

Helicobacter pylori
Omeprazole

**Effect of Omeprazole Quadruple Therapy on
Eradication of *Helicobacter pylori***

**Hyo Min Yoo, M.D., Yong Chan Lee, M.D., Sang In Lee, M.D.,
Young Myung Moon, M.D., Jin Kyung Kang, M.D. and In Suh Park, M.D.**

*Departments of Internal Medicine and Institute of Gastroenterology,
Yonsei University College of Medicine, Seoul, Korea*

Background/Aims: The optimal regimen for the eradication of *H. pylori* remains unclear. Thus the authors evaluated the effect of one-week course of omeprazole quadruple regimen on eradication of *H. pylori* in Korea. **Methods:** We investigated the outcome of quadruple therapy on eradication of *H. pylori* in 93 patients with *H. pylori* positive gastritis or peptic ulcer diseases. We tried three different quadruple regimens. Regimen A (OBMA) including omeprazole 20 mg *b.i.d.*, amoxicillin 1 g *b.i.d.*, metronidazole 500 mg *t.i.d.* and bismuth 240 mg *b.i.d.* was used for 64 patients. Another regimen (OABC) including omeprazole 20 mg *b.i.d.*, amoxicillin 500 mg *t.i.d.*, bismuth 240 mg *b.i.d.* and clarithromycin 250 mg *b.i.d.* was used for 18 patients and the third regimen (OAMC) including omeprazole 20 mg *b.i.d.*, amoxicillin 1 g *b.i.d.*, metronidazole 500 mg *t.i.d.* and clarithromycin 250 mg *b.i.d.* (OAMC) was applied for 11 patients. **Results:** The overall eradication rate of quadruple regimens was 84.9%. Eradication rates of each regimen were 94.4% in OABC, 81.9% in OAMC and 82.8% in OBMA. Eradication was successful in 85.2% of 61 patients who used quadruple regimen as first line treatment and in 84.4% of 32 patients who used quadruple regimen for retreatment. The side effects were observed in 16.1% of the patients and the compliance rate was 98.9%. **Conclusions:** One-week course of quadruple regimens was effective in the eradication of *H. pylori* and showed good compliance. Quadruple regimen was also effective in patients who failed to eradicate *H. pylori* with dual or triple regimen. (**Kor J Gastroenterol 1999;33:473 - 481**)

Key Words: *Helicobacter pylori*, Quadruple regimen, Retreatment

Helicobacter pylori (H. pylori)

가 , H. pylori

2.

OBMA (omeprazole 20 mg b.i.d. +

bismuth 240 mg b.i.d. + metronidazole 500 mg t.i.d. + amoxicillin 1 g b.i.d.) 64 , OABC (omeprazole

20 mg b.i.d. + amoxicillin 500 mg t.i.d. + bismuth 240 mg b.i.d. + clarithromycin 250 mg b.i.d.) 18 ,

OAMC (omeprazole 20 mg b.i.d. + amoxicillin 1 g b.i.d. + metronidazole 500 mg t.i.d. + clarithromycin

250 mg b.i.d.) 11 .

H. pylori

.12

H. pylori

,

.3

bismuth, metronidazole

amoxicillin

(BMA)

가

metronidazole

가

.45 Omeprazole

61

H.

가

가

pylori

.4 ome-

32

BMA (bismuth, metronidazole,

prazole 가

amoxicillin)

omeprazole

,

가

(omeprazole +

1 2)

H.

,

가

H. pylori

4

omeprazole

rapid urease

H. pylori

가

1.

1996 7

1997 7

H. pylori

93

1.

. H. pylori

Omeprazole clarithromycin

hematoxylin &

OACB가 94.4% (n=18), OAMC가 81.9%

eosin

(n=11)

omeprazole 가

rapid urease

가

(OBMA) 82.8% (n=64)

H. pylori

84.9%

(Fig. 1).

47.3

2.

21 74

1.3:1

35

13

23

22

85.2% (n=61)

H. pylori

BMA

omeprazole

H. pylori (Fig. 3).
 84.4% (n=32)
 (Fig. 2).
 (BMA) *H.*
pylori OBMA 88.9% (n=45) ,
 77.8% (n=18) ,
 metronidazole
 OBMA
 92.9% (n=14)

Fig. 1. *H. pylori* eradication rates according to quadruple regimens. All of quadruple regimens have achieved eradication rate of over 80% but the difference of eradication rate among quadruple regimens was not significant.

Fig. 2. *H. pylori* eradication rates of quadruple regimens as the first-line therapy and retreatment. Retreatment with quadruple regimens was administered in failed patients with dual or triple regimens.

Fig. 3. *H. pylori* eradication rate of OBMA as the retreatment regimens in the failed first-line therapy with or without metronidazole. There was no significant difference in the eradication rate between two groups.

81.3% (n=48)
 .
 51.6 (n=14)
 50 92.9% (n=56) 50
 80.0% (n=37)
 (p=0.02). , ,
 (Table 1).
 4.
 80%
 가 98.9%
 . 15
 (16.1%) 5 , 2 , 2 ,
 1 , 1
 (Table 2).
 5.
H. pylori
 가 ,
 omeprazole 가 7
 clarithromycin
 7 14
 (Table 3).

Table 1. *H. pylori* Eradication Rate of Quadruple Regimens according to Various Factors (n=93)

Factors	Eradication rate (%)	p value
Sex		NS
Male (n=52)	88.5	
Female (n=41)	80.1	
Age		0.02
<50 (n=56)	92.9	
50 (n=37)	80.0	
Alcohol		NS
Non-drink (n=63)	82.5	
Social drink (n=22)	90.9	
Heavy drink (n=8)	87.5	
Smoking		NS
Non-smoker (n=61)	84.3	
Smoker (n=32)	85.2	
Endoscopic diagnosis		NS
Chronic gastritis (n=35)	85.7	
Gastric erosion (n=13)	69.2	
Gastric ulcer (n=23)	87.0	
Duodenal ulcer (n=22)	90.9	

Helicobacter pylori (*H. pylori*)

Table 2. Compliance and Side Effects of Quadruple Regimens

	No. of patients (%)
Compliance	
Compliant (80%)	92 (98.9)
Not compliant (<80%)	1 (1.1)
Side effects	15 (16.1)
Metallic taste	5 (5.4)
Diarrhea	5 (5.4)
Indigestion	2 (2.2)
Dyspepsia	2 (2.2)
Tongue discoloration	1 (1.1)

Table 3. The Cost of *H. pylori* Eradicating Regimens

Regimens	Duration (days)	Cost (won)
BMA	14	26,208
OBMA	7	41,552
OC	7	65,534
OC	14	131,068
OAC	7	67,830
OAC	14	135,660
OMC	7	66,598
OMC	14	133,196
OAM	7	31,808
OAM	14	63,616

BMA, bismuth + metronidazole + amoxicillin; OBMA, omeprazole + bismuth + metronidazole + amoxicillin; OC, omeprazole + clarithromycin; OAC, omeprazole + amoxicillin + clarithromycin; OMC, omeprazole + metronidazole + clarithromycin; OAM, omeprazole + amoxicillin + metronidazole; omeprazole 20 mg *b.i.d.*; amoxicillin 1 g *b.i.d.*; metronidazole 500 mg *t.i.d.*; clarithromycin 250 mg *t.i.d.*; bismuth 240 mg *b.i.d.*.

H. pylori .12
H. pylori
H. pylori bismuth proton-pump inhibitor , 가
 가 .7
 , , , ,
 ,389 80%
 , 90%
 .1012
 bismuth, metronidazole amoxicillin 가
 (BMA) , metronidazole
 , 가
 .4571314 Omeprazole 가
 가 .414 omeprazole
 가
 가
 ,
 가 .
 가 omeprazole 가
 , metronidazole
 .11,15-17
 omeprazole
 가
 .15,16 93
 1
 .
 95%
 ,15-17 metronidazole
 zole
 .18 60%
 .19
 omeprazole 가

가 *H. pylori*
 , *H. pylori*
 .6

(OBMA) 82.8% 20 (OBMA) ,
68.9%
95% . dazole 가 .
H. pylori
tetracyclin amoxicillin
, , tetracyclin 10% ,
amoxicillin 80% ,4
가 clarithromycin .431 Omeprazole (OACM)
90%
1 72%,21 2 76.1%,22 4 .32 omeprazole
91%23 7
84.4%
가
omeprazole H. pylori
가
.12 Omeprazole 가 ,
pH가 ,24 가 omeprazole 가 7
가 가 , clarithromycin 7
가 가 .25 pH가 14
bismuth
,26 omeprazole 가 urease H. pylori
.27,28
Metronidazole 가 .
.10 metronida-
zole 82%
29 metronidazole
.30 me-
tronidazole : H. pylori
(OBMA) ,
.29 metronidazole bis- H. pylori
muth 가 metronidazole omeprazole 가
가 .10 . : 1996 7 1997
metronidazole 7
, H.
pylori 77.8% pylori 93 (35 ,

13 , 23 , 22)

OBMA (omeprazole 20 mg *b.i.d.* + bismuth 240 mg *b.i.d.* + metronidazole 500 mg *t.i.d.* + amoxicillin 1 g *b.i.d.*) 64 , OABC (omeprazole 20 mg *b.i.d.* + amoxicillin 500 mg *t.i.d.* + bismuth 240 mg *b.i.d.* + clarithromycin 250 mg *b.i.d.*) 18 , OAMC (omeprazole 20 mg *b.i.d.* + amoxicillin 1 g *b.i.d.* + metronidazole 500 mg *t.i.d.* + clarithromycin 250 mg *b.i.d.*) 11

61 *H. pylori* 32 *H. pylori* .

OACB가 94.4% (n=18), OAMC가 81.9% (n=11), OBMA가 82.8% (n=64) 84.9% , . 85.2% (n=61) , 84.4% (n=32) . (BMA) *H. pylori* OBMA 77.8% (n=18) , metronidazole OBMA 92.9% (n=14) . 88.9% (n=45) , 81.3% (n=48) . 50 92.9% (n=56) 50 80.0% (n=37) (p=0.02). , , (98.9%), 16.1% 1 . : *H. pylori* 가 .

1. National Institute of Health Consensus Conference. *Helicobacter pylori* in peptic ulcer disease. JAMA 1994;272:65-69.
2. Tytgat GN. Review article: treatments that impact favourably upon the eradication of *Helicobacter pylori* and ulcer recurrence. Aliment Pharmacol Ther 1994;8:359-368.
3. de Boer WA, Tytgat GN. The best therapy for *Helicobacter pylori* infection: should efficacy or side effect profile determine our choice? Scand J Gastroenterol 1995;30:401-407.
4. van der Hulst RW, Keller JJ, Rauws EA, Tytgat GN. Treatment of *Helicobacter pylori* infection: a review of the world literature. Helicobacter 1996 1:6-19.
5. Noach LA, Langenberg WL, Bertola MA, Dankert J, Tytgat GN. Impact of metronidazole resistance on the eradication of *Helicobacter pylori*. Scand J Infect Dis 1994;26:321-327.
6. Labenz J, Borsch G. Highly significant change in the clinical course of relapsing and complicated peptic ulcer disease after cure of *Helicobacter pylori* infection. Am J Gastroenterol 1994;89:1785-1788.
7. Chiba N, Rao BV, Rademaker JW, Hunt RH. Meta-analysis of the efficacy of antibiotic therapy in eradicating *Helicobacter pylori*. Am J Gastroenterol 1992;87:1716-1727.
8. Graham DY. A reliable cure for *Helicobacter pylori* infection? Gut 1995;37:154-156.
9. . *Helicobacter pylori* . 1997;53(suppl 2):S455-S466.
10. Graham DY, Hoffman J, el-Zimaity HM, Graham DP, Osato M. Twice a day quadruple therapy (bismuth subsalicylate, tetracycline, metronidazole plus lansoprazole) for treatment of *Helicobacter pylori* infection. Aliment Pharmacol Ther 1997;11:935-938.
11. Peterson WL, Graham DY. *Helicobacter pylori*. In

- Feldman M, Scharschmidt BF, Sleisenger MH, eds. Gastrointestinal and liver disease. Volume 1. 6th ed. Philadelphia: Saunders, 1998: 604-619.
12. de Boer WA, van Etten RJ, Schade RW, Ouwehand ME, Schneeberger PM, Tytgat GN. 4-day lansoprazole quadruple therapy: a highly effective cure for *Helicobacter pylori* infection. *Am J Gastroenterol* 1996;91:1778-1782.
 13. Penston JG. Review article: *Helicobacter pylori* eradication: understandable caution but no excuse for inertia. *Aliment Pharmacol Ther* 1994;8:369-389
 14. Thijs JC, van Zwet AA, Moolenaar W, Wolfhagen MJ, ten Bokkel Huinink J. Triple therapy vs. amoxicillin plus omeprazole for treatment of *Helicobacter pylori* infection: a multicenter, prospective, randomized, controlled study of efficacy and side effects *Am J Gastroenterol* 1996;91:93-97.
 15. de Boer WA, Driessen WM, Jansz AR, Tytgat GN. Effect of acid suppression on efficacy of treatment for *Helicobacter pylori* infection. *Lancet* 1995;345: 817-820.
 16. Borody TJ, Andrews P, Fracchia G, Brandl S, Shortis NP, Bae H. Omeprazole enhances efficacy of triple therapy in eradicating *Helicobacter pylori*. *Gu* 1995;37:477-481.
 17. de Boer WA, Driessen WM, Jansz AR, Tytgat GN. Quadruple therapy compared with dual therapy for eradication of *Helicobacter pylori* in ulcer patients: results of a randomized prospective single-centre study. *Eur J Gastroenterol Hepatol* 1995;7:1189-1194.
 18. Hosking SW, Ling TK, Yung MY, et al. Randomised controlled trial of short term treatment to eradicate *Helicobacter pylori* in patients with duodenal ulcer. *BMJ* 1992;305:502-504.
 19. Phull PS, Griffiths AE, Halliday D, Jacyna MR. One week treatment for *Helicobacter pylori* infection: a randomised study of quadruple therapy versus triple therapy. *J Antimicrob Chemother* 1995;36:1085-1088.
 20. Lee DH, Park HJ, Song SY, et al. Evaluation of therapeutic regimens for the treatment of *Helicobacter pylori* infection. *Yonsei Med J* 1996;37:270-277.
 21. Tucci A, Corinaldesi R, Stanghellini V, et al. One day therapy for treatment of *Helicobacter pylori* infection. *Dig Dis Sci* 1993;38:1670-1673.
 22. Kung NN, Sung JJ, Yuen NW, et al. Anti *Helicobacter pylori* treatment in bleeding ulcers: randomized controlled trial comparing 2-day versus 7-day bismuth quadruple therapy. *Am J Gastroenterol* 1997;92:438-441.
 23. de Boer WA, Driessen WM, Tytgat GN. Only four days of quadruple therapy can effectively cure *Helicobacter pylori* infection. *Aliment Pharmacol Ther* 1995;9:633-638.
 24. Grayson ML, Eliopoulos GM, Ferraro MJ, Moelering RC Jr. Effect of varying pH on the susceptibility of *Campylobacter pylori* to antimicrobial agents. *Eur J Clin Microbiol Infect Dis* 1989;8:888-889.
 25. Westblom TU, Duriex DE. Enhancement of antibiotic concentrations in gastric mucosa by H₂ receptor antagonist: implications for treatment of *Helicobacter pylori* infections. *Dig Dis Sci* 1991;36: 25-28.
 26. Nwokolo CU, Lewin JF, Hudson M, Pounder RE. Transmucosal penetration of bismuth particles in the human stomach. *Gastroenterology* 1992;102:163-167.
 27. Nagata K, Satoh H, Iwahi T, Shimoyama T, Tamura T. Potent inhibitory action of the gastric proton pump inhibitor lansoprazole against urease activity of *Helicobacter pylori*: unique action selective for *H. pylori* cells. *Antimicrob Agents Chemother* 1993: 37:769-774.
 28. Nakshabendi IM, Zhang QB, Mokhashi M, Gemmel CG, Lee FD, Russell RI. Effect of omeprazole therapy on the survival of *Helicobacter pylori* urease activity, and antral gastric histology in patients with duodenal ulcer. *Helicobacter* 1996;1:155-158.
 29. van der Hulst RW, van der Ende A, Homan A, Roorda P, Dankert J, Tytgat GN. Influence of

- metronidazole resistance on efficacy of quadruple therapy for *Helicobacter pylori* eradication. Gut 1998;42:166-169.
30. de Boer WA. How to achieve a near 100% cure rate for *H. pylori* infection in peptic ulcer patients. A personal viewpoint. J Clin Gastroenterol 1996;22:313-316.
31. Huang JQ, Hunt RH. Review: eradication of *Helicobacter pylori*. problems and recommendations. J Gastroenterol Hepatol 1997;12:590-598.
32. Treiber G, Ammon S, Schneider E, Klotz U. Amoxicillin/metronidazole/omeprazole/clarithromycin: a new, short quadruple therapy for *Helicobacter pylori* eradication. Helicobacter 1998;3:54-58.
-