OMEPRAZOLE, FURAZOLIDONE, AND TETRACYCLINE: AN ERADICATION TREATMENT FOR RESISTANT *H. PYLORI* IN BRAZILIAN PATIENTS WITH PEPTIC ULCER DISEASE

Fernando Marcuz Silva, Jaime Natan Eisig, Ethel Zimberg Chehter, Júlio Jovino da Silva and Antonio Atílio Laudanna

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OBJECTIVES: To determine the efficacy of a simple, short-term and low-cost eradication treatment for *Helicobacter pylori* (*H. pylori*) using omeprazole, tetracycline, and furazolidone in a Brazilian peptic ulcer population, divided into 2 subgroups: untreated and previously treated for the infection.

PATIENTS AND METHODS: Patients with peptic ulcer disease diagnosed by endoscopic examination and infected by *H. pylori* diagnosed by the rapid urease test (RUT) and histological examination, untreated and previously unsuccessfully treated by macrolides and nitroimidazole, were medicated with omeprazole 20 mg daily dose and tetracycline 500 mg and furazolidone 200 mg given 3 times a day for 7 days. Another endoscopy or a breath test was performed 12 weeks after the end of treatment. Patients were considered cured of the infection if a RUT and histologic examination proved negative or a breath test was negative for the bacterium.

RESULTS: Sixty-four patients were included in the study. The women were the predominant sex (58%); the mean age was 46 years. Thirty-three percent of the patients were tobacco users, and duodenal ulcer was identified in 80% of patients. For the 59 patients that underwent follow-up examinations, eradication was verified in 44 (75%). The eradication rate for the intention-to-treat group was 69%. The incidence of severe adverse effects was 15%.

CONCLUSION: The treatment provides good efficacy for *H. pylori* eradication in patients who were previously treated without success, but it causes severe adverse effects that prevented adequate use of the medications in 15% of the patients.

DESCRIPTORS: **Peptic Ulcer. Treatment. *Helicobacter pylori.* Eradication. Tetracycline. Furazolidone. Omeprazole.**

INTRODUCTION

The eradication of *H. pylori* in patients with peptic ulcer disease linked to such bacterium cures the disease[1,2]. At present, the treatments for *H. pylori* eradication consist of the association of 2 antibiotics with an acid supressor[3-5]. Clarithromycin and amoxicillin with a proton pump inhibitor or clarithromycin with or without amoxicillin and bismuth-ranitidine provide high eradication rates in Brazil[6,7]. For the patients in whom the bacterium cannot be eradicated, considering the high prevalence of primary resistance to nitroimidazoles in our country[8] and the expected secondary resistance to macrolides [9], the furazolidone option[10,11] is attractive, due to its low cost and high efficacy, and it has been proposed as the first or second choice of treatment[12-22].

The aim of this study was to test the efficacy of a treatment schedule that uses furazolidone with tetracycline and omeprazole for 7 days in untreated peptic ulcer patients and in those previously treated without success using nitroimidazoles and macrolides.

From the Department of Medicine and the Department of Clinical Gastroenterology, Hospital das Clínicas, Faculty of Medicine, University of São Paulo.

PATIENTS AND METHODS

Patients with a diagnosis of scarred

or active gastric or duodenal peptic ulcer disease, confirmed by upper digestive endoscopy, performed at the Gastroenterology Unit of São Paulo University Medical School Hospital, and infected by *H. pylori* were invited to participate in the study. Patients untreated for *H. pylori* infection or previously treated without success for the infection with nitroimidazoles and macrolides were included in the study. Patients with prior antibiotic therapy up to 3 months prior to the study start date, patients under 14 years old, patients with severe disease, pregnant or lactating patients, and patients with prior gastric surgery were excluded. The Hospital Committee on Ethics and Science approved the study, and all patients signed the informed consent statement.

Infection diagnosis:

Diagnosis of *H. pylori* infection was made by histologic examination in all cases, (H & E staining), and the rapid urease test (RUT)[23] was performed on mucosal biopsy specimens of the gastric antrum that were obtained through upper digestive endoscopy.

Treatment:

Treatment consisted of tetracycline 500 mg and furazolidone 200 mg administered 3 times a day after each meal, with omeprazole 20 mg once a day before breakfast, for 7 days. At end of the treatment, patients were required to avoid all anti-ulcer medications, except for the symptomatic use of antacid pills. Patients were then questioned about the occurrence and intensity of adverse effects, and the remaining pills were counted.

Treatment assessment:

H. pylori infection was considered cured if TRU and the histologic examination by upper endoscopy performed 12 weeks after the end of treatment proved to be negative or a ^{14}C-urea breath test[24] performed 12 weeks after the end of treatment was negative.

Statistical determinations were made by SPSS, software package version 8.0 (SPSS Inc. USA).

RESULTS

The clinical data of the studied population are shown in table 1. The female sex was predominant, and the percentage of duodenal ulcer was high. The mean age was similar to the median age. Smokers made up one third of the total patient number. Five patients did not show up for follow-up examinations. The eradication rates were good: 75% for the per protocol group (Table 2). The differences regarding eradication rates between the previously treated group (77%) and the previously untreated group (74%) did not reach statistical significance (P = 0.71).

Adverse effects were reported by 34% of patients: 14% were of mild intensity and 5% moderate intensity. Severe adverse effects, mainly nausea and vomiting episodes, were reported by 15% of the patients.

Table 1 - Clinical data of patients.

Patients		64
Age (years)	Mean	46
	Median	44
	Interval	14 - 75
Women		58%
Previously treated		60%
Duodenal ulcers		80%
Scarred ulcers		66%
Tobacco users		33%
Alcohol users		10%

Table 2 - Eradication rates.

	n / %	Confidence Interval (95%)
Per protocol	44/59(**75%**)	63% - 86%
Intention to treat	44/64 (**69%**)	57% - 80%

DISCUSSION

Even though it is possible to effectively treat the symptoms of peptic ulcer disease using acid suppressors, treatment with antibiotics[25] is more cost effective. Additionally, for complicated ulcers, the latter treatment also reduces risk of bleeding ulcers, stenosis ulcers, perforating ulcers, etc.[26,27]. Therefore, even when considering the greater difficulty in treating resistant *H. pylori* infection (the retreatment schedules are more complex, have lower efficacy, higher costs, and more frequent adverse effects[28,29]), it is important to seek effective treatment schedules for such cases. A high rate of primary resistance of *H. pylori* to nitroimidazole compounds[8] and recently also amoxicillin[9] has been described in our country. The low cost and simplicity of this treatment schedule are very important attributes for the eradication of *H. pylori*, if one considers the low cultural and social status and the low income of the majority of the Brazilian people. The choice of the treatment schedule with tetracycline, furazolidone, and omeprazole involved consideration of these issues. The eradication rate obtained for previously treated patients, which did not differ from that of untreated patients, can be considered satisfactory for a retreatment schedule.

The high incidence of adverse effects, also observed by another author[14], is a noteworthy outcome of this study, especially considering the severity of the adverse effects. The treatment schedule with clarithromycin, tinidazole, and proton pump inhibi-

tor[30] resulted in 18% adverse effects, and only 1 patient discontinued the medications. This fact was a possible limitation for the achievement of better eradication rates. Adverse effects are more frequently related to furazolidone use[14], a main drug of the treatment schedule in our study. The addition of another drug to prevent adverse effects, if possible, will change this schedule into a new complex one. Nevertheless, this treatment does not promote secondary bacterial resistance to the antibiotics[31], and it is a short-term and low-cost treatment; therefore, it is an interesting option for a great number of Brazilian patients with peptic ulcers due to *H. pylori* infection, particularly those who have antibiotic-resistant infection.

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RESUMO RHCFAP/3094

SILVA FM e col. - Omeprazol, Tetraciclina e Furazolidona, um tratamento para erradicação do *H. pylori* resistente em pacientes ulcerosos do Brasil. **Rev. Hosp. Clín. Fac. Med. S. Paulo 57**(5): 205-208, 2002.

OBJETIVO: Testar a eficácia de um esquema simplificado e de baixo custo para erradicação do *H. pylori* utilizando omeprazol, tetraciclina e furazolidona, em uma população de ulcerosos do Brasil, já tratados e não tratados previamente para a infecção.

PACIENTES E MÉTODOS: Pacientes portadores de úlcera péptica, documentada por exame endoscópico e infectados pelo *H. pylori* confirmado pelo teste da urease e exame histológico, não tratados previamente ou já tratados sem sucesso com macrolídeos e nitroimidazólicos, foram tratados com Omeprazol 20mg em dose única diária, associado à Tetraciclina 500mg e Furazolidona 200mg dadas três vezes ao dia, por três dias. Uma nova endoscopia ou um Teste Respiratório foi realizado 12 semanas após o término do tratamento e foram considerados erradicados da infecção os pacientes que apresentaram o teste da urease e exame histológico negativos ou o Teste Respiratório negativo para a bactéria.

RESULTADOS: Sessenta e quatro pacientes foram incluídos no estudo, 26 deles não previamente tratados. As mulheres predominaram (58%), a idade média foi de 46 anos, 33% dos pacientes eram tabagistas e a úlcera duodenal foi identificada em 80% dos pacientes. Nos 59 doentes que realizaram o exame de controle, a erradicação foi constatada em 44 (75%). Por intenção de tratamento o índice foi de 68%. O grupo não tratado previamente não diferiu do grupo previamente tratado. A incidência de efeitos adversos intensos foi de 15%.

CONCLUSÃO: O esquema proporciona boa eficácia na erradicação do *H. pylori* em pacientes já previamente tratados sem sucesso, porém apresenta efeitos adversos intensos, que impediu o uso adequado dos medicamentos em 15% dos pacientes.

DESCRITORES: **Úlcera Péptica. Tratamento. *Helicobacter pylori.* Erradicação. Tetraciclina. Furazolidona. Omeprazol.**

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