

article

Amoxycillin Triple Therapy versus Clarithromycin Triple Therapy, for H. Pylori related Duodenal ulcer Prospective , Randomized , Controlled study

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ABSTRACT

Objective: The aim of this prospective open study was to compare the effectiveness of two regimens; Amoxycillin, Metronidazole, and Omeprazole (AMO), and Clarithromycin, Metronidazole, and Omeprazole (CMO) on healing and eradication of helicobacter pylori related duodenal ulcer.

Methods: Sixty patients with proven duodenal ulcer were randomized to one of two regimens. Thirty patients "group A" were given amoxycillin 1 gm before meal bd and metronidazole 400 mg after meal bd for one week plus omeprazole 20 mg before meal bd for one month. The other thirty "group B" were given clarithromycin 500 mg before meal bd, metronidazole 400mg after meal bd for one week plus omeprazole 20 mg bd before meal bd

For one month. Endoscopy was performed six weeks after the initiation of therapy, and the presence or absence of H. pylori was determined with biopsy specimens.

Results: All patients completed the study. In clarithromycin treated patients both the healing and eradication rate was higher than in amoxycillin treated group (97 and 89 versus 87 and 70%).

Side effects were few in both treatment groups.

Conclusion: One week clarithromycin and metronidazole plus omeprazole for four weeks seems to be very effective treatment for healing and eradication of helicobacter pylori related duodenal ulcer in Iraq and superior to amoxycillin triple therapy.

INTRODUCTION

Helicobacter pylori infection is the most important cause of chronic active gastritis, active and inactive gastric and duodenal ulcers. Eradication of Helicobacter pylori has been established as an effective treatment for active duodenal ulcer (1,2) and result in marked reduction in ulcer recurrence (3-5). Accordingly, treatment of helicobacter pylori-positive duodenal ulcer is now considered standard.

Although triple therapy using bismuth salt with two antibiotics has been accepted as the gold standard for curing H. pylori infection (6) and more recently proton pump inhibitor in combination with two antibiotics has been reported as effective as the bismuth triple therapy (7-9), it is equally important to validate the success rate of a treatment regimen in every country, and perhaps even in the

Specific region of each country where its use is planned. Accordingly It has been decided to compare the effectiveness of two commonly used triple therapy one including amoxycillin, metronidazole and omeprazole and another one containing clarithromycin, metronidazole and omeprazole in an open prospective controlled clinical study.

MATERIALS & METHODS

This opened clinical prospective trial was conducted at Mosul Endoscopy Unit and Ninevah Private Hospital between Jan. 1998 and Dec. 1999. All patients with endoscopically proven duodenal ulcer with positive helicobacter pylori infection on three antral biopsy specimens were enrolled in this study. Patients with acute bleed, previous gastric surgery, chronic liver, renal and respiratory diseases as well as pregnant women were excluded ,

as well as those with deformed scarred duodenal bulb. The patients were allocated into two treatment groups:

Group A: given AMO:

Amoxicillin 1 gm orally bid before meal for one week. Metronidazol 400 mg bid after meal one week. Omeprazole 20 mg bid before meal for one month.

Group B. given CMO:

Clarithromycin 500 mg bid before meal for one week. Metronidazol 400 mg bid after meal for one week. Omeprazole 20 mg bid before meal for one month.

All patients were requested to come back after one week to check for pain relief, side effects of drugs, and to advise for further treatment. They were asked specifically about the following side effects: nausea, vomiting, metallic taste in the mouth, dry mouth, malaise, lassitude, dysuria, headache, dizziness, abdominal pain or colic, diarrhoea and skin rash. All patients were asked to return again five weeks later for recheck endoscopy and six biopsies taken from antral mucosa for the presence of *H. pylori* and inspection of duodenal bulb for ulcer healing. Eradication is defined as absence of organism on these six biopsies on gram stain.

Randomization, clinical examination and endoscopy and treatment all were done by one doctor. The two groups were matched for age, sex, and duration of ulcer disease as well as the endoscopic findings. The endoscopic findings were registered including ulcer size & number, plus the antral mucosal changes. Ulcer was regarded as healed if completely epithelialized or scarred.

Although it is invasive; histological confirmation of the presence or absence of *H. pylori* was chosen in this study not only because it is the only way available but easy to do and associated with high sensitivity & specificity (10)

RESULTS

A total of 60 patients was enrolled into the study. Thirty patients in Amoxicillin group and thirty patients in Clarithromycin group. All the patients in both groups completed the study. Table(I) shows the patients details, and both groups were comparable in all variables i.e., both groups were very well matched. After one week all patients

in both groups lost their pain, acidity and felt very well. Table (II) shows the reported side effects which were though mild but high in both groups. However in general the drugs were well tolerated and non of patients discontinued the treatment. Of importance to note that nausea was high in both group (40%) and metallic taste was very high in Clarithromycin group (60%).

After six weeks all patients in both groups were free from pain and acidity. Ulcer healing was higher in Clarithromycin treated patients than amoxicillin ones (97%) versus (87%) and *Helicobacter pylori* eradication rate as well was higher (89%) versus (70%). All patients were symptom free whether they have healed or unhealed ulcer while on therapy but pain and acidity recurred soon after stopping omeprazole in those with unhealed ulcer and in whom eradication have failed.

DISCUSSION

Treatment regimens for *H. pylori* infection have been evolving since the early 1990s, when monotherapy was first recommended. Ever since, the number of regimens suggested for its eradication has been increasing. Dual therapy which is a combination of antibiotic and proton pump inhibitor using omeprazole and amoxicillin for two weeks has resulted in inconsistent results. Initial studies suggested that infection was cured in over (80%) of patients (11) and Bayerdorffer et al using a very high dose of omeprazole reported over (95%) cure (12), but such good results have not been confirmed (13, 14) and this regimen can no longer be recommended (15).

In this controlled study using two regimens and including adequate number of patients in each group, it was very clear that triple therapy including clarithromycin, metronidazol and omeprazole gave a very good eradication rate of (89%) and very high healing rate of (97%). This goes favorably with result obtained in MACH I study which is a large European Trial compares five different regimens as containing two antibiotics + omeprazole given for 7 days (89.8%) (9). However, amoxicillin triple therapy gave a low eradication rate probably because of resistance of *H. pylori* due to widespread use of amoxicillin in general practice a results commonly seen in the United State and some middle east trials of (58%) (16, 17).

In this study omeprazole was given for four weeks in an attempt to increase the eradication rate as this drug is known to have synergistic effect with antibiotics. Although the result in this study is not superior to other trials using omeprazole for one week yet in a very recent study (MACH II) published in 1999 it was shown that the addition of PPI to two antibiotics increased the efficacy of *H. pylori* eradication whether amoxicillin / clarithromycin combination or a metronidazole / clarithromycin combination were used, and more interesting in the same study the finding that the addition of PPI to antibiotics improved the eradication rate even in the presence of resistant strains compared to a combination without PPI (18).

Accordingly; it was recommended at the Asia-Pacific consensus on *H. Pylori*, that the first - line therapy for *H. pylori* infection should be a proton pump inhibitor (PPI) or ranitidine-bismuth citrate (RBC) in combination with any two of the following three antimicrobials: amoxycillin, clarithromycin, and metronidazole (19). Side effects were relatively high in both treatment regimens probably because both regimens contain metronidazole, but they were mild and did not lead to discontinuation of treatment in any patients.

In conclusion triple therapy using clarithromycin, metronidazole for one week and omeprazole for four weeks is very effective therapy for healing and eradication of *Helicobacter pylori* related duodenal ulcer. However multi center trial using non-metronidazole containing regimens in order to decrease the incidence of side effects is needed in this country.

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Table I. Patients characteristics

	Treated group	
	A "Amo"	B "CmO"
Male / female	20 / 10	20 / 9
Age " mean " yrs.	38	40
Duration of disease (yr)	7	6.5
Gastritis " % "	100	110
Ulcer size "mm"	10	9
Multiplicity "no"	10	9
Bulb deformity "no"	0	9

Table II. Side effects of treatment

	Group A AMO	Group B AMO
Nausea	20 %	30 %
Vomiting	0 %	1 %
Dry lips & mouth	40 %	45 %
Metalic test	30 %	60 %
Headache	10 %	15 %
Diarrhoea	10 %	10 %
Pruritus	10 %	10 %
Skin rash	6 %	7 %
Interruption of therapy	0 %	0 %
Therapy completed	100 %	100 %
Multiplicity "no"	110 %	110 %

Table III. Patients characters

	Group A AMO	Group B AMO
Ulcer Healing	26 / 30 (87 %)	29 / 30 (97 %)
Eradication of H. Pylori	21 / 30 (70 %)	27 / 30 (89 %)

* P. Value < 0.001