg/mL , 1
 7.1% clarithromycin
 metronidazole 35.7% clarithromycin
 26.3%, 43.5% , 6 clari-

thromycin *H. pylori* 가 , metronidazole
 .3436 *H. pylori*
 가 .2
 , , , , , ABO , , 가 , ,
 , omeprazole , , 가 가 ,
 .235 BMA 가
 96% , *H. pylori*
 69% 가 가 ,
 가 5
 가 89%, 가 *H.*
 50% , *pylori* ,
 가
 2 . 80%
 가 가 71.9%
 가 20% : 가 *H. pylori*
H. pylori
 가 , . 가
*H. pylori*가
 .233
 가 : 1997 6 1997 12
H. pylori .34
H. pylori 63 ,
 .2 omeprazole , metronidazole
 pH가 *H. pylori* clarithromycin :
 가 , 29 (46%),
 'coccoid persister'가 21 (33%), 13 (21%) ,
 omeprazole *H. pylori* 42 metronida-
 .222 *H. pylori* zole 35.7%, clarithromycin 7.1%
 가 .21235 *H. pylori*
 pH가 , 36 . 가 71.9% *H.*
pylori 가 20%

metronidazole (0.94 µg/mL)
 (64.0 µg/mL)
 : *H. pylori*
 , *H. pylori*
 가 가

H. pylori

: *Helicobacter pylori*,

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