**EVALUATION OF THE EFFICACY OF CLARITHROMYCIN IN THE ERADICATION OF HELICOBACTER PYLORI (Hp).**

C. Spillios (1), S. Georgopoulos (1), F. Stamatakis (2), A. Manis (3), G. Gianakaki (2), Z. Manisi (5), N. Skandalis (6). Department of Gastroenterology (1) and Pathology (2), General Hosp. of Athens Department of Bacteriology (2), Hepatitis Pasteur Institute, Athens.

The triple treatment regimen (metronidazole, tetracycline and colloidal Bismuth subcitrate) is considered effective. It has a lower efficacy in the eradication of Hp although it is associated with undesirable events (such as glossitis, vertigo, diarrhea etc.). Recent studies have shown that clarithromycin (CL), particularly in combination with omeprazole (OM), has a similar efficacy in the eradication of Hp. The aim of this study was to evaluate the efficacy of CL alone and in combination with colloidal Bismuth subcitrate (CBS) comparatively with the triple treatment regimen for the eradication of Hp in patients with a healed duodenal ulcer (DU) after treatment with OM.

Patients-Methods: A hundred and two patients (73/29, men/women) with a documented Hp infection (by CLO-test, histology and culture) had a 14 days treatment with OM 20mg x 2. Ninety seven (97) patients with endoscopically healed DU were randomly assigned to one of the three treatment groups: the group A received CL alone 250mg x 4, the group B CL 250mg x 4 in combination with CBS 300mg x 4 and the group C metronidazole 500mg x 3, tetracycline 500mg x 4 plus CBS 300mg x 4. The eradication treatment was of 14 days duration in all the three groups. All the patients underwent a gastroscopy with biopsies 1 month after treatment completion, in order to assess the presence or absence of Hp. Results: Group A: eradication of Hp is in 22% patients (7%), and of the remaining 9 (29%) Hp positive patients, 4 (13%) had a recurrence of DU after the post treatment control. Group B eradication of Hp in 29/32 patients (90,4%), and from the 3 (9,6%) Hp positive patients, 1 (33%) had a recurrence of DU. Group C eradication of Hp in 29/43 patients (85,3%), and from the 5 (14,7%) Hp positive patients, 2 (53%) had a recurrence of DU. The response of treatment was significantly increased in group B compared to group A (P<0.05). The therapeutic response was not significantly different between patient groups C and patients of the two other groups. Five (5) patients of group C presented adverse events compared to no patient in groups A and B.

Conclusions: The combination therapy with CL and CBS has clear advantages over monotherapy withCBS in the eradication of Hp in patients with healed DU after post-treatment with OM. 2. Compared to classical triple therapy, the therapeutic regimes including CL has an equal efficacy and a better tolerability.

**ERADICATION OF HELICOBACTER PYLORI INFECTION: IS A DOUBLE THERAPY STILL SUITABLE?**

Caroli A, Kustatscher S\*, Boni M, Grasso GA\*, Sperti C, Di Mario F\*, Puglisi A. Institute of Surgical Semiotics, Feltre and Gastroenterology Division, Padua, Italy

The association of amoxicillin (A) and omeprazole (OM) has been proposed for the treatment of Helicobacter pylori (Hp) infection. Several factors, including doses and duration of the treatment can explain the wide range of the eradication rates obtained by different authors. The aim of this study was to evaluate if there is a dose dependent correlation between the amoxicillin dose and the eradication rate. One hundred and twenty consecutive duodenal ulcer (DU) patients were randomized in 3 different groups of treatment (40 patients each one). Hp infection was determined no gastric biopsies by CP tests and Giemsa stain all the DU patients received (O 20mg twice a day) for 4 weeks. In addition to the antisecretory treatment all the 3 groups received for the first 2 weeks: group A (A 500 mg three times a day), group B (A 1000 mg twice a day) and group C (1000 mg three times a day). All the groups were comparable for sex, age and smoking-habit. From the 4th to the 8th week all patients received ranitidine 150 mg at bedtime. A follow up endoscopy was performed after 8 weeks. And only when histology (H&E and Giemsa stains) and CP test were both negative the infection was considered to be cured. RESULTS: Hp infection was eradicated in 51.2% (20/39), 61.5% (24/39) and 78.9% (30/38)(*) in group A, B and C, respectively. (*)P<0.01 vs. group A). Only 4 out of 120 patients (3.3%) spontaneously discontinued the suggested therapy because of the side effects. **CONCLUSIONS:** 1) Amoxicillin in combination with omeprazole (40 mg/day) dose dependently increase Hp eradication rate. 2) Amoxicillin, even at the dose of 3 mg/day, confirmed to be a very safe antibiotic characterized by a very low side-effect rate. 3) A double therapy with amoxicillin for Hp eradication, in duodenal ulcer patients, might be suggested only at the highest (3 mg/day) dose.
ALTERNATIVE TRIPLE THERAPY FOR HELICOBACTER PYLORI (Hp) RELATED DUODENAL ULCERS (DU). G.L.S.U. (Interdisciplinary Study Group for Ulcer Study), Italy. It has been demonstrated a close correlation between Hp-infection and DU. Successful antimicrobial treatment has been shown to dramatically reduce the frequency of DU recurrences. The majority of antimicrobial schedules consist of in the association between Pylorin Pump Inhibitors (PPI) and one or two antibiotics like Amoxicillin (AMO) and Metronidazole (METRO), good results have also been reported with Amoxicillin plus antibiotics. No studies comparing H2-antagonists triple therapy with PPI double, triple or quadruple therapies.

AIM: To compare Hp-eradication rates using two doses of H2- antagonists (Ranitidine, RAN) triple therapy with Omeprazole (OME) double, triple or quadruple therapy.

METHODS: 151 active DU patients with Hp-infection consecutively referred to different Endoscopy Units in North-East of Italy and randomly assigned to one of the following treatments:
1) OME 40mg plus AMO 4 x 500mg
2) OME 40mg plus AMO 4 x 500mg plus METRO 4 x 250mg
3) OME 40mg plus AMO 4 x 500mg plus METRO 4 x 250mg plus BCS 4 x 120g
4) RAN 300mg plus AMO 4 x 500mg plus METRO 4 x 250mg
5) RAN 2 x 300mg plus AMO 4 x 500mg plus METRO 4 x 250mg plus BCS 4 x 120g

All antibiotic treatments persisted for 2 weeks while antisecretory treatments lasted 4 weeks. The diagnosis of Hp-infection was based on 7 biopsies (gastric antrum, angulus, body) for histology (Giemsa method modified and rapid urease test). Endoscopy was repeated 1 month (T1) and 4 months (T5) after the beginning of therapy.

RESULTS: All pts. completed the treatment. At endoscopy T1, 10 pts. were healed (8 Hp-negative; 2 Hp-positive) and left the study. At endoscopy T3, 7 pts. presented DU recurrence (1 Hp-negative; 6 Hp-positive) and 1 gastric ulcer Hp-positive (high grade lymphoma revealed by histological assessment).

133 pts. persisted healed (98 Hp-negative; 35 Hp-positive). The percentage of Hp-eradication for each regimen were as follows: 1) 56%; 2) 88-98%; 3) 89-89%; 4) 75-10.2%.

CONCLUSIONS: 1) Double therapy Omeprazole plus Amoxicillin cannot be proposed for Hp-eradication, having proved an eradication rate lower than 60%. 2) Omeprazole triple and quadruple therapy have comparable eradication rates (both over 80%); 3) Triple therapy with H2-antagonists revealed good effectiveness in eradicating Hp-infection of about 70%.

EFFECT OF HPYLORI ERADICATION ON THE SEVERITY OF DYSPESPERIC SYMPTOMS IN DU PATIENTS - A ONE YEAR FOLLOW UP STUDY. E. El-Omar, A. Witz, K.E.L. McCall, University Department of Medicine and Therapeutics, Western Infirmary, Glasgow, Scotland.

Eradication of H pylori markedly reduces the DU relapse rate. However, very little data is available regarding the effect of eradication therapy on the severity of dyspeptic symptoms in DU patients. We have recently developed and validated a new tool for the global measurement of dyspepsia (The Glasgow Dyspepsia Severity Score). This scores the severity of dyspeptic symptoms on the basis of: frequency and severity of symptoms, frequency of medical consultation and investigations, time off work, and usage of prescribable and off-the-counter medication. Each category is scored on a sliding scale giving a combined maximum possible score of 21. We used this tool to study the symptomatic response in DU patients receiving eradication therapy.

Subjects and Methods: Thirty one endoscopically proven DU patients with H pylori had their dyspeptic symptoms scored before and at one year following eradication therapy consisting of two weeks treatment with Tripletratium Citratobismuthate 120mg t.i.d., Metronidazole 400mg t.i.d and Amoxicillin 500mg t.i.d. The DU dyspeptic scores were compared with those from eighty age and sex matched healthy subjects selected randomly from the same catchment area; thirty of the healthy subjects had sought medical advice for dyspepsia though 28 (35%) were positive for H pylori infection. H pylori status of all subjects was determined by the 13C urea breath test.

Results: The mean dyspeptic score in the 31 DU patients before eradication therapy was 12.7 (range: 7-17) compared to 1.7 (range: 0-3) in the 80 healthy subjects. (p=0.001). In 25 DU patients the infection was successfully eradicated and their mean dyspeptic score fell to 1.8 (range: 0-9) which is equivalent to that in the healthy subjects. In the three DU subjects in whom the infection was not eradicated their dyspeptic scores were similar before [9.1±1.1] and one year after receiving the therapy (10.1±1.1 respectively).

Conclusions: H pylori markedly reduces dyspeptic symptoms in DU patients, restoring their severity and frequency to that of the general population.


Introduction: Bismuth triple therapy achieves 85-95% Helicobacter pylori eradication (HPE) rate, but is encumbered with side effects. MTZ resistance is reported to lower HPE rates. Aim: To compare two triple therapies of 14 days duration in patients with HP positive duodenal ulcer disease and the significance of primary MTZ susceptibility on HPE rates: 1) "BTM" (bismuth substrate 75mg qid, oxytetracycline 500mg qid, metronidazole 400mg bid) and 2) "OAM" (omeprazole 20mg bid, amoxicillin 750mg bid, metronidazole 400mg bid).

Methods: HP infection was confirmed by biopsy cultured up to 12 days, microscopy and urease test. MTZ susceptibility was determined by the Epiometer test, and MTZ resistance defined as MIC>16mg/l. Patients completed a self-assessment questionnaire with grading of side effects. Follow up endoscopy with HP status was performed 6 weeks after treatment.

Results: HPE rates with bismuth triple therapy were 90% (n=50) for MTZ sensitive strains and 95.7% (n=23) for resistant strains. In omeprazole triple therapy HPE rates for MTZ sensitive strains were 97.7% (n=44) and for resistant strains 63.6% (n=11). There were differences in reported severe side effects; "BTM" 25% and "OAM" 7% (p=0.015).

Conclusions: 1) Triple therapy with bismuth is efficient in HP eradication in both sensitive and primary MTZ resistant HP strains. 2) HP rates with omeprazole triple therapy are reduced in MTZ resistant strains. 3) "OAM" therapy seems more tolerable than "BTM" therapy.

TWICE A DAY THERAPY WITH OMEPRAZOLE FOR CURE OF HELICOBACTER PYLORI (HP) INFECTION. F. Lerang, B Mouni, E Raghfildstveni, T Hauge, P Tölls, E Aubert, M Henriksen, P S Efiskind, K Nasciotes, Fredrikstad Hospital, T Torslanda, Norway.

Introduction: Cure of HP infection reduces the rate of ulcer relapse. Triple therapy with bismuth cures HP infection in 85-95%, but is encumbered with side effects and inconvenience of dosage.

Aim: To compare two triple therapies of 2 weeks duration in patients with HP positive duodenal ulcer (DU) disease. Bismuth substrate 75mg qid, oxytetracycline 500mg qid and metronidazole 400mg bid ("BTM") and omeprazole 20mg bid, amoxicillin 750mg bid and metronidazole 400mg bid ("OAM").

Methods: Patients with DU and HP infection, were randomised to treatment with "BTM" or "OAM" after ulcer healing treatment with H2-blocker. HP infection was confirmed by biopsy cultured up to 12 days, microscopy and urease test. MTZ susceptibility was determined by the Epiometer test, and MTZ resistance defined as MIC>16mg/l. The patients completed a self-assessment questionnaire with grading of side effects. Follow up endoscopy with HP status was performed 6 weeks after treatment.

Results: Of the 128 patients included in this study, 27% had MTZ resistant HP strains. Eradication rates irrespective of MTZ susceptibility: 91.8% for "BTM" and 90.9% for "OAM". There were differences in reported side effects; 25% in "BTM" vs. 7% in "OAM" (p=0.015). Six patients interrupted the treatment (five in "BTM" and one in "OAM").

Conclusions: 1) Both treatment regimens are highly efficient for cure of HP infection. 2) Triple therapy with omeprazole is more tolerable than triple therapy with bismuth.
HIGH EFFICACY OF A CLARITHROMYCIN-AMOXICILLIN-OMEPRAZOLE ASSOCIATION FOR H. PYLORI ERADICATION AND TREATMENT OF ULCER-LIKE OR REFLUX-LIKE DYSPTEptic SYMPTOMS.

E. Trespi, L.Villani, F. Broglio, O. Lainez, C. Colla, B. Fiocca, E. Soldati. Digestive Endoscopy and Pathology Services, IRCCS Policlinico San Matteo and Department of Pathology, University of Pavia, 27100 Pavia, Italy.

Among a series of 179 patients undergoing endoscopy for dyspeptic symptoms, 117 were found to be H. pylori positive by both urease test and histology (Giemsa stain and immunoperoxidase test on 7 antral, angulus or corpus biopsies). All the 117 patients were treated for 10 days with omeprazole 20 mg b.i.d., amoxicillin 500 mg qds or tetracycline 500mgds and metronidazole 500 mg tds. One patient was lost to follow-up.

Treatment: 1) Omeprazole 20 mg bd, amoxicillin 500 mg tds and metronidazole 400 mg for one week.

2) Standard triple therapy of a) bismuth 120mg qds, amoxicillin 500mg qds or tetracycline 500mgds and metronidazole 500 mg tds.

3) Omeprazole 20 mg bd, amoxicillin 500 mg tds and clarithromycin 250 mg tid and 400mg for one week, all patients in whom previous course had failed.

Side effects (diarrhea, rash and headache) were reported in 205/668 (30.6%) and the incidence was the same in treatment success and failures (31% and 30%, NS).

CONCLUSIONS: Simple one week Helicobacter pylori eradication regimes are successful in everyday practice, and one week course not containing metronidazole was highly successful in those whose treatment had failed.

THE ERADICATION OF HELICOBACTER PYLORI IN PRACTICE: AN AUDIT OF THREE YEARS CLINICAL EXPERIENCE WITH PEPTIC ULCER PATIENTS.

TG. Reilly, V. Poxx & R.P. Wait. Department of Medicine, Queen Elizabeth Hospital, Birmingham.

AIM: To compare the performance of different eradication regimes in the everyday management of Helicobacter-positive peptic ulcer.

Between February 1992 and February 1994, 668 unselected patients with proven peptic ulcer (467 males, 201 females, median age 53, range 18-83) of whom 574 had duodenal ulcer (4 perforations, 3 GI bleed) and 90 gastric ulcer, 103 both, 3 unspecified, underwent a course of eradication therapy and had a subsequent 13C-urea breath test at least 4 weeks after finishing. Age, date, type of treatment, test result and side effects were recorded. The main therapeutic regimes were as follows:

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Eradicated</th>
<th>Failed</th>
<th>Rate (%)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>OAT1</td>
<td>359</td>
<td>65</td>
<td>83.9</td>
<td>80.3-87.5</td>
</tr>
<tr>
<td>SST2</td>
<td>149</td>
<td>46</td>
<td>76.4</td>
<td>70.1-82.8</td>
</tr>
<tr>
<td>OAT1</td>
<td>19</td>
<td>0</td>
<td>100</td>
<td>82.4-100</td>
</tr>
<tr>
<td>Overall</td>
<td>344</td>
<td>124</td>
<td>81.4</td>
<td>75.8-84.4</td>
</tr>
</tbody>
</table>

TREATMENT OF PATIENTS WITH NEW DSPYPTIC SYMPTOMS AND DDOENAL ULCERS: GUIDELINES FOR THE GENERAL PRACTITIONER.

B. Raithe, Dept Gastroenterology, Leicester Royal Infirmary, England on behalf of the H. pylori Review Group.

Peptic ulcer disease affects 5% to 10% of the British population at some time during their lives with 70% to 80% of those having a 25% chance of duodenal ulcer pts infected by H. pylori. As our understanding about the causal relationship between H. pylori and peptic ulcer disease has evolved over the last five years, so have approaches to the management of H. pylori associated disease. While H. pylori associated ulcer disease is now curable, strategies for patient selection and management are in evolution. The H. pylori Review Group, nine clinicians representing academic centres, hospitals and general practices in Britain was formed to develop, based on clinical data and experience, consensus treatment (tx) guidelines for use by GPs caring for pts with new symptoms of dyspepsia and duodenal ulcer. The results of their efforts are presented. Among pts with newly presenting dyspeptic symptoms, those <45 yrs old should be considered for H. pylori detection (by serologica carbon dioxide breath test) and eradication tx.

<table>
<thead>
<tr>
<th>Symptom</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
</tr>
</thead>
<tbody>
<tr>
<td>a) Pain relieved by food/antacids</td>
<td>37</td>
<td>5</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>b) Periodic pain</td>
<td>12</td>
<td>6</td>
<td>4</td>
<td>0.001</td>
</tr>
<tr>
<td>c) Postprandial pain</td>
<td>41</td>
<td>3</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>d) Nocturnal pain</td>
<td>18</td>
<td>0</td>
<td>0</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>e) Heartburn</td>
<td>22</td>
<td>3</td>
<td>2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>f) Acid regurgitation</td>
<td>18</td>
<td>2</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>g) Nausea and/or vomiting</td>
<td>26</td>
<td>4</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>h) Early satiety and/or anorexia</td>
<td>43</td>
<td>37</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>i) Abdominal distension</td>
<td>42</td>
<td>34</td>
<td>2</td>
<td>NS</td>
</tr>
<tr>
<td>j) Excessive belching</td>
<td>18</td>
<td>14</td>
<td>1</td>
<td>0.044</td>
</tr>
</tbody>
</table>

Patients with symptom before (A) persisiting after (B) therapy and patients with newly aquired symptom after therapy (C)