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Increased Prevalence of Helicobacter pylori 23s rRNA Gene Mutations in

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M1090 Rifabutin Resistance of *H. pylori* Isolated from Japanese Patients
Shoji Suzuki, Hidekazu Suzuki, Tsushito Nishizawa, Fumihiko Kaneko, Yoshimasa Saito, Sumire Ootani, Hiroe Muraoka, Inetsu Kobayashi, Mamoru Miyari, Tsushihumi Hibi
Background and Aim. Recently, the number of *Helicobacter pylori* ( *H. pylori*) isolates showing antibiotic resistance has rapidly increased. Rifabutin is a novel antibiotic that has shown promise in several controlled. Aim: To perform a systematic review and meta-analysis to determine the therapeutic efficacy of rifabutin as a component of *H. pylori* eradication therapy. Methods: Patients with *H. pylori* infection were assigned to 6 regimens: 1) placebo, 2) rifabutin 450 mg once daily for 7 days, 3) rifabutin 450 mg once daily for 2 weeks, 4) rifabutin 450 mg once daily for 4 weeks, 5) rifabutin 450 mg once daily for 8 weeks, and 6) rifabutin 450 mg once daily for 12 weeks. The primary outcome was *H. pylori* eradication as determined by the urease test and biopsy. Results: Of the 48 strains (MIC<0.015). On the other hand, seven of the 46 strains (15.2%) isolated from the patients at National Minami-Yokohama Hospital showed point mutations in the resistance-determining regions of the *rpf* gene of rifabutin, and the MICs of rifabutin were high (MIC > 0.5) for five of these seven strains (71.4%) with point mutations in the *rpf* gene (PPV: 71.4%, NPV: 97.7%: sensitivity: 71.4%; specificity: 97.7%; p<0.001). In particular, the MICs were high for strains isolated from patients with a past history for treatment with rifampicin (PPV: 85.7%, NPV: 98.9%: sensitivity: 85.7%; specificity: 98.9%; p<0.001). And, the relationship between the MICs of RB (more than 0.01 μg/ml) and RFP for the strains is a significant linear correlation. Conclusion: rifabutin might be a potential candidate component of a new regimen for *H. pylori* eradication therapy following failure of the first-line and/or second-line regimens, it should be used only after the patient is checked for a past history of treatment with rifampicin.

M1091 Ten-Day Sequential Therapy Is Superior to Triple Therapy for the Eradication of *Helicobacter pylori*: Systematic Review and Meta-Analysis
Luigi Gatta, Dino Vara, Nimish Vakil
Background: The success of the current recommended therapy for *H. pylori* infection (PPI-triple therapy) has declined to unacceptable levels. Sequential therapy is a novel treatment strategy that has shown promise in several controlled. Aim: To perform a systematic review and meta-analysis to determine the therapeutic efficacy of sequential therapy compared to the PPI-triple therapy in adults and children. Data Sources: Studies were identified by searching the Cochrane Trial Register (Issue 3, 2007), MEDLINE (1966 - September 2007), EMBASE (1980-September 2007), two relevant灰色的期刊abstracts from the major US and European gastroenterology conferences. Study Selection: Randomized controlled trials comparing sequential therapy to PPI-triple therapy in adults and children *H. pylori* infected. Data Extraction: Two investigators separately performed the search, selected the studies, and performed data extraction. Quality assessment was performed using a scale described by Jadad. A third investigator arbitrated in the event of a lack of agreement. Subgroup analyses were performed evaluating age, patients, duration of triple therapy, Jadad score, presence of NUD or PUD, number of tests performed to confirm the eradication. Results: 70 randomized controlled trials enrolled adult patients and the pooled relative risk for eradication of *H. pylori* with sequential therapy compared to triple therapy was 1.22 (95% CI 1.03 to 1.43), 12% (p<0.001) with a number needed to treat of 6 (95% CI: 5 to 7). 2 studies enrolled children and adolescents, and the pooled relative risk for eradication of *H. pylori* with sequential therapy compared to triple therapy was 1.21 (95% CI 1.01 to 1.40), 12% (p<0.001) with a number needed to treat of 6 (95% CI: 5 to 6). Conclusion: Sequential therapy is superior to triple therapy in the eradication of *H. pylori*. It should be evaluated further as a potential new first-line therapy in infected patients

M1092 A Randomized Double Blinded Clinical Trial with Omeprazole, Levofloxacin and Escalated Dose of Rifaximin for *Helicobacter pylori* Infection in Treatment-Naive Population
F. Patrick Basu, Krishna Rayapudi, Jose Estevez
Purpose: *Helicobacter pylori* (H pylori) is an innocuous with a significant progression to gastric carcinoma, lymphoma and peptic ulcer disease. Aims: To evaluate the efficacy and safety of an ESC Rubin-dosed rifaximin (Rifaximin 800 mg, Omeprazole 20 mg and Levofloxacin 250 mg) all twice daily for 10 days and the other arm (n=15) with Rifaximin 800 mg, Omeprazole 20 mg, and Levofloxacin 250 mg all twice daily for same duration. Follow up stool testing for *H pylori* antigen was performed after cessation of Omeprazole for at least 2 weeks. Results: 6 patients(46%) and 8 patients(53%) cleared *H pylori* in the 600mg Rifaximin and 800mg Rifaximin arms respectively. 10 patients(33%) experienced mild to moderate side effects but completed the full course. Conclusion: There is no statistically significant benefit with escalated doses of rifaximin for eradication of *H. pylori*. These regimen's eradication rate compared with 50% in the standard 800mg daily, daily, rifaximin may need higher doses of rifaximin to achieve a similar efficacy.

M1093 Levofloxacin- and Amoxicillin-Based Quadruple Therapy for the Third-Line Treatment of *Helicobacter pylori*, Infection
Ping-I Hsu, Deng-Chyang Wu
Background: A standard third-line therapy for *Helicobacter pylori* (H pylori) infection is lacking, and antimicrobial sensitivity data for patients failing eradication are often unavailable in clinical practice. We therefore designed the prospective study to assess the efficacy of a novel third-line levofloxacin- and amoxicillin-based quadruple therapy. Patients and methods: From January 2005 to August 2007, 42 consecutive patients with *H pylori* infection who had failed standard first-line and second-line treatments underwent a 10-day quadruple therapy comprising rabeprazole 20 mg b.d., bismuth subcitrate 300 mg q.d.s., amoxicillin 500 mg q.d.s., and levofloxacin 500 mg o.d. Follow-up endoscopy with rapid urease test, histological examination and culture were performed at six weeks after the end of treatment to evaluate the response to therapy. Results: *H pylori* was successfully eradicated in 37 out of 42 patients (88% by both intention-to-treat analysis and per-protocol analysis) in all patients (100%) completed with the eradication therapies, and none (0%) patients complained of mild-to-moderate side events. Amoxicillin- and levofloxacin-resistant strains were observed in 17% and 22% clinical isolates, respectively. There were no significant differences between *H pylori* eradication rates and antibiotic resistances. Conclusions: The 10-day levofloxacin- and amoxicillin-based quadruple therapy is well tolerated and achieves a high eradication rate in third-line empirical treatment for *H. pylori* infection.

M1094 Increased Prevalence of *Helicobacter pylori* 23s RNA Gene Mutations in Patients with Gastritis in Pakistan
Javed Yakoob, Waisim Jafri, Zaigham Abbas, Shahid Abid, Rustam Khan, Nida Jafri, Zaigham Ahmad
Background The major cause of *Helicobacter pylori* treatment failure is clarithromycin resistance which is attributed to point mutations within the phosphoriberanase-encoding region in domain V of the 23sRNA gene. Several distinct point mutations including A2142G, A2143G, A2142C, A2115G and G2141A have been described. The aims of this study was to determine the prevalence of clarithromycin point mutations A2142G, A2143G and A2142C in patient presenting nonulcer dyspepsia, gastric and duodenal ulcer and gastric carcinoma and lymphoma. Methods PCR restriction fragment length polymorphism (PCR-RFLP) was used to allow the identification of mutations A2142G and A2143G using the Bsd1 and BsaI restriction enzymes, respectively and for detection of the *mcmR* mutation A2115G using the BceAI. A 267-bp fragment was amplified by PCR using primers 5'-ACGTTAAGGATGTTTGG CAGTC-3' (HPY-B3) and 5'-CCTGATATTTCCCCAT- TAGC AGT-3' (HPY-A), corresponding to nucleotides 1931 to 1952 and 2197 to 2175, respectively, of the 23S rRNA gene of *Helicobacter pylori*. Differences in proportion were assessed by Pearson Chi square, Fisher exact or likelihood ratio test where appropriated. P value was 0.05.

Population
In the study population of 30 patients of diverse ethnic background with stool antigens positive in 74(80%) and lymphoma 3 (3%), respectively. 7(8%), gastric carcinoma 15(16%) and duodenal ulcer in 5(5%). Histology showed acute gastritis in 34(37%) patients. Mutations were common in patients with symptoms p=0.008 Endoscopically, antral gastritis was present in 32(34%), gastritis 34/37%, gastric ulcer 7(8%), gastric carcinoma 15(16%) and duodenal ulcer in 9(5%). Histology showed acute on chronic inflammation in 57(62%), chronic inflammation 18(19%), gastric adenocarcinoma 15(16%) and lymphoma 3 (3%), respectively. *Helicobacter pylori* was positive on histology in 74(80%) and *H pylori* qmPCR in 93(100%) patients. CLR mutations were significantly
present in patients with gastritis 30(88%) as compared to gastric carcinoma 11(3%) and peptic ulcers 3(9%) (p < 0.02). On histology, 24 (71%) patients with chronic active gastritis had C. pylori compared to 29(20%) in patients with chronic inflammation and gastric carcinoma and lymphoma 1(3%) (p < 0.004). Conclusion: Clarithromycin mutations were present in clinical isolates of H. pylori. They were significantly associated with endoscopic gastritis with chronic active gastritis compared to peptic ulcer and gastric carcinoma.

M1095
Empirical Rescue Therapy After H. pylori Treatment Failure: A 10-Year Single Center Study of 500 Patients
Javier P. Guberti, Jose-Luis Guberti, Eusebio Marcos, Isabel Jimenez-Alonso, Adrian G. McNicholl, Rodrigo Moreno-Otero, Jose-María Pajares

BACKGROUND: The most commonly used first-line eradication therapies may fail in up to 20-30% of patients. Several “rescue” therapies have been recommended, but they still fail to eradicate H. pylori in more than 20% of the cases. Currently, a standard third-line therapy is lacking, and international guidelines recommended culture in these patients to select a third-line treatment according to microbial sensitivity to antibiotics. However, cultures are often not obtained only in research centers, and the use of this procedure as “rescue” therapy in patients who failed several treatments is not feasible. AIM: To evaluate the efficacy of different “rescue” therapies empirically prescribed (antibiotic susceptibility was unknown) during 10 years to 500 patients in whom at least one eradication regimen had failed to cure H. pylori infection. METHODS: Design: Prospective single-center study. Patients: Consecutive patients in whom at least one eradication regimen had failed. Intervention: Rescue regimens included: 1) Quadruple therapy with omeprazole-bismuth-tetracycline-metronidazole; 2) ranitidine bismuth citrate-tetracycline-metronidazole; 3) omeprazole-amoxicillin-levofoxacin, and 4) omeprazole-amoxicillin clarithromycin. Antibiotic susceptibility was unknown (rescue regimens were chosen empirically). Outcome: Eradication was defined as a negative 13C-urea breath test 4-8 weeks after completing therapy. RESULTS: Five-hundred patients were included (76% functional dyspepsia, 24% peptic ulcer). Compliance with 2nd, 3rd, and 4th-line regimens was 92%, 92%, and 95%. Adverse effects were reported by 30%, 37%, and 55% of the patients receiving 2nd, 3rd, and 4th-line regimens. Overall, H. pylori cure rates with the 2nd, 3rd, and 4th-line rescue regimens were 70%, 74%, and 76%. Cumulative H. pylori eradication rate with 4 successive treatments was 99.5%. CONCLUSION: It is possible to construct a rescue treatment strategy to maximize cure rates on the administration of four consecutive empirical regimens; thus, performing bacterial culture even after a second or third failure of cure may not be necessary.

M1096
High Dose vs. Standard Dose Proton Pump Inhibitor Triple Therapy for Helicobacter pylori Infection: A Meta-Analysis
Albert Villoria, Xavier Calvet, Pilar Garcia, Javier P. Guberti, Valenti Puig Divi

Introduction: The usefulness of using high-dose proton pump inhibitor (PPI) in triple therapy for H. pylori eradication is controversial. Objective: To review the evidence on the possible usefulness of high dose PPI in standard triple therapy for Helicobacter pylori eradication. Methods: A systematic search was performed in multiple databases (MEDLINE, ISI Web of Knowledge, Embase, Cochrane Database of Randomized trials and CINAH), and in the abstracts submitted to the Digestive Diseases Week and the European Helicobacter Study Group congresses between 2000-2007. The references of the relevant articles or reviews were also assessed. Randomized trials comparing a standard dose PPI (omeprazole, rabeprazole or esomeprazole 20 mg, lansoprazole 30 mg or pantoprazole 40 mg) twice a day, or high dose PPI (esomeprazole, rabeprazole or omeprazole 40 mg, lansoprazole 60 mg or pantoprazole 80 mg) twice a day, in triple therapy, strategies combining a PPI plus clarithromycin and either amoxicillin or metronidazole were selected. Results: Six studies including 1703 patients (76% functional dyspepsia, 24% peptic ulcer) were included (76% functional dyspepsia, 24% peptic ulcer). Compliance with 2nd, 3rd, and 4th-line regimens were chosen empirically). Outcome: Eradication was defined as a negative 13C-urea breath test at 4-8 weeks after completing therapy. RESULTS: Results were compared to our previous analyses from the PHS database over the years 1992-2000. Results: There were 2,361,578 hospital discharges from 2002-2007 compared to 2,052,743 from 1992-2000 (32 US pediatric hospitals included). The proportion of discharged patients with diagnoses of PUD, gastritis, and HP are shown in Table 1, overall PUD prevalence increased significantly for this period. 1121 (0.047%) patients had a discharge diagnosis of bleeding ulcers from 2002-2007. From 2002-2007, HP infection was associated with a greater number of children hospitalized with duodenal ulcer (DU; 16.5%) than with gastric ulcer (GU; 6%). Of 1578 children with a diagnosis of HP, 1191 (75.5%) had a concurrent diagnosis of gastritis or duodanitis, 314 (19.9%) had a diagnosis of gastrointestinal bleeding, 94 (6%) had a diagnosis of GU, and 178 (11.3%) had a diagnosis of DU. Yearly percentages of total discharges significantly declined in PUD, and gastric duodenitis plus HP between 2004 and 2005 (p=0.005 and p=0.002 respectively), which mirrors a decline in HP (p=0.001) these same years. These discharge diagnoses increased subsequently. Gender, race/ethnicity, and age all affected rates of discharges due to PUD, gastritis, and HP. Discussion: Rates of discharge diagnoses of PUD, HP, and gastritis have increased significantly in hospitalized children over the past 15 years. The decline in HP seen in pediatric hospitals from 2004 to 2005 is similar to adult studies over the same years. The case for this temporary decrease in HP-related discharge diagnoses is unclear. Prospective studies are needed to determine if such epidemiologic data of PUD and the impact of HP infection among children in outpatient populations. Future PHS analyses will include extensive demographic information and financial impact that PUD and associated complications have on the pediatric health system.

Table 1. Percentages of total discharges, PHS

<table>
<thead>
<tr>
<th>Years</th>
<th>PUD(%)</th>
<th>Gastritis(%)</th>
<th>HP(%)</th>
</tr>
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<tbody>
<tr>
<td>1992-2000</td>
<td>0.12</td>
<td>0.6</td>
<td>0.03*</td>
</tr>
<tr>
<td>2000-2007</td>
<td>0.13*</td>
<td>0.72*</td>
<td>0.07*</td>
</tr>
</tbody>
</table>

*Only data from 1995-2000 is available, *p < 0.0001

M1097
Symptom Association During Impedance Testing (pH-MII) Is Not Useful in Predicting Outcome After Fundoplication
Rachel Rosen, Phillip Levine, Paul D’Amico, Samuel Nurko

Background: Causal relationships between symptoms and gastroesophageal reflux are difficult to prove. Previous pilot data has suggested that the number of reflux events detected by pH-MII may not predict outcome after fundoplication. The purpose of this study was to determine if symptom association during pH-MII testing is useful to predict which patients will improve symptomatically after fundoplication.

Methods: Children with peptic ulcer disease were given pH-MII testing between January 2002 and October 2007. Records for patients who underwent fundoplication with preceding pH-MII testing were reviewed. 34 children were included in the analysis. pH-MII tracings were blindly reviewed and the symptom index (SI) and the symptom sensitivity index (SSI) were determined for each patient. Patients were categorized as improved or not improved after surgery. Patients who improved were further classified as improved or not improved after surgery. Results were compared to our previous analyses from the PHIS database over the years 1992-2000. Data were analyzed using Student’s t-test for continuous variables and the chi-square test for categorical variables. Conclusion: Symptom association during pH-MII testing is not useful in predicting outcome after fundoplication.