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Oral and Intravenous Eradication of *Helicobacter pylori*

[1]M. Amini and [2]A. Tajik
[1]Department of Gastroenterology, Baqiyatallah University of Medical Sciences, Tehran, Iran
[2]Department of Community Medicine, Medical College, Tehran University of Medical Sciences, Tehran, Iran

Abstract: The aim of this study was to determine the efficacy of oral regimens in patients without active gastric bleeding and those of intravenous regimens in a group with active gastric bleeding. This study was performed as an interventional investigation in Tehran between April 2004 and March 2008. The patients who had active peptic ulcer were included and divided into two groups. One group included 26 subjects with active gastric bleeding and the other included 29 patients without active gastric bleeding. The intravenous treatment included metronidazole, ampicillin, ranitidine and orally administered bismuth for five days. The oral regimen included metronidazole, amoxicillin, ranitidine and bismuth sub-citrate for 14 days. In intravenous group 24 patients (92.3%) and in oral group 24 subjects (82.8%) had no drug adverse events. The successful treatment was seen in 61.5% (16/26) and 55.2% (16/29) in intravenous and oral methods, respectively. Finally, it may be concluded that both five-day intravenous therapeutic regimen in patients with active gastric bleeding and 14-day oral regimen in patients without active gastric bleeding would have good efficacy and low rate of drug adverse events.

Key words: *Helicobacter pylori*, intravenous, oral, treatment

INTRODUCTION

Helicobacter pylori (HP) is one of the most common gastric pathogenic microorganisms in developing countries (Jafarzadeh *et al*., 2007; Novis *et al*., 1998). Peptic ulcers and gastrointestinal malignancies are the most common and most serious consequents of HP infections, respectively (Bafandeh *et al*., 2005; Rhead *et al*., 2007). These infection-related morbidities are bothersome entities. Diagnosis and treatment especially in countries with high frequency of HP infection are important issues for eradication of HP. It is due to easy fecal-oral transmission of disease in such countries (Siavoshi *et al*., 2005).

Generally, there are three steps in the treatment of HP infection including diagnosis, treatment and follow up for successful eradication of HP infection (Amini *et al*., 2005). Nowadays, there are many therapeutic regimens including quadruple and triple therapies. But, recent investigations are focused on the reduction of the number of drugs in used regimens and also decreasing the duration of treatment (Ley *et al*., 2005). These matters would result in better patients' compliance and also lower costs for both governments and the patients (Romero Gómez *et al*., 2000). It may be more attentive when we consider the cultural characteristics of Iranian patients who live least duration of drug consumption.

In the other hand, the used regimens are generally prescribed orally. But it may not be possible for some clinicians to treat a number of critically ill patients with oral regimens. Also, the injection treatments due to faster effect of used drugs would have a more rapid onset of action, but with lower rate of therapeutic complications and higher patients' compliance due to shorter period of treatment (Barkun *et al*., 2004).

Some regimens are now available for injection purposes. Vast majority of earlier reports have compared the efficacy of injection regimens with oral ones but in patients with similar admission conditions (Adamek *et al*., 1994). Comparison of therapeutic efficacy of injection regimens in critically ill patients with effectiveness of oral regimens in outpatients was not performed earlier. Nevertheless, physicians need to know that whether efficacy of injection regimens is similar to those seen by oral ones in emergency cases. If approved, this matter would help them to treat their critically ill patients with a rational and equally effective method, lower costs and more patients' compliance. This investigation was conducted to determine the efficacy of oral regimens in patients without active gastric bleeding and those of intravenous regimens in a group with active gastric bleeding.

Corresponding Author: Mohsen Amini, Department of Endoscopy, Baqiyatallah Hospital, Mollasadra Street, Tehran, Iran
Tel: +98 (21) 88464434 Fax: +98 (21) 88464434

MATERIALS AND METHODS

This study was performed as an interventional investigation in Tehran between April 2004 and March 2008. The patients who had active peptic ulcer were included and divided into two groups. One group included 31 subjects with active gastric bleeding and the other included 34 patients without active gastric bleeding. At the end of the study, there were only 26 patients in the first and 29 subjects in the latter. Before the treatment, all the 55 individuals had positive Rapid Urease Test (RUT) and the histological findings for HP and a gastric ulcer and different upper gastrointestinal manifestations.

After the informed consent form was signed, the patients were included. This study was approved by ethical committee of Baqiyatallah University of Medical sciences. Helsinki Declaration was respected all over the study. The exclusion criteria were use of NSAIDs and anti-coagulants, need to surgery during the study, severe adverse drug events, severe congestive heart failure and history of seizure or active neurological disorder.

A pilot study was initially performed on three-day intravenous treatment which showed low eradication rate. So, we decided to use a five-day intravenous regimen. The intravenous treatment included metronidazole (500 mg every 6 h), ampicillin (100 mg/kg/dose in four divided doses), ranitidine (50 mg every 4 h) and orally administered bismuth (120 mg every 6 h) for five days. The oral regimen included metronidazole (250 mg every 6 h), amoxicillin (500 mg every 6 h), ranitidine (150 mg every 6 h) and bismuth sub-citrate (120 mg every 6 h). This regimen was prescribed for 14 days.

After the treatment was completed, the histological examination for HP was performed again. Those cases that were negative in histological evaluation, their RUT test after 8-12 weeks from the treatment was negative and their clinical findings were alleviated, were considered as successful treatments. After the data were collected, the SPSS (version 14.0) software (Statistical Procedures for Social Sciences; Chicago, Illinois, USA) was used for statistical analysis. Differences in each group (intra-group differences) were tested by Mann-Whitney-U test and were considered statistically significant at p-values less than 0.05.

RESULTS

Mean±SD ages were 48.36±22.1 years and 46.23±21.7 years in intravenous and oral regimens, respectively. In intravenous group 76.9% and in oral group 62.1% were male. Mean before-treatment histologic scores were 2.9 and 3.1 in intravenous and oral treatment groups, respectively. Mean after-treatment histologic score was 1.9 in both intravenous and oral treatment groups. The mean before and after-treatment histologic scores were significantly different within the groups (Table 1).

Table 1: Before and after-treatment histologic scores of the patients in two groups

	Intravenous group		Oral group	
Score	Before -treatment	After -treatment	Before -treatment	After -treatment
1 (%)	1 (3.8)	13 (50)	1 (3.4)	16 (55.24)
2 (%)	9 (34.6)	6 (23.1)	7 (24.1)	5 (17.2)
3 (%)	9 (34.6)	4 (15.4)	11 (37.9)	4 (13.8)
4 (%)	5 (19.2)	2 (7.7)	7 (24.1)	3 (10.3)
5 (%)	2 (7.7)	1 (3.8)	3 (10.3)	1 (3.4)
Mean*	2.9	1.9	3.1	1.9

*The mean histologic scores were significantly decreased in both groups ($p<0.05$). Values in brakets are percentage

Table 2: Frequency of symptom relief in the patients of two groups

Symptoms	Intravenous group	Oral group
Regurgitation (%)	14 (53.8)	15 (51.7)
Burning (%)	12 (46.2)	12 (41.4)
Epigastric pain (%)	16 (61.5)	17 (58.6)

Values in brakets are percentage

Seventeen subjects (65.4%) had reduction in histologic score in intravenous treatment and 24 patients (83%) in oral treatment group. After-treatment RUT was negative in 23 patients (88.4%) in intravenous treatment group and 23 patients (79.33%) in oral treatment group. The frequencies of symptom relief after treatments are shown in Table 2. The successful treatment was seen in 61.5% (16/26) and 55.2% (16/29) in intravenous and oral methods, respectively.

In intravenous group 24 patients (92.3%) and in oral group 24 subjects (82.8%) had no drug adverse events. There were no severe drug-related side effects leading to cessation of treatment in any cases.

DISCUSSION

This study showed that intravenous regimen in patients with active gastric bleeding and also oral regimens in those without active bleeding are effective for eradication of *H. pylori* both histologically and clinically. Also the drug-related side effects had a low frequency rate in both regimens.

The various drugs used in the injection regimens would result in a differed therapeutic efficacy for eradication of HP infection, as well as oral ones (Adamek *et al*., 1994). So, lack of the efficacy in an investigation for injection regimens may not be an ending of performing more trials with other drugs used as injections. Especially if it be considered that those

regimens with lower costs are selected in this study. A lower cost and no much longer period of treatment (five-day instead of three-day injection regimens) may lead to better therapeutic efficacy and patients' compliance.

In this study the success rate and complication rate in both intravenous and oral therapies were acceptable. The good efficacy and low rate of therapeutic side effects is interesting when it is considered that the patients who received injection treatment had bad general condition. They had active gastric bleeding and were admitted as emergent cases.

The obtained results in this study about the injection group were similar to those previously reported by some authors (Adamek *et al*., 1994; Metz *et al*., 2006). However, the success rates of oral treatment were higher in those studies. Romero-Gómez *et al*. (2003) reported that a three-day intravenous triple therapy is not effective for the eradication of HP infection in patients with bleeding gastro-duodenal ulcer. They reported that intravenous treatment is effective in only 50% of the patients in comparison with success rate 86% in oral treatment group. But Riuz Gómez *et al*. (2002) reported that intravenous 3-day HP eradication therapy is highly effective in patients with bleeding peptic ulcer. They reported a success rate of 87.5%; which is a good outcome and higher than our obtained success rate (61.5%). Sheu *et al*. (1999) reported eradication rates of 43.8 up to 58.1% according to three different three-day intravenous regimens. All these rates were lower than obtained success rate in this study. However, they concluded that 3-day intravenous regimens may achieve clearance of *H. pylori* quickly. Obviously, there are some differences in the detailed drugs that were prescribed in previous articles. Some were triple and some were quadruple. It may be the main cause of a better or worse response and/or lower or higher drug adverse events rate in different studies. Nevertheless, prescribing the anti-HP therapies would have an important role for lowering the recurrence rate of gastrointestinal bleeding and also complication of peptic ulcers when the HP-infection is established (Riuz Gómez *et al*., 2002).

Finally, it may be concluded that both five-day intravenous therapeutic regimen in patients with active gastric bleeding and 14-day oral regimen in patients without active gastric bleeding would have good efficacy and low rate of drug adverse events. The findings in this investigation are in support of vast majority of earlier studies. However, further studies should be carried out for approving the results obtained in this study.

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