ΠΡΟΣΚΕΚΛΗΜΕΝΕΣ ΞΕΝΟΓΛΩΣΣΕΣ ΑΝΑΚΟΙΝΩΣΕΙΣ ΕΛΛΗΝΩΝ ΕΡΕΥΝΗΤΩΝ

● IS THERE AN ASSOCIATION BETWEEN *HELICOBACTER PYLORI* INFECTION AND INFLAMMATORY BOWEL DISEASE: A META-ANALYSIS

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Background: There are epidemiologic data suggesting a protective effect of *Helicobacter pylori (H. pylori)* infection against the development of autoimmune disease. In addition laboratory data illustrate *H. pylori's* ability to induce immune tolerance and limit inflammatory responses. Numerous studies have examined the association between *H. pylori* infection and inflammatory bowel disease (IBD).

Aim: The aim of this study was to perform a meta-analysis on the association between *H. pylori* infection with Crohn's disease (CD) and ulcerative colitis (UC).

Methods: Extensive Medline and EMBASE English language medical literature searches for human studies were performed through April 2010, using suitable keywords. Pooled estimates were obtained using fixed or random effects models as appropriate. Heterogeneity between studies was evaluated with the Cochran Q test whereas the likelihood of publication bias was assessed by the Begg and Mazumdar adjusted rank correlation test and by the Egger's regression test.

Results: For CD the pooled odds ratio (OR) with 95% conflidence intervals (CI) were 0.405 (0.316-0.520), test for overall effect Z = -7.124, p<.0001. The heterogeneity Q value was 48.118, I^2 = 60.514, p<.0001. For UC the pooled Ors were 0.516 (0.403-0.660), Z=-5.62, p<.0001. The heterogeneity Q value was 28.059, I^2=50.105, p<.0001. There was no publication bias.

Conclusions: These results suggest a protective role of *H. pylori* infection against the development of IBD. Therefore, further studies investigating the effect of eradication of *H. pylori* on the development of IBD are warranted and also studies in *H. pylori* experimental models are necessary to further define the mechanism of this negative association.

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● IMPLICATION OF CAGTA EPIYA-C PHOSPORYLATION IN IL-8 INDUCTION BY GASTRIC EPITHELIAL CELLS

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New findings suggest that presence of CagA in *H. pylori* strains is required for full IL-8 induction. Our aim was to investigate the impact of CagA tyrosine phosphorylation of repearing EPIYA-C domains, on IL-8 activation and secretion by gastric epithelial cells. Based on *H. pylori* strain P12, we constructed genetically modified isogenic mutants expressing CagA protein with variable IPIYA-C phosphorylation motifs (AB, ABCC, ABCCC) and their respective EPIFA-C phosphorylation deficient counterparts (ABFFF). These strains were used to infect AGS cells for 0, 2, 4 and 24 hours. IL-8 gene activation was quantified by Quantitative Real Time PCR and concentration of secreted IL-8 was determined in supernatants with ELISA. The presence of EPIYA-C phosphorylation, independent of the motifs number (2 or 3) significantly increased the activation of IL-8 gene by approximately 120 times in 2 hours post infection (p.i.). However, strains expressing CagA without EPIYA-C motifs (AB) or carrying phosphorylation deficient motifs (ABFFF), failed to fully activate IL-8 gene transcription. Moreover, the ABFFF strain failed to induce IL-8 protein. At 4 hours p.i. IL-8 gene activation reached background levels in all cases, except for ABCCC type which retained about 50% activation of IL-8 gene. No IL-8 gene activity was detected at 24 hours p.i. but IL-8 concentration in supernatants appeared dependent on the number of EPIYA-C motifs. Time-dependent NF-kB activation analysis was concordant with these findings. In conclusion, phosphorylation of CagA on EPIYA-C motifs, plays an important contributing role in the full transcriptional activation of IL-8 gene and subsequent secretion of IL-8.

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● PRIMARY ANTIBIOTIC RESISTANCE AND HELICOBACTER PYLORI VIRULENCE FACTORS – IS THERE AN ASSOCIATION?

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Our aim was to study any potential association between the presence of H. pylori virulence factors and primary H. pylori antibiotic resistance to amoxicillin (AMO), clarithromycin (CLA), tetracycline (TET), metronidazole (MET) and levofloxacin (LEV) in Greek adult and children patients. A total of 133 clinical H. pylori strains were isolated from 69 adults (age 53.8 $\pm$ 14) and 64 children (age 10.7 $\pm$ 2.8) following gastroscopy. None of the patients had received any previous eradication therapy of PPIs. Antibiotic susceptibility was determine by E-test. MIC breakpoints adopted were >0.5 mg?L for AMO, CLA and LEV, >1mg/L for TET and >8 mg/L for MET (3rd European Multicentre Study on *H. pylori* antibiotic susceptibility). *VacA* genotypes (s, I and m) as well as *cagA* presence and EPIYA status were determined by polymerase chain reaction. Eighty eight (66.2%) strains exhibited resistance to one or more antimicrobial agents, mainly to CLA (adults: 18/69, 26.1%; children 29/64, 45.3%), MET (adults: 28/69; 40.6%; children 18/64, 28,1%) and LEV (adults: 11/69, 15.9%; children 1/64, 0.2%). No association was detected between *vacA* genotypes and antibiotic resistance. However, a significant association between *cagA*-negative status and the presence of antibiotic resistance to at least one antimicrobial agent was observed within our population (p=0297, OR: 1.346, 95% CI: 1.07-1.69). This was evident in the adult (p= .0297, OR: 1.469, 95% CI: 1.09-1.97) rather than the children group (p= .2907). High primary resistance rates to clarithromycin and metronidazole were observed. Absence of *cagA* gene might be a risk factor in the development of antimicrobial resistance.

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● PREVALENCE OF *HELICOBACTER PYLORI* INFECTION IN PATIENTS WITH LIVER CIRRHOSIS

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Background: *Helicobacter pylori (HP)* infection plays a crucial role in the pathogenesis of a variety of gastric diseases ranging from dyspepsia and peptic ulcer to gastric adenocarcinoma and gastric MALT lymphoma. The role of HP in liver cirrhosis is still conflicting.

Aim: To investigate the prevalence of HP infection in patients with liver cirrhosis and to correlate it with gastric pathology.

Methods: Data from 72 patients with cirrhosis, who had been investigated with upper GI endoscopy for a variety of symptoms and signs were collected and *Helicobacter pylori* infection was confirmed either with a rapid urease test (RUT) and/or histology specimens and Wright-Giemsa staining.

Results: The global prevalence of *H. pylori* infection in cirrhotic patients was 31.9%, less than what is generally recorded in patients with non-ulcer dyspepsia or peptic ulcer. The prevalence of HP infection in patients with Child-Pugh class A, B and C liver cirrhosis was 35.7%, 28.5% and 31.5%, respectively. The prevalence of peptic ulcer disease in patients with cirrhosis was 20.6%. The prevalence of *H. pylori* infection did not differ significantly between patients with or without peptic ulcer (32.9% vs 30.9%).

Conclusions: *Helicobacter pylori* does not seem to play the main role in the pathogenesis of peptic ulcer disease in patients with liver cirrhosis.

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● CLINICAL EVALUATION OF A 10 DAY REGIMEN WITH ESOMEPRAZOLE, METRONIDAZOLE, AMOXICILLIN, AND CLARITHROMYCIN FOR THE ERADICATION OF *H. PYLORI* (E-MACH STUDY)

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Aims: We aimed to assess effectiveness and safety of a 10 day quadruple non bismuth containing therapy for H.pylori in a population with relatively high resistance to metronidazole (M) and clarithromycin (C).

Patients and methods: We included 96 consecutive patients who had upper GI endoscopy. Excluded patients had: eradicated H.pylori, recent use of antibiotics, bismouth, NSAID or aspirin, allergy, gastrectomy, pregnant women. All eligible patients were CLO-test and either histology or culture positive and were prescribed: Esomeprazole 40mg, Metronidazole 500mg, Amoxicilin 1000mg, and Clarithromycin 500mg, twice daily, for 10 days. Compliance to treatment and adverse effects were recorded. Eradication was tested 4-6 weeks later by means of histology and/or ^{13}C-UBT and/or stool test.

Results: Ninety three patients (41F/52M, aged 18-81, mean: 51.8years) were evaluated for eradication (35.5% smokers, 21.5% with ulcer disease). Adherence to treatment was 97,7% (95%CI 95,9-99,6). Six (6.2%) patients experienced severe side effects. Overall PP and ITT eradication rates were 90.3% (95%CI 84.2-96.4) and 87.5% (95%CI 80.7-94.2) but were significantly higher when the regimen was prescribed as a first line therapy (92.6% PP, 90.4% ITT) than in the remaining cases (63.6% PP, 58.3% ITT) ($p<0.001$). Positive cultures and antibiotic sensitivity tests were carried out in 40/47 (85.2%) patients. Eradication rates were significantly higher in sensitive and single resistance strains (12/12, 100% and 18/19, 94%) than in those with double resistance (5/9, 55%) ($p<0.0001$).

Conclusions: The 10 days concomitant regimen is effective and safe as first line *H. pylori* eradication therapy although double (M and C) resistance may compromise its effectiveness.

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● COELIAC DISEASE PATIENTS HAVE HIGHER RE-INFECTION RATE AFTER SUCCESSFUL HELICOBACTER PYLORI ERADICATION FOR PEPTIC ULCER DISEASE

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Introduction: Currently available eradication regimes for HP infection have been proven particularly effective and with low re-infection (or recrudescence) rate which is estimated to about 1-3% per year after successful eradication.

Aims & Methods: Aim of the study was to assess long-lasting maintenance of the eradication with currently available regimes in patients with celiac disease. In 24 patients (13 male, 9 female, age range 21-59 years) with celiac disease benign peptic ulceration (17 duodenal, 7 stomach) was diagnosed endoscopically over a 5 years period. All patients were in clinical and histological (with distal duodenal biopsies) remission on a gluten-free diet and none was on long-term NSAID'S.

Results: 20/24 patients were HP (+) by histology and CLO test and received for both healing and HP eradication first-line triple schemes (PPI, clarithromycin, amoxicillin) and those who failed (6/20) to become HP (-) second-line quaqdruple schemes (PPI, bismuth compounds, amoxicillin, metronidazole). First and second-line schemes were given at the recommended dose and duration of treatment. All patients had their ulcers healed and became HP (-) by histology/CLO test and/or ^{13}C-UBT. All patients were re-evaluated for their HP status with ^{13}C-UBT after a mean observation period of 42 months (range 28-64 months). 12/20 (60%) remained HP (-) while 8/20 (40%) became HP (+). The observed re-infection rate for matched non-coeliac patients and for similar observation period was 5%. 8/20 patients, 4 HP (-) and 4 HP(+), were re-endoscoped because of dyspeptic symptoms and in 2/8 recurrence of duodenal ulcer was diagnosed. Both these patients were HP(+).

Conclusion: Even if the number of patients studied is relatively small, it seems that patients with celiac disease have higher re-infection (or recrudescence) rate than expected compared to non-coeliac patients. Genetic factors influencing susceptibility to HP infection (i.e. IL-10 production) by modulating the host immune response might be implicated to explain this observation.

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