4A: Clinical pharmacological aspects of H. pylori treatment

4A.01 AZITHROMYCIN AND INCREASING DOSES OF OMEPRAZOLE FOR THE ERADICATION OF HELICOBACTER PYLORI

M. Castelli 1, M. Ruina 1, L. Gallerani 1, P. Fabbri 1, P. Gaudenzi 1, V. Alviti 1, 2, School of Gastroenterology, University of Ferrara, Italy

Background: Helicobacter pylori is implicated in different gastroduodenal pathologies, such as peptic disease and gastric cancer, and it is associated with ulcer relapse. This background makes the eradication of bacterial colonisation desirable in any clinical and endoscopical condition, also when associated with problems of mild entity. An effort should be made to make apt the eradication therapy to single problems.

Objectives: To evaluate the efficacy and tolerability of short-term dual therapy with azithromycin and increasing doses of omeprazole.

Methods: Two selected group of 50 H. pylori-positive patients matched for age, sex and rate were compared for the prevalence of bacterial eradication rate after dual therapy with a standard dose of azithromycin (500 mg/day for 3 days) and increasing dose of omeprazole (20 mg b.i.d. or 40 mg b.i.d. for one week). H. pylori presence before and after treatment was determined by urease test and histology.

Results: Five-seven weeks after treatment, H. pylori had been eradicated in 29 of 50 patients (58%) who taken azithromycin and 40 mg/day of omeprazole, and in 44 of 50 patients (88%) who taken azithromycin in the same way and 80 mg/day of omeprazole (P = 0.001).

Conclusions: Short-term dual therapy with high dose of omeprazole combined with standard dose of azithromycin appears to have an high success eradication rate of H. pylori colonisation, very good compliance and it appears to be without side-effects. Azithromycin seems to represent interesting antibiotic agent for future dual and triple therapy trials.

4A.02 THE ROLE OF H2-RECEPTOR ANTAGONIST IN THE ERADICATION OF H. PYLORI


Introduction: The addition of an antisecretory drug to anti-H. pylori (HP) regimens have been reported to increase eradication rates due to enhanced effectiveness of some antimicrobials. In contrast to proton pump inhibitors (PPI), however, H2-receptor antagonists (H2RA) have rarely been studied in combination with antimicrobials to eradicate HP.

Aim: (1) To verify the efficacy of ranitidine in combination with amoxicillin and metronidazole for eradication of HP. (2) To elucidate the simplest and cost-effective amoxicillin dosage and duration of treatment.

Methods: 131 patients (95 males; 36 females, mean age ± SE 45.2 ± 1.0 yrs) with active DU and HP infection were enrolled in this prospective, randomized study. HP infection was confirmed by positive rapid urease test and presence of bacteria in modified Giemsa staining from antral biopsy. All the patients were randomly allocated to 4 groups of regimens (see below). Eradication was defined as negative results of rapid urease test, modified Giemsa staining and 13C-UBT at least 4 weeks after the completion of therapy.

Results:

<table>
<thead>
<tr>
<th>Treatment/group</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ranitidine bid</td>
<td>300 mg</td>
<td>150 mg</td>
<td>150 mg</td>
<td>150 mg</td>
</tr>
<tr>
<td>Amoxicillin qid</td>
<td>500 mg</td>
<td>250 mg</td>
<td>500 mg</td>
<td>500 mg</td>
</tr>
<tr>
<td>Metronidazole qid</td>
<td>250 mg</td>
<td>250 mg</td>
<td>250 mg</td>
<td>250 mg</td>
</tr>
<tr>
<td>Duration</td>
<td>2 weeks</td>
<td>2 weeks</td>
<td>2 weeks</td>
<td>1 week</td>
</tr>
<tr>
<td>HP eradication (%)</td>
<td>48%*</td>
<td>90%</td>
<td>85%</td>
<td>77%</td>
</tr>
<tr>
<td>Side-effect (%)</td>
<td>19%</td>
<td>15%</td>
<td>20%</td>
<td>18%</td>
</tr>
</tbody>
</table>

*P < 0.05

Conclusions: (1) Ranitidine is as effective as PPI in achieving high HP eradication rates in triple therapy. (2) Low dose amoxicillin (1 g/day) in combination with ranitidine and metronidazole (RAM) is a very effective regimen for eradicating HP infection. (3) The efficacy of RAM decreases when treatment duration is shortened to one week. (4) Dual therapy with ranitidine plus amoxicillin is ineffective.

4A.03 COMPARISON OF OMEPRAZOLE AND CLARITHROMYCIN VERSUS OMEPRAZOLE, CLARITHROMYCIN AND METRONIDAZOLE IN THE TREATMENT OF HELICOBACTER PYLORI

R.A. Veenendaal 1, J.M. Goez 1, J.L. Meijer 1, I. Biemond 1, A.T. Bernard 1, G.J.A. Offerhaus, C.B.H.W. Lamers 1, 2, University Hospital Leiden, The Netherlands; 2, Spaarne Hospital Hertmeede, The Netherlands; 3, Academic Medical Centre Amsterdam, The Netherlands

We investigated the efficacy of a high dose two week regimen consisting of Omeprazole (OM) and Clarithromycin (CLA) versus a combination of OM, CLA, and Metronidazole (MET) in the treatment of H. pylori. The efficacy of the two regimens was examined in a multicentre, double-blind, randomized study including 50 patients with H. pylori infection. H. pylori status was assessed before and eight weeks after treatment by culture (antrum and corpus) and histology (Sydney classification). All patients received OM (20 mg) twice daily, CLA (500 mg) thrice daily, and either placebo or MET (500 mg) thrice daily for two weeks.

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hp eradication*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>OM, CLA</td>
<td>16/25 (64%)</td>
<td>42.5–82</td>
</tr>
<tr>
<td>OM, CLA, MET</td>
<td>24/25 (96%**</td>
<td>80–100</td>
</tr>
</tbody>
</table>

*P < 0.01, chi-square

Two patients (from one group) were lost to follow up. No patients discontinued because of adverse events. Minor side effects, however, were common. Treatment failure (double therapy) was in a significant number of patients accompanied by CLA resistance post-treatment.

Conclusions: Ulcer (OM, CLA, MET) is superior to high dose double therapy (OM, CLA) in the treatment of H. pylori.

4A.04 CLINICAL AND ECONOMIC EFFECTS OF IMMEDIATE HELICOBACTER PYLORI ERADICATION FOR PATIENTS WITH DOCUMENTED PEPTIC ULCER DISEASE BUT UNKNOWN HELICOBACTER PYLORI STATUS

A.M. Fendrick, J.T. McCort, B.S. Bloom 1, University of Michigan, Ann Arbor, Michigan; 1, University of Pennsylvania, Philadelphia, Pennsylvania

Background: Nearly all persons with peptic ulcer disease who have not been treated for H. pylori infection experience an ulcer recurrence. Once H. pylori is eradicated, patients may no longer experience ulcer-related symptoms. Recurrence of ulcers may be due to lack of medication compliance, among other reasons. The recurrence rate of H. pylori infection may also be related to the eradication therapy.

Methods: A decision analytic model estimated the clinical and economic effects of treatment alternatives for asymptomatic patients with previously documented peptic ulcer but unknown H. pylori status receiving maintenance therapy for 4 weeks. Two decision strategies were evaluated: 1 – immediate H. pylori eradication therapy and cessation of maintenance therapy, and 2 – continued maintenance therapy with subsequent H. pylori eradication therapy reserved for those patients at first symptom recurrence.

Results: At one year the model estimated that a strategy of immediate H. pylori eradication therapy (Strategy 1) led to 22% fewer patients with ulcers (28.7 vs. 36.8 ulcer months/100 patient years), 10% fewer patients with ulcer symptoms (21.0 vs. 23.1), and 24% lower per-patient expenditures ($587 vs. $767 per patient year) than a strategy of maintenance therapy with eradication therapy (Strategy 2). Immediate H. pylori eradication therapy resulted in 14% more patients with symptoms from all causes (37.9 vs. 33.2 symptom months/100 patient years) than Strategy 2, because maintenance therapy was effective in treating symptoms from causes other than peptic ulcer disease.

Conclusions: Ulcer-related outcomes for patients receiving maintenance therapy for documented peptic ulcer disease can be improved at reduced direct medical cost with the prompt eradication of H. pylori infection.
A THREE-DAY COURSE OF INTRAOPERATIVE OMEPRAZOLE PLUS ANTIBIOTICS FOR H. PYLORI-POSITIVE BLEEDING DUODENAL ULCER

Bor-Shyang Sheu, Hsiao-Bai Yang, I-Ben Su, Xi-Zhang Lin. National Cheng Kung University Hospital, Tainan, Taiwan

Purposes: To determine the efficacy of 3-day intraoperative omeprazole plus antibiotics for H. pylori eradication in bleeding duodenal ulcer (DU). Methods: From Jul. 1995 to Mar. 1996, 50 patients with H. pylori-positive bleeding DU were allocated into 2 groups: Gr 1 (n = 25) cases received a 3-day course of intraoperative omeprazole (80 mg loading then 40 mg q 9 am & 9 pm) plus ampicillin (1.5 gm iv loading then 750 mg q 9 am, 3 pm, & 9 pm); Gr 2 (n = 25) followed protocol as Gr 1 except the antibiotics to be metronidazole and eritromycin (both 500 mg iv q 9 am, 3 pm, & 9 pm). In each case, gastric biopsies over antrum, body, and cardia were done for histologic density of H. pylori (score 0~5), before (to assess pre-treatment bacterial rate), 1 day after therapy (to test the clearance) and 2 months later (to test the eradication). The total H. pylori density (THPD) is a sum of scores from 3 biopsies (range 0~15). The 24 hr intragastric pH meter (MIC Inc. Gastrografin Spark III, Swiss) was inserted on the 2nd day of therapy. Results: The clearance rates of group 1 & 2 were 92% (23/25) & 88% (22/25), and the eradication rates were 64% (16/25) & 80% (20/25). The percentage of intragastric pH > 5.3 during 24 hr was not different between H. pylori non-eradicated and eradicated cases (59.5 ± 15.9% vs. 63.8 ± 15.2%, p > 0.05). The H. pylori eradicated cases had lower THPD than non-eradicated ones (5.6 vs 8.1, p < 0.05). Conclusion: This 3-day intraoperative course of anti-H. pylori therapy achieves quick clearance of bacteria. The individual response to omeprazole in such dose disclosed insignificant variations in intragastric pH elevation to alter the success of eradication. To improve eradication rate, prolonged course or add-up of subsequent oral route would be rational and especially indicated for patients with higher bacterial loads.

TWO-DAY VERSUS ONE-WEEK ANTI-HECILIBACER THERAPY IN CONTROLLED BLEEDING ULCERS: A PROSPECTIVE RANDOMISED TRIAL

N.S. Kung, J.J.Y. Sung 1, P.W. Ng, W.F. Yuen, E. Chung, B.H. Lim, S.P.Y. Kwok, H.C. Ma. United Christian Hospital, Hong Kong; 1 Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong

One-week bismuth triple therapy is highly effective in curing H. pylori infection. Recently, a two-day regimen using bismuth, amoxicillin and tinidazole has achieved a 90% eradication rate. For patients hospitalised for ulcer bleeding, an effective ultra-short regimen allows medications to be completed before discharge.

Aim: To compare 2-day versus One-week triple therapy in curing H. pylori infection and bleeding peptic ulcers.

Methods: 80 patients (pts) with endoscopically proven non-actively bleeding DU or GU and confirmed H. pylori infection were randomised to receive EITHER BISMUTH SUBCITRATE 120 mg, tetracycline 500 mg and metronidazole 400 mg four times daily for 1 week (BTM-7) OR bismuth subcitrate 240 mg, tetracycline 500 mg and metronidazole 400 mg four times daily for 2 days (BTM-2). Both pts groups also received omeprazole 20 mg twice daily for the first week. Endoscopy was repeated 5 weeks after randomisation to determine ulcer healing and H. pylori status by rapid urease test, culture and histology.

Results: 92 pts had DU, 5 had GU and 3 had DU plus GU. The ulcers showed a visible vessel and/or adherent clot in 15 pts. Baseline characteristics and drop-out rates were similar in both groups. Ulcer healing at 5 weeks was 44/46 (95.7%) in BTM-2 and 49/50 (98%) in BTM-7 (intention to treat, p = 0.61). H. pylori eradication was achieved in 35/46 (76.1%) in BTM-2 and 50/50 (100%) in BTM-7 (intention to treat, p = 0.00024). No patient had bleeding in either groups.

Conclusion: Despite similar efficacy in ulcer healing, the 2-day anti-heciliber regimen is less effective than the one-week triple therapy in curing H. pylori infection.

COMPARISON OF TWO DOUBLE THERAPIES (RANITIDIN PLUS AMOXICILLINE VS OMEPRAZOLE PLUS AMOXICILLINE) IN PATIENTS WITH HELICOBACTER PYLORI POSITIVE DUODENAL ULCER

N. Popovic, M. Glisic, P. Popovic, T. Milosavljevic, K. Todoric, O. Matejc. Clinic for Gastroenterology and Hepatology, Clinical Center, Belgrade, Yugoslavia

The eradication of Helicobacter pylori (HP) may be presently achieved with many therapy schedule. Pepsite suppression is one of the factors responsible for the in vivo efficacy of combined therapy for eradication of HP. There are, however, controversies regarding the influence of the acid lowering drug on HP eradication rates. Omeprazole /OME/ has been generally the antisecretrory drug preferred in most of the clinical trial performed. The purpose of the present study was to determine if protonpumpinhibitors are more potent in HP eradication therapy as compared to H2-receptor antagonist. Ranitidin 300 mg with one antibiotic? 80 patients with the endoscopical diagnosis of duodenal ulcer (DU) and positive HP status were randomized into two treatment groups. I RAN 300 mg/b.i.d. for 15 days + Amoxycillin /AMO/ 1 gr/b.i.d. for 10 days and after RAN 300 mg/b.i.d. for 15 days. II OME 20 mg/b.i.d. for 10 days plus AMO 1 gr/b.i.d. for 10 days and after OME 20 mg/b.i.d. for 20 days. All patients were endoscopically assessed at the end of treatment. HP status was assessed by means CLO-test and antral/body histology. Results: One patient had diarrhoas side effect. Healing of DU was observed in 34/40 (85%) patients of the group I and in 37/40 (92%) patients of group II. Eradication of the HP occurred in 27 (67.5%) patients of the group I and 29 (72.5%) patients of the group II. There was no significant difference between both groups. Conclusion: The results show that under controlled condition there is no difference between RAN + AMO vs OME + AMO in eradication of HP and in ulcer healing rate.

OMEPRAZOLE VS TWO DIFFERENT DOSES OF LANSOPRAZOLE IN TRIPLE THERAPY ON H. PYLORI POSITIVE DUODENAL ULCER

F. Catalano, U. Privitera 1, G. Brandicorte, R. Catanzaro, C. Bentivegna, A. Brogna, A. Blasi. University of Catania, Catania, Italy; 1 Endoscopy Unit of Cannizzaro Hospital, Catania, Italy

Purpose of this paper was to describe the effect of Omeprazole (OME) 40 mg vs Lansoprazole (LAN) at two different doses (30 and 60 mg) in H. pylori positive duodenal ulcer (DU). We enrolled 200 H. pylori +ve DU pts and randomized in 3 groups: 70 pts (40 M-30, F mean age 47.11 yrs, range 18-74) treated with OME 40 mg for 20 days plus Amoxicillin (AMO) 2 g and Clarithromycin (CL) 1 g for 10 days (Group A); 64 pts (36 M-28 F, mean age 47.04 yrs, range 23-72) treated with LAN 30 mg for 20 days plus AMO and CLA at same dose of Group A (Group B); 66 pts (30 M-36 F, mean age 45.95 yrs, range 21-75) treated with LAN 60 mg plus AMO and CLA at same dose of Group A and B (Group C). Patients were reassessed by endoscopy, histology, CP-test at 6 weeks after the end of therapy. Data were analyzed using chi-square test and a p < 0.05 was considered significant. Eight pts in Group A, 4 pts in Group B and 8 pts in Group C dropped out. Our results show that 60/62 pts (96.8%) in Group A, 54/59 pts (90%) in Group B and 56/58 pts (95.6%) in Group C healed: no significant difference was found statistically. H. pylori was eradicated in 58/62 pts (95.6%) in Group A, 42/62 pts (70%) in Group B and 52/58 pts (89.7%) in Group C. Statistical analysis shows a p = 0.002 (OME 40 vs LAN 30); a p = 0.015 (LAN 60 vs LAN 30); and no significant difference between OME 40 and LAN 60. The histological grade of all treated pts showed improvement. In conclusion we evidence that OME 40 and LAN 60 plus AMO and CLA are effective in H. pylori eradication. All used treatment are effective in healing DU.

WHAT'S THE CLINICALLY FAVORED TRIPLE THERAPY?

A.S. Ho 1, S.C. Lee 2, C.T. Hsu 1, 1 Tri-Service General Hospital, Taipei, Taiwan, R.O.C.; 2 Institute of Nuclear Energy Research, A.E.C., Taipei, Taiwan, R.O.C.

Purpose: To find the fewer dosage, lesser side effect and shorter duration with high eradication regimen among the recent triple therapies.

Methods: Endoscopically proved 90 duodenal ulcer patients were randomly assigned with one of three regimens (Group A: DeBro 120 mg qid + amoxicillin 500 mg gid + metronidazole 250 mg gid for 14 days, n = 30; Group B: Lansoprazole 30 mg bid + clarithromycin 500 mg bid + amoxicillin 500 mg gid for 14 days, n = 30; Group C: omeprazole 20 mg bid + clarithromycin 250 mg bid + metronidazole 500 mg bid for 7 days, n = 30). The H. pylori infection status was proved by CLO test and 13C-urea breath test (UBT) with the excess 13CO2 excretion of 5 per mil as upper limit. Eradication of H. pylori was assessed by two consecutive 13C-UBT at 4 and 8 weeks after the finishing treatment respectively.

Results: In Group A, 21 patients (70%) had successful triple therapy, while in Group B and C, 24 patients (80%) and 29 patients (97%) respectively had successful triple therapy. Difference is significant (p < 0.01).
side effect regimen with the shorter duration and saving cost. The newer triple therapy with omeprazole 20 mg bid + clarithromycin 250 mg bid + metronidazole 500 mg bid of 7 days duration is a good choice for H. pylori eradication.

**4A:10 EFFICACY OF ONE WEEK TRIPLE THERAPY WITH CLARITHROMYCIN, FURAZOLIDONE PLUS LANSOPRAZOLE OR COLOIDAL BISMUTH SUBCUTRTE FOR ERADICATION OF HELICOBACTER PYLORI**

W.Z. Liu, S.D. Xiao, W.W. Xu, Y. Shi. Shanghai Institute of Digestive Diseases, Shanghai, P.R. China

The optimal drug regimen for eradication of Helicobacter pylori (Hp) remains uncertain.

**Aim:** 1) To evaluate the efficacy of two drug regimens in eradication of Hp and healing of duodenal ulcer (DU).

**Patients and Methods:** 60 patients with DU or non-ulcer dyspepsia and Hp infection were randomly received one-week triple therapy with Clarithromycin (Cia) 500 mg/d, Furazolidone 200 mg/d plus Lansoprazole 30 mg/d (group A) or CBS 480 mg/d (group B). Before and four weeks after end of therapy, patients were investigated with endoscopy and biopsy (4 from antrum and 2 corpus) for Hp culture and histology.

**Results:** 57 patients completed the study. The rates of Hp eradication in group A and B were 92.6% (25/27) and 90.0% (27/30) respectively (P < 0.05). The primary resistant rate of Hp strains to Cia was 7.5% (4/53), and no patient infected with resistant Hp strain to Cia succeeded in eradication. The healing rates of DU were 94.4% (17/18), in group A and 100% (18/18) in group B (P > 0.05). Only two patients complained of mild nausea.

**Conclusions:** (1) Both of the regimens are highly effective in the eradication of Hp and the healing of DU, and are well tolerated. (2) The primary resistance of Hp strains to Cia is the main cause of the treatment failure.

**4A:11 TRIPLE THERAPY (OMEPRAZOL + AMOXICILLIN + CLARITHROMYCIN) FOR HELICOBACTER PYLORI ERADICATION IN PATIENTS WITH CHRONIC GASTRITIS. TWELVE DAYS BETTER THAN SIX**

C. Hermeda, J.A. Moreno, P. Carpentero, J.M. Mateos, R. GoGrávalos, J.M. Pajares. Servicio de Medicina Digestiva, Hospital Universitario de La Princesa, Universidad Autónoma de Madrid, Spain

**Intro:** Modern therapies for eradication of Helicobacter pylori try to be more effective and to achieve better compliance being shorter and cheaper. Some seven-days regimens with omeprazole, amoxicillin and clarithromycin have proved high eradication rates. In Spain available packaging of both antibiotics uses carried 12 capsules in. If we use 7 days regimens we need double number of packages and lots of pills are wasted.

**Aim:** To ascertain the efficacy of a triple therapy with omeprazole, amoxicillin and clarithromycin for Helicobacter pylori eradication in regimens of 6 and 12 days.

**Patients and Methods:** We conducted a clinical trial to eradicate Helicobacter pylori infection in patients with chronic gastritis. 105 consecutive patients (58 M/47 F; mean age: 47, 53, range: 15-83) submitted to upper digestive tract endoscopy because symptoms of dyspepsia, were included in the study. Diagnosis of Helicobacter pylori infection was achieved when, at least, two of the following tests were positive: histologic examination of antral biopsy specimens in frozen tissue sections on H-E and Giemsa, rapid urease test (Jatrom-test) and C13 urea breath test. Triple therapy consisting in omeprazole 20 mg/bid, amoxicillin 1 g/bid and clarithromycin 500 mg/bid was given to patients at the time of diagnosis. Duration of treatment was non-randomized assigned for 6 and 12 days. Control of eradication was assessed by C13 urea breath test after 6 weeks of finishing treatment. Statistical analysis was performed using x2 test with Yates correction.

**Results:** Eradication rates in the different groups are:

- 6 Days: 61.1% (33/54)
- 12 Days: 84.3% (43/51)

**Statistical difference of eradication (p < 0.008) was found between both regimens (6 vs 12 days).** Costs of the 2 regimens were 85 and 170 $ respectively for 6 and 12 days.

**Conclusion:** In patients with chronic gastritis a 12 days triple therapy (Omeprazol + Amoxicillin + Clarithromycin) eradicates Helicobacter pylori better than a shorter 6 days regimen.

**4A:12 SHORT-TERM LOW-DOSE TRIPLE THERAPY FOR THE ERADICATION OF HELICOBACTER PYLORI: A RANDOMIZED, DOUBLE BLIND, CONTROLLED STUDY**


**Background:** a simple safe and effective short-term (1 week) low dose triple therapy, Omeprazole 20 mg u.i.d. + Clarithromycin 250 mg b.i.d. + Tinidazole 500 mg b.i.d. (OCT), has been developed for the eradication of Helicobacter (H.) pylori (Eur J Gastroenterol 1994; 6: 773-7) in response to the problems seen with standard triple and dual therapies. Consistent results have been reproduced by several investigators in different countries with the same regimen, whilst increasing dosages and duration of treatment does not seem to improve success rate. **Aim:** This is a double blind, randomized controlled trial to evaluate the efficacy and safety of OCT in comparison to even simpler combinations of the three considered agents. **Methods:** 128 patients (68 males, 60 females, age (yrs) range 22-76, mean 53) with non ulcer dyspepsia and Hp pylori infection were randomly allocated in four treatment groups receiving for 1 week: clarithromycin 250 mg b.i.d. (group C, n = 32) or omeprazole 20 mg u.i.d. clarithromycin 250 mg b.i.d. (group OC, n = 32) or clarithromycin 250 mg b.i.d. tinidazole 500 mg b.i.d (group CT, n = 32) or omeprazole 20 mg u.i.d. clarithromycin 250 mg b.i.d. tinidazole 500 mg b.i.d (group OCT, n = 32). H. pylori infection as well as eradication was assessed by histology (Haematoxylin/Eosin, Giemsa), culture, quick urease test and 13C-Urea Breath Test (13C-UBT) before and 4 weeks after the end of treatment. Drug tolerability was evaluated by patient interview and compliance by pill counting at the end of treatment.

**Results:** The four groups of patients had similar demographic and clinical characteristics. All patients completed the treatment and took more than 90% of the prescribed medication. One patient discontinued treatment due to side effects.

**Treatment**

<table>
<thead>
<tr>
<th></th>
<th>Eradication rate</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>6.3% (2/32)</td>
<td>0-14.6</td>
</tr>
<tr>
<td>OC</td>
<td>31.3% (10/32)</td>
<td>15.2-47.3</td>
</tr>
<tr>
<td>CT</td>
<td>59.4% (19/32)</td>
<td>42.4-76.0</td>
</tr>
<tr>
<td>OCT</td>
<td>93.8% (30/32)</td>
<td>85.4-99.9</td>
</tr>
</tbody>
</table>

** Differences in eradication rate in the four groups were statistically significant (at least p < 0.025). Conclusions: this randomized double blind, controlled study confirms that the combination of omeprazole, clarithromycin and tinidazole at low dosages and just for one week is highly effective for H. pylori eradication. Simpler combinations of the same agents are far less effective. The high success rate is probably linked to lack of side effects, patient compliance and synergy of all three agents.**

**4A:13 LANSOPRAZOLE (30 mg OD vs BID) WITH AMOXICILLIN AND CLARITHROMYCIN TO CURE HELICOBACTER PYLORI INFECTION**

A. Burete 1, V. Lamy 2, B. Ramdani 1, J. Cappelli 3, C. De Prez 2, Y. Cholcyrisksky 2, N. Clin. Basileu, Belgium; 3 Hôpital Civil de Jumet, Belgium; 4 Hôpital A. Vésale, Charleroi, Belgium

In this double-blind, multicenter study, 99 patients with Helicobacter pylori (Hp) associated NUD, DU or GU were randomly assigned to one of the three triple therapies administered for 10 days: Group 1: lansoprazole (LA) 30 mg od (before meals) + amoxicillin (AM) 1 g bid (after meals) + clarithromycin (CL) 500 mg tid (after meals); Group 2: LA 30 mg bid + AM 1 g bid + CL 500 mg tid. The Hp status was assessed before treatment and 4-6 weeks post-treatment in antral and corporeal biopsies by urease test, culture and histology. Eradication was defined as the absence of Hp in all post-treatment samples. 13C-urea breath test was performed 3 months post-treatment to confirm Hp eradication. Susceptibility testing of putative post-treatment isolates to CL was performed by disc diffusion method. Patients were considered as compliant if they took > 80% of the treatment. **Results:** 7/99 patients were lost to follow-up. Among the 84/92 patients who completed the study (48 M, mean age: 48 years, 24 DU, 8 GU), 76 were considered compliant to the treatment. Cure of Hp infection was respectively achieved in 71/76 (93%, 95% CI: 88-99) and 77/84 (92%, 95% CI 86-98) of the patients according to the Per Protocol and the Intention To Treat analyses. Pre-treatment resistance to CL was found in 8/81 (10%) of the Hp strains. Cure of Hp infection was achieved in 4/7 of these cases. Mild adverse events, including dysgeusia (18%) and diarrhea (16%), occurred in about 50% of the patients but treatment was discontinued in only 2 of them. **Conclusion:** Triple therapies with LA, AM and CL for 10 days are very effective regimens to cure Hp infection. The overall cure high rate observed in this study suggests that both regimens (LA 30 mg od or bid) are very successful. Treatment failure occurs in about 50% of the cases when the infecting Hp strain is CL-resistant.
4A: Clinical pathological comments of H. pylori treatment

4A: OVER 95% OF PATIENTS REMAIN H. PYLORI NEGATIVE 6 MONTHS AFTER ONE WEEK LOW-DOSE ERADICATION THERAPY

J.J. Misiewicz 1, A.W. Harris 1, K.D. Bardhan 2, S. Levi 3, H. Langworthy 3, 4, Central Middlesex Hospital, London, UK; 2 Rotherham General Hospital; 3 Welsh Park Hospital, Slough, 4 Lederle, UK

Introduction: We have previously shown that H. pylori (Hp) can be eradicated in the majority of patients with a 7 day low dose triple therapy containing a proton pump inhibitor (PPI) in combination with 2 antibiotics. It is unclear whether patients remain free of infection 6 months after treatment with these regimens. This study investigated the Hp re-infection or recrudescence 6 months after different one week regimens.

Methods: A multicentre, prospectively randomized, parallel group, single blind study was conducted in Hp positive (positive CLO® and positive 13C urea breath test [UBT]) patients with endoscopic DU and for one ulcer gastritis. Treatment was either Lansoprazole (L) 30 mg plus 2 of clarithromycin (C) 250 mg, amoxicillin (A) 1 g, metronidazole (M) 400 mg or omeprazole (O) 20 mg plus A 1 g and M 400 mg; all give twice daily for one week. Endoscopy and UBT were performed ≥6 months after treatment in those patients in whom UBT had been negative ≥28 days after treatment. Ethics approval and written informed consent obtained. Results: 304 patients returned for UBT ≥6 months after treatment. The proportion of patients remaining Hp negative is shown below:

<table>
<thead>
<tr>
<th>LAC n (%)</th>
<th>LAM n (%)</th>
<th>LCM n (%)</th>
<th>OAM n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>80/83 (96.4%)</td>
<td>68/70 (97.1%)</td>
<td>77/78 (98%)</td>
<td>72/73 (96.6%)</td>
</tr>
</tbody>
</table>

There were no significant differences (p > 0.05) between treatments. Conclusion: 6 months after treatment with LAC, LCM, LAM or OAM > 96% of patients remain Hp negative. This research was funded by Lederle Laboratories, UK.

4A: ONE WEEK LOW-DOSE H. PYLORI ERADICATION THERAPY HEALS 90% OF DUODENAL ULCERS

J.J. Misiewicz 1, A.W. Harris 1, K.D. Bardhan 2, S. Levi 3, H. Langworthy 3, 4, Central Middlesex Hospital, London, UK; 2 Rotherham General Hospital, UK; 3 Welsh Park Hospital, Slough, UK; 4 Lederle, UK

Introduction H. pylori (Hp) can now be eradicated in the majority of patients with 7 days of treatment with a proton pump inhibitor (PPI) in combination with 2 antibiotics. It is unclear if PPI treatment should be continued beyond 7 days in patients with duodenal ulcer (DU). This study investigated the efficacies of 4 one week Hp eradication regimens in the healing of DU. Methods A multicentre, prospectively randomized, parallel group, single blind study was conducted in the UK and Eire in Hp positive (defined as a positive CLO® and positive 13C urea breath test [UBT]) patients with endoscopic DU. Treatment was either Lansoprazole (L) 30 mg plus two of clarithromycin (C) 250 mg, amoxicillin (A) 1 g, metronidazole (M) 400 mg or omeprazole (O) 20 mg plus A 1 g and M 400 mg; all give twice daily for one week. Endoscopy and UBT were performed ≥28 days following the end of treatment. Ethics approval was given and written informed consent obtained. Results: 262 patients fulfilled the entry criteria, of whom 237 returned for follow-up endoscopy. The proportion of patients in whom DU was healed, is shown below with Hp eradication status:

<table>
<thead>
<tr>
<th>LAC n (%)</th>
<th>LAM n (%)</th>
<th>LCM n (%)</th>
<th>OAM n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>53/60 (88.3%)</td>
<td>52/56 (92.9%)</td>
<td>49/55 (89.1%)</td>
<td>60/66 (90.9%)</td>
</tr>
<tr>
<td>3/7 unhealed</td>
<td>4/4 unhealed</td>
<td>2/6 unhealed</td>
<td>3/6 unhealed</td>
</tr>
<tr>
<td>Hp±ve</td>
<td>Hp±ve</td>
<td>Hp±ve</td>
<td>Hp±ve</td>
</tr>
</tbody>
</table>

There were no significant differences (p > 0.05) in DU healing between treatments. Conclusion: Treatment with LAC, LCM, LAM or OAM for one week heals DU in about 90% of patients. This research was funded by Lederle Laboratories, UK.

4A: ONE-HOUR TOPICAL TREATMENT vs OMEPRAZOLE PLUS AMOXICILLIN IN ERADICATION OF H. PYLORI IN DUODENAL ULCER PATIENTS

K. Przyulkoski, J. Regula, A. Marek 1, J. Ostrowski, A. Nowak 1, E. Butruk. Medical Centre for Postgraduate Education, Institute of Oncology, Warsaw, Poland; 1 Silesian Medical Academy, Katowice, Poland

One-hour topical method (described in Am J Gastro 1995, 90, 63) was effective in eradication of H. pylori in 97% of gastritis patients. Omeprazole plus amoxacillin eradication rate in duodenal ulcer patients varies from 0 to 62%. The aim of this trial was to compare the two methods in a randomised, prospective study.

Eighty patients (21 female, 59 male; median age: 43, range 18–73) with duodenal ulcer were randomised into one of the following groups. Group 1: 40 patients were given ranitidine 150 mg bid for 6 weeks and then omeprazole 20 mg b.i.d. plus promose 30,000 units b.i.d. for 2 days. On the next day a solution (100 ml) of 7% natrium bicarbonate containing 4000 mg of amoxicillin, 2000 mg of bismuth substrate, 1000 mg of metronidazole and 30,000 units of promose was instilled into the stomach for 1 hour using an intestinal tube with the balloon occluding duodenal outlet. Group 2: 40 patients treated with omeprazole 20 b.i.d. and amoxicillin 1000 mg b.i.d. for 2 weeks, followed by ranitidin 150 mg b.i.d. for next 4 weeks. Eradication was regarded as successful when urease test, histology and urea breath test results were negative.

Eradication rates in groups 1 and 2 were 2.5% and 35% in "intention-to-treat" analysis, respectively. Minor side-effects (nausea, vomiting, diarrhoea) were encountered in 40.5% and 15.3% of patients, respectively. Topical method was poorly tolerated in 54% of patients.

One-hour topical method as well as omeprazole/amoxicillin treatment are ineffective in eradication of H. pylori in duodenal ulcer patients.

4A: COMPARISON OF THE EFFICACY OF TWO, SHORT-TERM, TRIPLE THERAPIES BASED ON CLARITHROMYCIN, IN THE ERADICATION OF HELICOBACTER PYLORI (HP): A RANDOMIZED STUDY

S. Georgopoulos 1, A. Menis 1, S. Karatapanis 1, A.S. Mylonakis/Katranis 2, V. Artikis 2, G. Dept 1, Dept. of Internal Medicine of Athens "ELPIS" Hospital, 2 Dept of Bacteriology, Hellenic Pasteur Institute, Athens, Greece

Recent studies have shown that newer, one week, triple therapies based on Clarithromycin (CL) are highly effective and safe in treating Hp infection. The aim of our study was to compare the Hp eradication rates achieved by two, one week, triple regimens that involve either one or two antibiotic agents.

Patients - Methods: Seventy-eight patients (aged 19-83 yrs, mean 45.6) with a documented Hp infection (by CLO-test, histology and culture) were randomized in two treatment groups: Group A (n = 40, 25f, 62.5% smokers) received Omeprazole (Ome) 20 mg bid + CL 500 mg bid + Metronidazole (Met) 500 mg bid, for one week. Group B (n = 38, 24f, 61.3% smokers) received Ome 20 mg bid + CL 500 mg bid + TDB (De Nol) 120 mg bid, for one week. Patients underwent a new endoscopy 4 weeks after the end of treatment to assess eradication of Hp. Antibiotic sensitivity test was performed whenever Hp isolates were successfully cultured.

Results: Eradication of Hp was achieved in 34/40 (85%) patients of group A vs 34/38 (89.5%) of group B (p = NS). Culture and antibiotic sensitivity test revealed 12/32 (37.5%) Met resistant (MetR) Hp strains in group A and 13/31 (41.9%) in group B (p = NS). In contrast, only one patient (1.63%) had an Hp strain with primary resistance to CL and notably didn’t respond to both therapies. The regimens were comparable according to their efficacy on Met sensitive (MetS) strains (20/20 (100%) vs 17/19 (89.5%), p = NS). In contrast, the response to treatment of patients with MetR strains was significantly lower in group A compared to group B (7/12 (58.3%) vs 12/13 (92.3%), p < 0.05). Five patients in group A experienced mild to moderate adverse events compared to one patient in group B. Conclusions: The efficacy of the new, short- term treatments involving two antibiotics probably is dependent on the incidence of MetR Hp strains. In area with low CL resistance of Hp, an alternative mono-antibiotic triple regimen may be equally effective and well tolerated.

4A: DUODENAL ULCER HELICOBACTER PYLORI (HP) POSITIVE: THERAPY WITH RANITIDINE (R) + CLARITHROMYCIN (C) + METRONIDAZOLE (M) VERSUS OMEPRAZOLE (O) + CLARITHROMYCIN + METRONIDAZOLE

N. Sacc, A. De Medici, S. Rodino, M. De Siena, A. Giglio. Servizio di Endoscopia Digestiva, Ospedale Cucci, Catanzaro, Italy

To compare two different therapeutic regimens and to evaluate their effects on Hp eradication we conducted a prospective study on 123 patients with duodenal ulcer and Hp associated gastritis. The patients were randomly assigned to the following treatment groups: A) Ranitidine 150 mg b.i.d. for a month + C 250 mg b.i.d. for a week + M 250 mg t.i.d. for a week; B) Omeprazole 20 mg for a month + C b.i.d. for a week + M t.i.d. for a week. 58 patients were assigned to the regimen A and 65 patients to the regimen B. The patients underwent endoscopy at the beginning of the study and 2 months after the end of the therapy. Hp status was determined with urease test and histology (2 biopsies each one taken from the antrum and corpus of the stomach. Eradication was achieved as follows: Group A 47/58 = 80.7% and group B 25/26 = 96.2% The patients were completely healed in all patients. Both regimes were tolerated. No statistically significant differences (X2 test) were found between the two groups.
**4A: Clinical pharmacological aspects of H. pylori treatment**

Conclusions: Ranitidine 150 mg b.i.d. + C + M is as effective for HP eradication as omeprazole 20 mg + C + M. The patients compliance to one week therapy is excellent.

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**4A:19 THE ROLE OF QUADRUPEL THERAPY IN THE TREATMENT OF HELICOBACTER PYLORI**

G. Dassopoulos, Y.Y. Ho, D. Mehanna, K. Chen. Inner West Endoscopy Centre, Sydney, Australia

Introduction: The definitive treatment for H. pylori has yet to be established. Triple therapies either with bismuth or a proton pump inhibitor currently appear to be the most often used treatments. There have, however, been several studies with quadruple therapy which seem to confirm more consistent higher eradication rates. There have been no comparative studies into which quadruple therapies may be more effective. Aim: To compare three different quadruple therapies in the eradication of H. pylori.

Methods: 161 patients with dyspeptic symptoms confirmed at endoscopy with biopsy as having H. pylori between June 94 and July 95 were entered into the study. Patients were randomised to one of three treatment groups. Each treatment was given for 2 weeks. (A) Colloidal bismuth 1 qid, tetracycline 250 mg qid, metronidazole 200 mg tid, lansoprazole 30 mg bd, (BTML- 45 patients). (B) Colloidal bismuth 1 qid, tetracycline 250 mg qid, metronidazole 200 mg tid, lansoprazole 30 mg bd, (BTM- 45 patients). (C) Colloidal bismuth 1 qid, tetracycline 250 mg qid, metronidazole 150 mg bd (BTMR - 36 patients). (C) Colloidal bismuth 1 qid, tetracycline 250 mg qid, metronidazole 200 mg qd, (BTMR - 12 patients).

Lamouliatte, (60.7%) in the LCT resistance with 110/128 therapy (BTML - 45 patients). Saint-Andrl, (0.05). BTRL the fundus Roxithromycin (I.T.T.) Per group, the trial was stopped because of comparable but insufficient eradication rates (HP-ER). In contrast to most studies our groups were matched for age, sex, weight, smoking habits, initial diagnosis, liver/renal function and history of previous ulcers. In 54/60 patients, total HP-ER is 44.4%: 59% (LA), 42% (OA) and 53% (RA), n.s. LA and OA produced higher mean (4.6 vs 5.3 vs 3.8) and median (4.4 vs 5.3 vs 3.8) pH values than RA and gave a longer acid suppression (time with pH > 4: 68% vs 75% vs 47%), all differences p < 0.01. Surprisingly, this resulted in comparable HP-ER between these groups. In patients becoming HP- and remaining HP+: no significant differences were found for mean and median pH. Time of acid suppression was lower with a pH > 4, initial UBT values were extremely good (93%). Conclusions: Acid inhibition is important in dual therapy with amoxicillin, but apparently not its extent. Ranitidine adequately dosed is as effective for HP-eradication as proton-pump inhibitors. There are neither pharmacokinetic nor -dynamic differences in patients being HP+ or HP- after therapy. In a subgroup of ulcer patients over 50 years with a previous history of PU dual therapy has an HP-ER of around 80%.

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**4A:20 RANDOMISED STUDY COMPARING TWO SEVEN DAYS TRIPLE THERAPIES WITH LANSPRAZOLE AND LOW DOSE OF CLARITHROMYCIN PLUS AMOXICILLIN OR TINIDAZOLE FOR H. PYLORI ERADICATION**

H. Lamouliatte, P. Talbi, R. Cayla, F. Zerbib, F. Megraud. Hôpital Saint-André, Bordeaux, France

For H. pylori (HP) eradication (HPE), two seven days triple therapies with PPI and two antibiotics have obtained eradication rate higher than 90%: 1/PPI-Clarithromycin (Clari) 250 mg bid and Tinidazole (Tin) or Metronidazole (Metro) 2/PPPI-Clari 500 mg bid and Amoxicillin (Amox). The aim of this study was to compare two seven days triple therapies using low dose of Clari.

Methods: HP infection was assessed on antral and fundic biopsies at the inclusion and 4 weeks after the end of the treatment by 4 methods: CLOtest at the inclusion, histology, culture and PCR. Clari resistance was defined by a contact resistance with an agar diffusion method and Metro resistance by a MIC > 8 mcg/ml (E-test). HP positive patients were randomly allocated to receive either: 1/Lansoprazole (Lanso) 30 mg bid + Clari 250 mg bid and Tin 500 mg bid (LCT group) or 2/Amox 1 bid (LCA group) during 7 days. Patients were allocated to one of the following 2 treatment schedules: 1) OME 40 mg plus AMO 4 x 500 mg plus METRO o x 250 mg; 2) OME 40 mg plus AMO 4 x 500 mg plus METRO o x 250 mg; 3) OME 40 mg plus AMO 4 x 500 mg plus METRO o x 250 mg plus BCS o x 120 mg; 4) RAN 300 mg plus AMO 4 x 500 mg plus METRO o x 250 mg; 5) RAN 2 x 300 mg plus AMO 4 x 500 mg plus METRO o x 250 mg. All antibiotics treatment lasted for two weeks while antisecretory treatment did four. HP eradication was confirmed by histology on 6 biopsies (2 gastric antrum, 2 antrum and 2 body; Hematoxilinosin and Giemsa modified stain) and by rapid urease test (CLO test). An endoscopy was performed at baseline and 1 and 4 months after the beginning of the treatment. Results. All patients completed the therapy. After 1 month 23 patients were unahealed (13 Hp-cleared and 10 Hp-positive) and left the study. After 4 months 17 patients presented DU recurrence (2 Hp-negative and 15 Hp-positive). 30 patients persisted healed (600 HP-negative) and 20 (1 HP-positive). The percentage of Hp eradication for each regimen were as follows: 1) 55.6; 2) 78.4; 3) 81.4; 4) 76.8; 5) 74.6. Conclusions: 1) Omeprazole triple and
ERADICATION OF H. PYLORI INFECTION WITH FIVE DIFFERENT DRUG REGIMES

M. Katičić, V. Prešeczki, M. Marušić, M. Prskalo, M. Tićak, B. Šabaric, V. Čolić-Cvijje, M. Dominia, S. Kalenic, S. Dzabo, B. Papa. Clinical Hospital “MURKUR”, Medical School, University of Zagreb, Croatia

The aim of our study was to compare the efficacy and tolerability of five different triple therapy regimens for H. pylori eradication.

Methods: 468 consecutive patients (MF: 395/233, mean age 51), undergoing endoscopy, were screened for H. pylori. 402 (86%) patients, with confirmed H. pylori infection by rapid urease test (CLO), histology (2-corpus, 2-antrum), serology (IgG) and microbiology were allocated to one of 5 regimens: A) Omeprazole 20 mg bd., Amoxicillin 1 g bd. for 14 days (n = 130), B) Omeprazole 20 mg bd., Amoxicillin 1 g bd. for 14 days, metronidazole 500 mg bd. for 10 days (n = 146), C) Omeprazole 20 mg bd., Amoxicillin 1 g bd., Clarithromycin 500 mg bd. for 14 days (n = 32), D) Same regimen (O + A + C) - 10 days (n = 46), E) Same regimen (O + A + C) - 7 days (n = 48).

Results: H. pylori eradication rates were: in group A, 43% (56/130), group B, 68% (99/146), group C, 94% (30/32), group D, 83% (38/46) and group E, 81% (39/48). The most common side effects were diarrhea and taste disturbances. All eradicated patients showed improvement in histology without significant differences, although eradication was statistically higher (p < 0.02) in groups C, D, E.

Conclusion: Combination Omeprazole + Amoxicillin had a low efficacy in H. pylori eradication. One week Omeprazole + Amoxicillin + Clarithromycin therapy is effective enough, simple and relatively well tolerated.

HIGH CURE RATES WITH RANITIDINE BISMUTH CITRATE (PYLORID) PLUS CLARITHROMYCIN GIVEN TWO TWICE DAILY

K.D. Bardhan, 1 H. Wurzer, 2 M. Marcelino, 3 J. Jahnsten, 4 N. Lotay. 5
1 Rotherham General Hospital, Rotherham, UK; 2 Graz General Hospital, 2 Med. Dept., Graz, Austria; 3 Hospital De Sao Marcos, Braga, Portugal; 4 Medical Department Aker Sykehus, Oslo, Norway; 5 Glaso Welcome R&D, UK

Introduction: H. pylori (Hp) eradication rates were compared for two dual therapies and one triple therapy in this double-blind, randomised, multicentre, parallel group study. Patients received ranitidine bismuth citrate (RBC) 400 mg bd in co-prescription with clarithromycin 500 mg bd (CL bd) or 250 mg qds (CL qds) or clarithromycin 500 mg bd plus metronidazole, 400 mg bd (CL + MT) for 14 days, followed by 14 days of RBC 400 mg bd alone to facilitate ulcer healing. Patients and Methods: A total of 646 patients with active DU (634 with confirmed Hp infection) entered the study. Patients with healed ulcers were further endoscoped at least 28 days after the end of treatment and Hp status was assessed by 13C-UBT and histology (Giems) on 2 antral and 2 corpus biopsies. Crude (worst case) and observed (evaluable follow-up) intention-to-treat analyses of Hp eradication and 4 week DU healing rates were calculated.

Results

<table>
<thead>
<tr>
<th>RBC + CLqds</th>
<th>RBC + CLbd</th>
<th>RBC + CL + MT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eradication (crude), % (n)</td>
<td>69 (254)</td>
<td>70 (252)</td>
</tr>
<tr>
<td>Eradication (observed), % (n)</td>
<td>84 (207)</td>
<td>97 (190)</td>
</tr>
<tr>
<td>Healing (crude), % (n)</td>
<td>90 (260)</td>
<td>91 (257)</td>
</tr>
<tr>
<td>Healing (observed), % (n)</td>
<td>95 (247)</td>
<td>95 (243)</td>
</tr>
<tr>
<td>Any adverse events, %</td>
<td>21</td>
<td>31</td>
</tr>
</tbody>
</table>

*p = 0.014 for comparison with RBC + CL qds. n = number of patients in the analysis.

Conclusion RBC in co-prescription with CL-500 mg bd was statistically superior to CL-250 mg qds and as effective as triple therapy. All regimens were well tolerated.

HIGHLY EFFECTIVE TRIPLE THERAPY WITH OMEPRAZOLE, AMOXICILLIN AND CLARITHROMYCIN IN PREVIOUS H. PYLORI TREATMENT FAILURES

F. Lerang1, B. Moum1, J.B. Haug2, T. Berge1, 1 Dept. of medicine, Østfold Central Hospital, Fredrikstad, Norway; 2 Dept. of microbiology, Østfold Central Hospital, Fredrikstad, Norway

Objectives: To compare cure of H. pylori (Hp) infection of two clarithromycin-based triple therapies for 10 days in previous treatment failures.

Methods: Thirty-three patients with duodenal ulcer disease were randomised to 1) omeprazole 20 mg bid, amoxicillin 750 mg bid and clarithromycin 250 mg bid (OAC) or 2) bismuth subcitrate 240 mg bid, oxytetracycline 750 mg bid and clarithromycin 250 mg bid (BTC). Previous failed regimens included combinations of bismuth, omeprazole, tetracycline, metronidazole, amoxicillin or clarithromycin in BTM (n = 22), OAM (n = 11), OA (n = 7), OCM (n = 2) or BCM (n = 1). Twenty-eight patients had received one course and five had received three courses. Diagnosis of Hp infection was based on culture with susceptibility testing (E-test) of antrum and corpus biopsy specimens. All but one patient had metronidazole resistant strains and none were resistant to clarithromycin or tetracycline.

Results: Cure of Hp infection was achieved in 18/18 patients (100%) in OAC and in 8/15 (53%) in BTC (p = 0.004). Side effects was a minor problem and all patients completed the treatment. The seven patients who failed BTC (with strains still sensitive to clarithromycin) have later received OAC and in 5 of 7 H. pylori was eradicated.

Conclusion: Ten-days OAC bid is highly effective and superior to BTC in previous Hp treatment failures. Addition of a proton pump inhibitor to antimicrobials may be critical in second line therapy. The efficacy of OAC other than clarithromycin-based therapies needs to be investigated.

HIGH vs STANDARD DOSE OMEPRAZOLE PLUS AMOXICILLIN FOR TREATMENT OF H. PYLORI POSITIVE DUODENAL ULCER. A MULTICENTRE, randomised, TRIALIZED RANDOM

Duodenal Ulcer Study Group and Schering-Plough, Italia, Italy

Background. Treatment of H. pylori with an association of omeprazole and amoxicillin gave conflicting results. The causative factors remain still unknown although one of the most important seems to be the dosage of omeprazole.

Aim. Purpose of the present nationwide, multi-center, randomized, single blind study was to compare two omeprazole (OM)-amoxicillin (A) schemes with different doses of omeprazole in the eradication of H. pylori, healing of duodenal ulcer and prevention of duodenal ulcer relapse.

Patients and methods. 332 patients (229 males, 93 females; mean age ± SD: 46.5 ± 13.1 yrs) with active H. pylori positive duodenal ulcer were randomly treated with either omeprazole 40 mg bid or 20 mg bid and amoxicillin 500 mg qid over 2 weeks, followed by omeprazole 20 mg om for another 4 weeks. Endoscopic control examination and gastric antral and corporeal biopsies for Giemsa staining were performed at the study entry, at the end of treatment, at 2 months and 9 months after termination of treatment.

Results. Duodenal ulcer healing was achieved at the end of treatment in 95.4% (149/152) of patients of OM 40 group and in 95.9% (144/147) of OM 40 group.

Table includes all patients who had the appropriate post-Rx visits

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Hp eradication at 2 months</th>
<th>DU relapse at 9 months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hp</td>
<td>OMR0 + A</td>
<td>63.6% (77/121)</td>
</tr>
<tr>
<td></td>
<td>OMR0 + A</td>
<td>26.9% (44/142)</td>
</tr>
<tr>
<td>Hp</td>
<td>OMR0 + A</td>
<td>44.5% (49/110)</td>
</tr>
<tr>
<td></td>
<td>OMR0 + A</td>
<td>32.2% (20/62)</td>
</tr>
</tbody>
</table>

H. pylori eradication in the OM 45 group was significantly different from the OM 40 group (p = 0.007).

Conclusions. Effectiveness of omeprazole plus amoxicillin gave modest results. However, higher doses of omeprazole seem to be associated with better Hp eradication rate. We confirm Hp eradication prevents ulcer relapse.

BISMUTH, METRONIDAZOLE AND TETRACYCLINE (BMT) ± ACID SUPPRESSION IN H. PYLORI ERADICATION: A META-ANALYSIS

N. Chiba, R.H. Hunt. McMaster University, Hamilton, Canada

We performed a meta-analysis of BMT alone or with H2-RA (H2-BMT) or PPI (OBMT only omeprazole data available).

Methods: Fully recursive search of literature using Medline to July 1995. Included abstracts from 1993-95 meetings. AQA, ASC, BSG, UEGW, WCG and European Hp meetings. Inclusion criteria: adults, prospective studies, per protocol data of number with Hp eradication per number of patients treated, assessed at least 4 wks after end of eradication therapy. Data pooled as mean % eradication with 95% CI.

Results: BMT therapy eradicated 81.8% (78.0-85.6). Eradication rate was not dependent on the daily dosage of metronidazole: < 800 mg/d (87%, 82.3-91.7), 1-1.2 g/d (77.2%, 70.3-84.1) or 1.5-1.6 g/d (82%,
H2-BMT was significantly better than BMT. Higher acid suppression with OMBT gave very consistent results and further significantly increased eradication rates over H2-BMT (95% CI for the difference 0.3–9.9). Withdrawals due to side effects (when reported) was low. Addition of acid suppression did not decrease any drop outs.

Conclusions: Overall mean efficacy of 81.8% is seen with BMT and MRT markedly reduces eradication rate. Significantly higher eradication rate is seen with increasing acid suppression with BMT. Overall withdrawals are low and not affected by addition of acid suppression.

4A:28
OMEPRAZOLE ONCE OR TWICE DAILY WITH CLARITHROMYCIN + METRONIDAZOLE IN H. PYLORI ERADICATION: A COHORT STUDY
N. Chiba, C. Marshall. Surrey GI Clinic, Guelph, Canada

As it is unclear whether omeprazole needs to be given once or twice daily in this promising new triple therapy, our aim was to study this.

Methods: Histology proven HP positive patients were given 7 days treatment with clarithromycin 250 mg and metronidazole 500 mg bid and allocated to omeprazole 20 mg, either once (01CM) or twice (02CM) daily. Side effects and medication compliance assessed at visit 2. Endoscopy with histology (antrum/body) repeated 4 weeks after pills completed to assess Hp status. Data given as all-patients treated (APT) analysis: includes patients who received at least 1 dose of medication.

Results: Group 01CM: 37 patients: 15 PUD, 15 gastritis, 7 GERD, age 53 y (22–78), m/f 15/22, 2 drop outs. All patients took all pills but did not return for final evaluation, included in APT. Eradication seen in 77.1% (27/35) patients. 32/35 took 100% of pills, two took only half the metronidazole dose by error. 12/35 (34.3%) had no side effects (SE) and 23 patients suffered 48 SE such as loose stools (9), nausea (7), headache (7), gas (4), epigastric pain, dry mouth and taste disturbance (3 each). Only 1 stopped metronidazole due to side effects (perspiring) but completed all other pills. Group 02CM: n = 37: 11 PUD, 22 gastritis, 4 GERD, age 55 y (31–78), m/f 20/17. 1 patient who did not return for the 2nd visit was withdrawn. A further 3 patients completed all pills but refused final evaluation. Thus, APT eradication 77.8% (28/36) and per protocol eradication 84.3%. Of 36 patients 100% of pills. 11 of 36 (30.6%) had no SE and 25 patients had 52 frequent, minor SE including taste disturbance (13), loose stools (9), nausea (7), headache (3) and leg tingling (3). No withdrawals occurred due to adverse drug effects.

Conclusions: Eradication rate equivalent whether omeprazole given once or twice daily. Excess variation of 77% is lower than reported in the literature. Possible explanations may be HP metronidazole resistance (estimated to be 20–30% in this area), larger doses of clarithromycin may be needed or need longer duration of treatment.

4A:29
OMEPRAZOLE PLUS ANTIBIOTICS IN THE ERADICATION OF H. PYLORI INFECTION: A META-REGRESSION
1MetaWorks Inc., Boston, MA, USA; 2Tufts-NEMC, Boston, MA, USA

Objective: To perform a systematic overview and meta-regression analysis of published studies of omeprazole (O) plus antibiotics (ab) in the treatment of H. pylori (HP) in patients with peptic ulcer disease and non-ulcer dyspepsia.

Methods: All relevant papers and abstracts were retrieved after a comprehensive electronic and manual search, inclusive of all languages and all languages, through September, 1995. Inclusion criteria are randomized control trials with ≥ 10 patients if parallel design, or ≥ 5 patients if crossover design, with at least one treatment arm containing an orally administered O + ab combination of ≥ 5 days duration. Lead-in intervals for O = 1 day were excluded, as were studies that did not report testing for HP eradication by treatment arm ≥ 4 weeks after completion of ab treatment. Probability of HP eradication was calculated for each study arm, and these probabilities were then compared with respect to different risk factors. For multivariate regression analysis, logistic regression based on the binomial outcomes from each study arm were performed, using all risk factors as candidate variables.

Results: Studies involving 141 study arms with 5633 patients treated with O + ab(s) were identified. Twenty-three (23) different ab regimens were identified, but the vast majority of treatment arms used amoxicillin (A) or clarithromycin (C) or both. Dual therapy (O + 1ab) was used in 92 treatment arms with 3363 patients; triple therapy (O + 2ab) was used in 45 treatment arms with 1914 patients. Eradicated 70.2% of the O + A dual regimens and 76% for the O + C dual regimens (p < 0.0001). Tripe therapy eradication rates were 82% for O + A + C; 84% for O + A + imidazole derivatives (M); and 90% for O + C + M. Generally, regardless of the ab combination used, treatment worked poorly in patients with ulcers than in those without (p < 0.0001). Duration of therapy past 1 week does not seem to add any benefit when doses of O + ab are higher. Higher doses of O + C in dual regimens may be equivalent to lower doses of O + 2ab in triple regimens. Test-ab and test-maintenance O interactions were seen, and require further studies to understand.

Conclusions: Tripe therapy with O is better than dual therapy with O in terms of Hp eradication rates achieved. In both dual and triple therapies, the higher the O dose, the higher the Hp eradication rates. Further investigation of low dose O triples vs. high dose duals is recommended, since this results suggest that dual therapy (O + 1ab) for 1 week at high doses may achieve equivalent results to triple therapy (O + 2ab) at lower doses for longer intervals. This may be important to understand in view of expected differences in compliance and cost.

4A:30
THE COST-EFFECTIVENESS OF H. PYLORI ERADICATION WITH DUAL AND TRIPLE THERAPY
S. Viergutz 1, P. Malferttheiner2, G.A. Gutz3, M. Schlender4, 1gmi, Munich, Germany; 2University of Magdeburg, Germany; 3Byk Gulden Pharmaceuticals, Konstanz, Germany

H. pylori (Hp) is broadly accepted as a major prerequisite for the development of peptic ulcer disease and its elimination prevents ulcer relapse in the vast majority of patients. This health economic study compares the cost-effectiveness of two extensively tested treatment schemata: a 14 days dual therapy with a proton pump inhibitor (PPI) and amoxicillin, which produced variable cure rates and a 7 days short term triple therapy (i.e. PPI and two antibiotics), which resulted in very high cure rates.

Methods: Possible therapy courses for Hp-cure were implemented by a decision tree model. The probabilities for the use of a particular course of treatment were determined by a survey of 100 office-based specialists in Germany. The underlying eradication and ulcer relapse rates were analysed by literature research and subsequent meta-analysis. For the analysis, direct costs (medication, diagnostics and consultations with the physicians) were considered.

Results: Taking only the medication costs into account, the daily costs of triple therapy were higher than those of dual therapy. However, the total medication costs of triple therapy were 34% lower than those of dual therapy. Carrying out a cost-effectiveness analysis, from the point of the German healthcare system, the total costs per year for a patient with successful Hp-eradication therapy were DEM 1082 with dual and only DEM 657 with triple therapy. The robustness of this result was validated by several sensitivity analyses.

Conclusion: This health economic analysis showed that triple therapy is not only more effective but also more efficient than dual therapy.

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COMPARISON OF TWO ALTERNATIVE STRATEGIES FOR THE MANAGEMENT OF DUODENAL ULCER: AN ECONOMIC MODEL
X. Lene1, T. Lebrun1, B. Requin1, M.A. Bigard2, R. Colin3, A. Cortot4, P. Zeiotun5, 1CRÈGUE (LABORES URA CNRS 362), France; 2Nancy, France; 3Rouen, France; 4Lille, France; 5Reims, France

This study aimed to compare 2 strategies for the management of duodenal ulcer 5 years after diagnosis with or without Helicobacter pylori eradication.

Methods: A cost-effectiveness (C/E) and cost-benefit (C/B) analysis were performed using simulated Markovian modelling on 100,000 individuals. Revealant clinical data introduced to the model were obtained from published data or from a consensus of experts. The C/E analysis evaluated the cost of one additional unit of efficacy, either the number of patients healed after the initial 4 week therapy, or the number of months before the first recurrence. The C/B analysis (from a collective point of view) evaluated the costs avoided per French Franc (FP) invested. The costs taken into account were the costs of treatment (H2 antagonists for the eradication strategy, omeprazole plus two antibiotics, followed in case of failure by H2 antagonists in eradication strategy), the cost of medical visits and the costs of gastroscopy. A sensitivity analysis was carried out to evaluate the effect of variations in clinical probabilities and costs, eg gastroscopy. The results presented are those where the strat-
Cost-effectiveness ratio* reduces per triple (HP) eradication. This strategy was evaluated within 17% of patients achieving 95% efficacy (max) and minimal maximal efficacy (max) (eradication: 95%).

Results: 5-year figures:

<table>
<thead>
<tr>
<th>Hyp. 1**</th>
<th>Hyp. 2**</th>
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<tbody>
<tr>
<td>Cost-effectiveness ratio*</td>
<td>Eрад (max eff)/AH2 (max eff)</td>
</tr>
<tr>
<td>Eрад (max eff)/AH2 (max eff)</td>
<td>3006 FF</td>
</tr>
<tr>
<td>Cost-benefit ratio***</td>
<td>Eрад (max eff)/AH2 (max eff)</td>
</tr>
<tr>
<td>Eрад (min eff)/AH2 (max eff)</td>
<td>-0.51 FF</td>
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</tbody>
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*p<0.001; **p< 0.05 Cochin-Manvel-Haenszel test.

Most common treatment related AE's were taste disturbance (MTT: 12; DT: 14); diarrhoea (MTT: 11; DT: 4) and increase in liver enzymes (MTT: 6; DT: 4). One-week MTT of PAN, CLA and MET is significantly superior to two-week DT with PAN and CLA in curing HP infection. Both treatments were similarly well tolerated.

4A: Clinical pharmacological aspects of H. pylori treatment

J.C. Yang 1, C.K. Yang 2, C.T. Shun 2, J.T. Wang 1, S.C. Lee, T.H. Wang 1,
1 Dept of Internal Medicine, National Taiwan University Hospital, Taipei, Taiwan, ROC; 2 Dept of Clinical Pathology, National Taiwan University Hospital, Taipei, Taiwan, ROC; 3 Dept of Pathology, National Taiwan University Hospital, Taipei, Taiwan, ROC; Institute of Nuclear Energy Research, Taoyuan, Taiwan, ROC

Recent reports suggest that omeprazole monotherapy partly suppresses and causes the redistribution of H. pylori (Hp) in the stomach. However, the effects of dual therapy and triple therapy containing omeprazole has not been well documented. The aim of this study was to analyze the intragastric distribution of Hp after treatment with regimens containing omeprazole. Methods: Ninety-eight patients with Hp(+)/ duodenal ulcer belonged to: grA (n = 29) received omeprazole 20 mg bid 2 wk; grB (n = 34) omeprazole 20 mg bid plus amoxicillin 500 mg qid 2 wk; grC (n = 35) omeprazole 20 mg bid plus amoxicillin 250 mg and metronidazole 250 mg qid 1 wk. All patients received 1C-Urea breath test and multiple endoscopic biopsies from antrum and body in each center (except for the first 4 weeks after anti-Hp therapy. Five specimens from each site were obtained: for culture using an improved culture system (sensitivity about 98%), one for CLO test, and two for histology. Results: The eradication rate of grA, grB and grC was 87.5%, 90%, and 91.4%, respectively. Totally, 46 patients remained Hp positive after treatment. The percentage of positive detection after treatment was 80% at antrum, 83% at body, and 90% with both sites by histology. These data were 83%, 78% and 85% by CLO test, and 98%, 98% by improved culture system. Conclusion: The detection rate was much higher and became constant with improved culture system. These data indicated that the difference of sensitivity between different tests may be one of the most important factors responsible for the lower detection rate. The so-called "patchy distribution" and "proximal migration from the antrum to the body after treatment" may in fact play a minor factor.