

## To compare the efficacy of triple therapy with furazolidone, amoxicillin and omeprazole for two weeks and three weeks in the eradication of *Helicobacter pylori* in Bangladeshi duodenal ulcer patients

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### Abstract

*Helicobacter pylori* eradication is the mainstay in the treatment of *Helicobacter pylori* associated peptic ulcer disease. Furazolidone was tried in several developing countries and showed good results in some trials. Increasing the duration of treatment has been shown to improve the eradication rate. This study was done to compare the efficacy of triple therapy for two weeks (Group-A) and three weeks (Group-B) consisting of omeprazole 20 mg b.d. amoxicillin 1gm b.d. and furazolidone 200 mg b.d. in the eradication of *Helicobacter pylori* in duodenal ulcer patient. A total of 70 duodenal ulcer patients with *Helicobacter pylori* infection were included in the study. Healing of duodenal ulcer was assessed three months after the end of treatment and at the same time *Helicobacter pylori* eradication assessed by Campylobacter Like Organism (CLO) test and histology. In group-A, duodenal ulcer was healed in 17(58.62%) patients and *Helicobacter pylori* was eradicated in 15(52%) patients. In group-B, duodenal ulcer was healed in 19(61.30%) patients and *Helicobacter pylori* was eradicated in 18(58%) patients. Healing of duodenal ulcer was not significantly different between two groups. Eradication of *Helicobacter pylori* was also not significantly different between two groups.

### Introduction

Duodenal ulcer disease is one of the most commonly encountered health problem in Bangladesh. The prevalence of duodenal ulcer was estimated to be 11.98%<sup>1</sup>. *Helicobacter pylori* is considered as one of the most important etiological factor responsible for duodenal ulcer<sup>2</sup>. *Helicobacter pylori* is widely prevalent in Bangladesh, with 60% of children being infected by the age 3 months and 80% being infected by the age of 3 years<sup>3</sup>. In adults, about 92% have been found to be seropositive for *Helicobacter pylori* antibody<sup>4</sup>.

Successful treatment aiming at the cure of *Helicobacter pylori* infection results in the healing of duodenal ulcer disease and very low recurrence rate<sup>5</sup>. Several international consensus conference<sup>6-8</sup> recommended that all patients with duodenal or gastric ulcer who have *Helicobacter pylori* infection should receive anti *Helicobacter pylori* therapy to cure the infection. In Bangladesh several trials have been conducted in the past with different regimens to treat *Helicobacter pylori*. Some studies showed high eradication rate<sup>9,10</sup> and other studies showed low

eradication rate<sup>11,12</sup>. In most of the studies in Bangladesh, the eradication was between 30-64%<sup>11,12</sup>.

Furazolidone, an antimicrobial agent belonging to nitrofurans group proved to be successful against *Helicobacter pylori* in several trials<sup>13,14</sup>. There is no incidence of resistant strains of *Helicobacter pylori* against furazolidone yet. This drug is very cheap and there are very few adverse effects. Amoxicillin resistance was found to be low in Bangladesh<sup>15</sup>. Increasing duration of treatment has been shown to improve the eradication rate<sup>16</sup>.

This study was designed to compare the efficacy of triple therapy with furazolidone in combination with amoxicillin and omeprazole for two weeks and three weeks in the eradication of *Helicobacter pylori* and also to compare the ulcer healing rate.

### Materials and Methods

This study was conducted in the department of Gastroenterology, Bangabandhu Sheikh Mujib Medical University from July 2002 to June 2004. A total of 70 patients with endoscopically proven duodenal ulcer, 15 to 60 years of age, of both sexes were included in this study when Campylobacter Like

Organism (CLO) test and histology gave positive result. Complicated duodenal ulcer, patients with gastric ulcer, severe concomitant illness, pretreatment with Proton Pump Inhibitors, H<sub>2</sub> receptor antagonist, bismuth preparation or antibiotics within 4 weeks prior to study, patients with regular intake of Non Steroidal Anti Inflammatory Drugs or steroids, pregnant or lactating women were excluded from the study. A complete medical history was obtained and physical examination was performed in each patient. Informed consent was taken from each patient. Socioeconomic status of the patients determined according to the yearly income of the patients. Low economic class-income <Tk 30,000 per annum, middle economic class-income Tk-30,000-Tk-59,900 per annum and high economic class-income Tk 60,000 and above.

Pretreatment endoscopy of upper Gastro Intestinal Tract was done with Olympus forward viewing video endoscope GIF-0145 to identify the presence, number, size and location of duodenal ulcer and two biopsies were taken from the antrum and one biopsy from the body of the stomach. One biopsy from antrum was used for Campylobacter Like Organism (CLO) test. One biopsy from the antrum and one from the body of the stomach used for histology. Those patients with duodenal ulcer who were found to be positive for *Helicobacter pylori* by Campylobacter Like Organism (CLO) test and histology were treated with omeprazole (20 mg b.d), amoxicilline (1gm b.d) and furazolidone (200 mg b.d.) for 2 weeks and 3 weeks.

Drug compliance was monitored by daily drug intake diary maintained by the patient in which the patient was required to mark each dose taken in the day and by counting of empty drug packages (each dose was supplied in one package). The patients were requested to note any adverse effect and to report.

Follow up endoscopy of upper Gastro Intestinal Tract was performed in all patients, three months after the end of therapy. Presence or absence of ulcer healing was checked. Biopsies from the antrum and body of the stomach were repeated. Biopsy samples were studied by Campylobacter Like Organism (CLO) test (one biopsy from antrum) and histology (one biopsy from antrum and one biopsy from body of stomach). Eradication was confirmed by negative result of the Campylobacter Like Organism (CLO) test and histology.

## Results

A total of 70 patients (35 patients in group-A for two weeks therapy and 35 patients in group-B for three weeks therapy) fulfilling the inclusion criteria were enrolled in this study. Base line characteristics of the patients are shown in the table-I. Among those patients, 6 patients from group-A and 4 patients from group-B didn't attend follow-up endoscopy at the end of 3 months (Table-II). The remaining 60 patients (85.71%) completed the trial. In group-A, 29 (82.85%) patients were follow-up, in group -B, 31 (88.57%) patients were followed-up. Total 36 (60%) patients out of 60 patients had their ulcer healed. In group-A, ulcer healed in 17(58.62%) patients. In group-B, ulcer healed in 19(61.30%) patients (Table-III). Comparison between two groups showed no significant difference of ulcer healing (P=0.833). *Helicobacter pylori* was eradicated in 33 (55%) patients out of 60 patients. In group-A, *Helicobacter pylori* eradication was found in 15 (52%) patients. In group-B, *Helicobacter pylori* eradication was found in 18 (58%) patients. Table-IV. Comparison between two groups showed no significant difference of *Helicobacter pylori* eradication (P= 0.622).

Patients who completed the trial were fully compliant. Some patients complained of nausea, loss of taste, headache and mild abdominal discomfort. All of these side effects were mild and did not require interruption of treatment. The reasons of dropout of patients in both groups from the study were not clear to us. Possibilities were they were noncompliant to the study. They thought that their symptoms were improved so repeat endoscopy would not help them. They were contacted but did not respond.

**Table I:** Baseline characteristics of the patients.

Parameters	Group A n=35	Group B n=35
Age		
Mean ± SD	33.71± 10.90	34.63± 13.36
Range	16-55	15-60
Sex		
Male	32	30
Female	3	5
Socioeconomic status		
Low	23	24
Middle	12	11
Smoking		
Yes	11	13
No	24	22

Group-A : Omeprazole, Amoxicillin and Furazolidone- 2 weeks.

Group-B : Omeprazole, Amoxicillin and Furazolidone- 3 weeks.

**Table II:** Patients attending at 3 months follow up.

Groups	Patients attended		Patients dropped out	
	No	(%)	No	(%)
A (n=35)	29	(82.86)	6	(17.14)
B (n=35)	31	(88.57)	4	(11.43)
Total	60	(85.71)	10	(14.29)

**Table III:** Duodenal ulcer healing in two groups:

Groups	Patients in whom duodenal ulcer healed		Patients in whom duodenal ulcer did not heal	
	No	(%)	No	(%)
A (n=29)	17	(58.62)	12	(41.38)
B (n=31)	19	(61.30)	12	(38.70)
Total (n=60)	36	(60)	24	(40)

**Table IV:** *Helicobacter pylori* eradication in two groups:

Groups	Patients in whom <i>Helicobacter pylori</i> eradicated		Patients in whom <i>Helicobacter pylori</i> not eradicated	
	No	(%)	No	(%)
A (n=29)	15	(52)	14	(48)
B (n=31)	18	(58)	13	(42)
Total (n=60)	33	(55)	27	(45)

## Discussion

Antimicrobial treatment of *Helicobacter pylori* is difficult because of the habitat occupied by the organism below the layer of mucous adherent to gastric mucosa. It is also difficult because of resistance of the organism to antimicrobial agent specially to nitroimidazole<sup>17,18</sup> and macrolides<sup>19</sup>. These factors have led to the concurrent use of several drugs as exemplified by triple and quadruple regimens. Even the most effective regimen available today fails in 5-20% cases<sup>20</sup>. This picture is more disappointing in Bangladesh with low eradication rates<sup>11,12</sup> and higher rates of re-infection<sup>21,22</sup>. In most of the studies in Bangladesh, the eradication rate was between 30–64%<sup>11,12</sup>. However, most studies in other developing countries showed also much lower eradication rates and higher rates of recurrence than those obtained in developed countries<sup>23-25</sup>. Increasing the duration of treatment has been shown to improve the eradication rate<sup>16</sup>. In India, study comparing two weeks therapy with three weeks therapy has found a better eradication rate in the three weeks group<sup>26</sup>.

In this prospective study we have compared the efficacy and safety of 2 weeks and 3 weeks of furazolidone based triple therapy. Furazolidone, an antimicrobial agent belonging to nitrofurans group proved to be successful against *Helicobacter pylori* in several trials<sup>12,13</sup>. There is no incidence of resistant strains of *Helicobacter pylori*-against furazolidone. Amoxicillin resistance was found to be low in Bangladesh<sup>15</sup>. This study has shown eradication rate of 52% in group-A and 58% in group-B, which is parallel with the rates of the most other studies in Bangladesh. But the rate is much lower than other countries.

Smoking has a relation with peptic ulcer healing. Ulcer healing is delayed in smokers. In our study ulcer healing was delayed in smokers. Smokers were advised to stop smoking during study but some patients did not stop due to addiction.

Socioeconomic status has a role in the prevalence of *Helicobacter pylori* infection. There is increased prevalence of *Helicobacter pylori* infection in low socioeconomic status. But socioeconomic status has no relation with peptic ulcer healing.

In one study<sup>13</sup> 30 patients with histologically documented *Helicobacter pylori* infection received combination of bismuth subcitrate 240 mg b.d. furazolidone 100 mg q.d.s. and amoxicillin 500 mg q.d.s. for 14 days. *H. pylori* eradication rate was 86%.

In another study<sup>14</sup> 140 patients were randomly assigned to received a one week course of furazolidone 100 mg b.d. and clarithromycin 250 mg b.d. with either tripotassium dicitrato-bismuthate 240 mg b.d. (FCB group) or lansoprazole 30 mg daily (FCL group) and clarithromycin 250 mg b.d. and omeprazole 20 mg daily with either furazolidone 100 mg b.d. (FCO group) or metronidazole 400 mg b.d. (MCO group). Four weeks after the end of therapy eradication rate was in the FCB, FCL, FCO and MCO groups were 91%, 91%, 86% 74% respectively. High eradication rate may be due to clarithromycin.

The optimal duration of treatment remains controversial. Two reports from the United States showed an improvement when the treatment is given for a longer time: 14 days greater than 10 days greater than 7 days<sup>27</sup>. In France, Lamouliatte et al.<sup>28</sup> compared regimens of Lansoprazole, amoxicillin and clarithromycin given for 7 days and 10 days and found a significant difference favoring a 10 days duration. In India compared regimens of Lansoprazole, amoxicillin and tinidazole given for 7 days, 14 days and 21 days and found better eradication rate in latter group<sup>29</sup>. In this study compared regimens of omeprazole, amoxicillin and furazolidone given for 14 days and 21 days and found no significant difference of *Helicobacter pylori* eradication between the 14 days and 21 days treatment duration.

From this study, it appears that adequate eradication rates are not achieved by *Helicobacter pylori* eradication therapy in duodenal ulcer patients with drug regimens shown to result in high eradication rates in developed countries. Low rates of eradication has been found in both two weeks and three weeks therapy. Eradication rate does not improve if duration of treatment increase from two weeks to three weeks. This low eradication rate may be due to development

of resistance to newer anti *Helicobacter pylori* regimen. A study from Mumbai reported resistance to amoxicillin 73% and furazolidone 91%<sup>29</sup>. Resistance to amoxicillin in developed countries is either nil or less than 1% indicating that it is not yet a problem<sup>30</sup>. Bangladesh is a developing country where it is difficult to eradicate *Helicobacter pylori* and therapy recommended for the developed countries may not be appropriate for the Bangladeshi population and regimens based on culture and sensitivity profile may be helpful. Another factor for low eradication rate may be due to bacterial virulence factors<sup>31</sup>. CagA negative strains have been shown to be a risk factor for treatment failure. Marais et al.<sup>31</sup> showed that *Helicobacter pylori* eradication was 87% of CagA positive strains while only 69% of CagA negative strains could be eradicated. However, the CagA and VacA status in this study was not known. It is also possible that other virulence factors may be involved in the bacterial response to *Helicobacter pylori* eradication therapy.

The present study of two weeks and three weeks triple therapy with furazolidone, amoxicillin and omeprazole did not show a markedly high *Helicobacter pylori* eradication rate at an acceptable level. Ulcer healing rate was also lower than that of other studies conducted in the different countries of the world. So further studies are needed to find out factor or factors responsible for the low eradication rate in Bangladeshi patients and to find out a more effective eradication therapy.

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