Success Rate of Furazolidone-Based Triple Therapy for Eradication of *Helicobacter Pylori* in Children

Mehri Najafi, MD*1; Ahmad Khodadad, MD1; Gholamhossein Fallahi, MD; Fatemeh Farahmand1, MD; Farzaneh Motamed, MD1; Mohammad Sobhani1, MD

1. Department of Pediatrics, Tehran University of Medical Sciences, Tehran, IR Iran

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**Abstract**

**Objective:** *Helicobacter pylori* (*H. pylori*) is now recognized as a major etiological factor in the pathogenesis of gastritis and peptic ulcer disease. There is concrete evidence that eradication of the bacterium reverses histological gastritis, and results in significant reduction of duodenal and gastric ulcer recurrence. Poor compliance and antibiotic resistance are the main causes for failure of anti *H. pylori* therapy. In this study we determined efficacy of omeprazole based triple therapy with b.i.d. dosing of furazolidone, amoxicillin for 2 weeks and omeprazole in Iranian children.

**Methods:** This prospective study included 37 children, in whom *H. Pylori* infection was diagnosed endoscopically. *H. Pylori* positive children were treated with a two weeks course of furazolidone (6 mg/kg/day) and amoxicillin (50 mg/kg/day) plus omeprazole (1-2 mg/kg/day). Eradication was assessed by 13C UBT.

**Findings:** Mean age of patients was 10.2 yr (5-15 yr), 25 (67.5%) patients were boys. *H. pylori* was eradicated in 34 children (per patient 91.9%, per protocol 86%). Side effects occurred in 3 (8.1%) patients, but these were mild and it was not necessary to discontinue treatment. Three children (8.1%) remained *H. pylori* positive.

**Conclusion:** Our study showed that the association of furazolidone plus amoxicillin with a proton-pump inhibitor could be a valuable alternative for eradication of *H. Pylori* infection in children. It is an effective, affordable treatment that allows good compliance and produces low adverse effect rates.

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**Key Words:** Helicobacter pylori; Furazolidone; Omeprazole triple therapy; Children
**Introduction**

*Helicobacter pylorus* is now recognized as a major etiological factor in the pathogenesis of gastritis and peptic ulcer disease [1]. There is concrete evidence that eradication of the bacterium reverses histological gastritis, and results in significant reduction of duodenal and gastric ulcer recurrence [1].

A recent meta-analysis concluded that recurrent infection is rare when eradication rates exceed 90% [2]. Eradication regimens for *H. pylori* must be effective, safe, with minimal induction of resistance. In Asia, *H. pylori* eradication is difficult and generally two weeks of treatment is necessary [3,4]. Metronidazole resistance is a common problem and clarithromycin is expensive [5,6] but *H. pylori* is sensitive to Furazolidone and reports of resistance have been scarce so far [6-8]. Furazolidone was effective against *H. pylori* in Iranian patients and was a good substitute for clarithromycin or metronidazole [9,10,11]. In addition to its efficacy, Furazolidone is a relatively inexpensive and easily affordable medication. In many reports furazolidone consumption for two weeks in adults was associated with adverse reactions such as anorexia, dizziness, urticarial rash, flu-like symptoms, and fever in 5–15% of cases, therefore, limiting its prescription [5,9].

The early childhood years are important with regard to exposure to *H. pylori* infection, with higher rates of acquisition than during the adult years [12,13]. When selecting a therapy to eradicate *H. pylori*, duration of treatment and adverse effects should be considered [1].

Until recently, the recommended duration of therapy for *H. pylori* eradication was one to two weeks. In this study we determined efficacy of triple therapy and two antibiotics (furazolidone, and amoxicillin) for 2 weeks.

**Subjects and Methods**

Children with chronic abdominal pain, hematemesis, and melena between 2.5 and 16 years of age were prospectively recruited during 2006 and 2007.

Children with *H. Pylori* infection confirmed by endoscopy and pathology entered the study. Patients who had undergone previous *H. Pylori* eradication therapy prior to the study or had a previous history of severe renal and hepatic disease were excluded from the study.

Upper gastrointestinal endoscopy was carried out after midazolam sedation (0.1 mg per kg). Gastric antral biopsy specimens were taken for histology examination, Giemsa staining and urease testing.

The presence of *H. Pylori* in histology was accepted as diagnostic for infection. *H. Pylori* positive children were treated with a two week course of amoxicillin (50 mg/kg/day b.i.d. as syrup or capsule) and furazolidone (6 mg/kg/day b.i.d. as syrup or tablet) plus four weeks omeprazole (1-2 mg/kg/day), and reinvestigated eight to ten weeks after accomplished treatment by urea breath test (13C UBT). This test was performed after a fasting period of 6 hours or longer. The patients swallowed capsules containing urea labeled 13C (non radioactive) and 13C in the expired air was measured 20 minutes later, using an infrared spectrophotometer (IRIS, Dr. Wagner, Bremen, Germany).

The difference between the values obtained at 20 minutes and at baseline was expressed as delta over baseline (DOB %). The cut-off value for negative UBT was less than 2.5 and for positive UBT more than 4.0 δ unit (delta over base).

Children, in whom *H. Pylori* persisted, were treated successfully with quadruple regimen (omeprazole, amoxicillin, bismuth subcitrate and clarithromycin).

The Ethics Committee of Tehran University of Medical Sciences approved the protocol. Statistical analysis: Chi-square test or Fisher’s exact test was used for qualitative variables and the Student t-test for quantitative variables. SPSS software for Windows version 15 was then used for processing of data. A P-value of less than 0.05 was considered significant.

**Findings**

Thirty seven children fulfilled inclusion criteria. Their mean age was 10.2 years, range 5 to 17 (10.9± 2.5) years and 25 (67.5%) of
them were boys. Characteristics of patients and endoscopic findings are shown in tables 1 and 2.

**Table 1: Characteristics of study patients**

| Characteristics   | No (|%|) |
|-------------------|-----|----|
| Median age (range) | 10.2 (5-17) |
| Sex (male)        | 25 (67.5%) |
| Abdominal pain (%) | 28 (75.7%) |
| Hematemesis/melena (%) | 8 (21.6%) |
| Vomiting (%)      | 8 (21.6%) |

**Table 2: Endoscopic findings in 37 patients with H. Pylori**

<table>
<thead>
<tr>
<th>Endoscopic findings</th>
<th>No (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>7 (18.9)</td>
</tr>
<tr>
<td>Antral nodularity</td>
<td>22 (73.3)</td>
</tr>
<tr>
<td>Gastric erythema</td>
<td>16 (53.3)</td>
</tr>
<tr>
<td>Duodenal ulcer</td>
<td>7 (23.3)</td>
</tr>
<tr>
<td>Gastric ulcer</td>
<td>0</td>
</tr>
</tbody>
</table>

All 37 children completed treatment protocol combined of amoxicillin and furazolidone and omeprazole. Side effects occurred in three (8.1%) children: (abdominal pain in two, vomiting, and headache each affected one child), but these were mild and it was not necessary to discontinue treatment.

Overall, the eradication was cleared in 34 of 37 children, giving an eradication rate of 91.9% (95% CI, 83%-98%) in ITT analysis. Three children (8.1%) remained *H. pylori* positive. All of these persistently *H. pylori* positive children had cleared from infection by a quadruple therapy (omeprazole, bismuth subcitrate, amoxicillin, clarithromycin).

**Discussion**

Treatment of *H. Pylori* infection is definitely indicated in children with proven *H. Pylori* gastritis, but also no ulcer need be treated is still debated. Treatment induces the eventual healing of inflammation and ulceration and significant reduction in the likelihood of developing gastric carcinoma [14]. However, after *H. Pylori* gastritis is diagnosed, the current approach is to treat the patient [15].

Triple treatment including a proton pump inhibitor (PPI) and clarithromycin, combined with either amoxicillin or metronidazole has been recommended to treat children with *H. pylori* infection [16].

In children all regimens should continue for 7-14 days [14]. However antibiotic resistance is increasing, so new therapeutic regimens are needed [17,18].

In this study we show that administering furazolidone for 2 weeks b.i.d. plus omeprazole and amoxicillin in a triple anti *H. pylori* treatment regimen has a high eradication rate (per patient 91.9%, per protocol 86%). One of the great impediments regarding the use of furazolidone is its association with some side effects, reported mainly from adults and studies carried out in Europe [9,19]. In our study however, no patient had to interrupt the treatment due to side effects.

The results of *H. Pylori* treatment in children are different from that in adults. So some authors concluded that treatment recommended for adults may be not suitable for children [20]. Bahreman et al, compared a triple therapy (omeprazole, amoxicillin, and clarithromycin) to a quadruple therapy (omeprazole, amoxicilline, metronidazole and bismuth subcitrate for 10 days), in Iranian children with *H. pylori* infection. The eradication rates were higher in triple versus bismuth quadruple therapy (92% vs. 84%) [21].

In the study of Arenz et al [22] one week esomeprazole–based triple therapy (amoxicillin, clarithromycin) was very effective in eradication of *H. Pylori* in children (92-93%).

The rate of resistance was 9% for clarithromycin and 16% for metronidazole. Triple therapy is more effective than dual therapy [23].

In Iranian children the rate of resistance to metronidazole was very high (72-79%), and
susceptibility to amoxicillin was 58% and 75% for clarithromycin [24]. In another study from Iran [25] the rate of resistance to metronidazole was (54.2%), and there was no resistance to furazolidone. Kawakami et al treated 38 children with omeprazole, clarithromycin and furazolidone for 7 days [26]. The rate of success was 84.8% per patient and 73.7% per protocol.

So treatment of *H. Pylori* in children needs more designed randomized placebo-controlled trials, especially in developing countries[27]. The high rate of resistance to antibiotics in these countries and also low compliance for drug intake are the main reasons for treatment failure[28].

Our limitations: Peptic disease in children is much less than in adults, and also some of the parents are not consent to endoscopy. So gathering sufficient sample is difficult.

**Conclusion**

Triple omeprazole based therapy (OAF) could be a valuable alternative to first line eradication therapy of *H. pylori* in children. It is an effective, affordable treatment that allows good compliance and produce low adverse effect rates, but further multicenter trials are needed to establish its role in the *H. Pylori* infection.

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**References**


