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## SAFETY AND CLINICAL EFFICACY OF PANTOPRAZOLE 40 MG IN PREVENTION OF RELAPSE OF REFLUX ESOPHAGITIS. SPANISH MULTICENTER STUDY.

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AIM: To investigate the safety and efficacy of pantoprazole 40 mg as relapse prophylaxis over 1 year for reflux esophagitis patients previously healed with pantoprazole or ranitidine. METHODS: Patients with reflux esophagitis (grade II or III according to Savary/Miller) previously healed with pantoprazole 40 mg or ranitidine 300 mg for four to eight weeks in a randomized multicenter study received pantoprazole 40 mg once daily for one year. Follow up visits were performed every 3 months. No regular endoscopies were carried out in the study. An endoscopy was only performed when patients perceived reflux esophagitis symptoms for at least 3 consecutive days. The main criteria for assessing safety were adverse events and laboratory values. Regarding efficacy, the criteria were time until occurrence of an endoscopic or symptomatic relapse. RESULTS: 118 patients with healed reflux esophagitis grade II or III were included in this study. Adverse events were reported by 28 patients (24%). Four adverse events were classified as possibly related to pantoprazole, none of these patients discontinued the study prematurely. No adverse event was assessed to be definitely related to pantoprazole. Only isolated changes in some patients occurred in the routine clinical laboratory values throughout the study. Pantoprazole was effective to maintain remission in patients with a history of reflux esophagitis. Endoscopic relapse was observed only in one patient (1%). At the end of study 95 patients were in remission. 22 patients were classified as lost-to-follow-up. Also, pantoprazole was effective to prevent symptoms associated to gastro-esophageal reflux disease. Symptomatic relapse rates were 2% and 7% after 3 and 6 months, respectively, and 8% after 9 and 12 months. CONCLUSIONS: These results confirm that pantoprazole 40 mg once daily is well tolerated after one year of treatment to prevent endoscopic and symptomatic recurrence of reflux esophagitis.

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## CLINICAL EFFICACY AND SAFETY OF PANTOPRAZOLE VERSUS RANITIDINE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE: SPANISH MULTICENTER STUDY.

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AIM:In this multicentre study, the objective was to compare the efficacy and safety of pantoprazole (PANTO) 40 mg once daily with ranitidine (RAN) 150 mg twice daily in the treatment of grade II and III (Savary/Miller classification) reflux esophagitis. METHODS: Randomized, double-blind, parallel group comparison. Outpatients with endoscopically assessed reflux esophagitis (grade II/III) were enrolled to receive either PANTO 40 mg once daily or RAN 150 twice daily for 4-8 weeks depending on healing. Double-blindness was enabled by the double-dummy technique. RESULTS: 165(PANTO 81, RAN 84) out of 187 patients (intention to treat: PANTO 94, RAN 93) completed the study protocol correctly. Complete reflux esophagitis healing after 4 weeks (per-protocol) was found in 77 patients (95.1%) of the PANTO group and in 56 patients (66.7%) of the RAN group. After eight weeks, corresponding figures were 80 (98.8%) and 65 (77.4%), respectively. The differences between groups were significant at week 4 ($p<0.01$) and after 8 weeks ($p<0.01$, Cochran-Mantel/Haenszel method). Symptom relief, as reported during study visits, was significantly better in the PANTO group, with 82.7% patients free of all primary symptoms (acid eructation, heartburn and pain on swallowing) at 2 weeks compared with 60.7% in the RAN group ($p<0.01$, per protocol, Fisher's exact test). After 4 weeks 91.3% patients in the PANTO group and 69.1% patients in the RAN group were free from these symptoms ($p<0.01$). Both treatments were equally well tolerated. No definitely related adverse event was reported. No patient discontinued the study in the PANTO group while 4 patients discontinued the study in the RAN group due to adverse events possibly related to the study medication. CONCLUSIONS:PANTO (40 mg s.i.d.) was clinically superior to RAN (150 mg b.i.d) in terms of healing rates and symptom relief in patients with reflux esophagitis, grade II and III. Both treatments were safe and well tolerated.

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## PREVALENCE OF *HELICOBACTER PYLORI* RESISTANCE TO METRONIDAZOLE, CLARITHROMYCIN, AMOXYCILLIN, TETRACYCLINE, AND FURAZOLIDONE IN BRAZIL.

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Background: *Helicobacter pylori* (*Hp*) infection is associated with a wide range of digestive diseases and is very prevalent in developing countries, although there is little data on the susceptibility of *Hp* to antimicrobials commonly used in eradication schedules in these countries. The aim of this study was to evaluate the resistance of *Hp* to metronidazole, clarithromycin, amoxycillin, tetracycline and furazolidone in dyspeptic Brazilian patients. Material and Methods: Ninety consecutive *Hp* positive patients were enrolled. Resistance was evaluated by an agar dilution test. Results: Resistance to metronidazole was detected in 38 patients (42%) to amoxicyllin in 26 individuals (29%), to clarithromycin in 6 patients (7%), to tetracycline in 6 patients (7%) and to furazolidone in 4 individuals (4%). Thirteen strains were resistant to 2 agents, and eight strains were resistant to 3 antimicrobials. Conclusions: These results confirm the need for culture and susceptibility testing to define *Hp* resistance patterns in particular geographical areas before the general use of an eradication schedule. They also suggest the possibility of resistance to antimicrobials like amoxycillin or tetracycline in geographical areas with a high prevalence of *Hp* infection and still not fully evaluated for antimicrobials susceptibility.

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## HELICOBACTER PYLORI (HP) SEROCONVERSION IN ASYMPTOMATIC BLOOD DONORS (BD). A FIVE-YEARS FOLLOW UP.

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The aim of this study was to assess the seroconversion by different techniques after five-eight years. Methods: In 1990, 588/1010 asymptomatic BD were found to be seronegative by ELISA, based on an HP whole-cell suspension lysate (sensitivity and specificity: 92% and 97%). In 1995 serum samples from 418/588 seronegative BD were collected and retested using the same antigen. 411 out of 418 samples were frankly negative; 7 BD were found to be seroconverted. This bunch of 7 sera represents the object of the study. Results: They were re-tested by ELISA and Western Blotting (WB) using a different antigen (NCTC). To standardise our techniques, sera from 43-HP+ve and 47 HP-ve patients according to culture, histology, urease test and UBT were used. The cut-off for ELISA-NCTC was 0.53 AI (Absorbance Index) (mean value + 2 SD), and for WB was negativity for CagA or $< 10$ bands (sensitivity and specificity: 95% and 96%; 98% and 81% for ELISA and WB respectively). According to the results obtained in 1990 and 1995, seven BD were found to be seroconverted by ELISA using sonicated antigen, in 5 the seroconversion was confirmed by ELISA using NCTC antigen and in two there was concordance with WB. Four out of 7 BD were contacted and asked to perform UBT and a further serum sample was drawn to be reassessed in 1998. A seroconversion was found in all four BD by ELISA, whilst WB and UBT confirmed the seroconversion in only three out of four BD. Conclusions: The "in house" ELISA used performed well compared to other theoretically better serologic assays and confirm the low seroconversion rate for HP infection in adult population living in developed countries.

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## EFFICACY AND TOLERABILITY OF 40 MG PANTOPRAZOLE VERSUS 2 × 150 MG RANITIDINE IN PATIENTS WITH REFLUX ESOPHAGITIS.

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AIM: To compare healing rates, symptom relief and tolerability of 40 mg pantoprazole (panto) once daily vs. 150 mg ranitidine (rani) twice daily in patients with endoscopically assessed gastro-esophageal reflux disease (GERD) grade II/III. METHODS: 256 outpatients with endoscopically proven reflux esophagitis, grade II or III (Savary/Miller), were randomly allocated to receive either 40 mg panto once daily or 150 mg rani twice daily. All patients underwent endoscopy after 4 weeks of treatment. If the esophageal lesion was not completely healed by this time, treatment was continued for another 4 weeks and a further endoscopy was performed by the end of treatment. Additional follow-up visits without endoscopy were performed 2 weeks after the start of treatment and, if not healed by the time of 4 weeks, 6 weeks after the start of treatment. At each visit, patients were asked about the presence and severity of the GERD key symptoms heartburn, acid eructation and pain on swallowing. Primary parameter was the endoscopically determined healing of the reflux esophagitis, i.e. the healing rates after 4 and 8 weeks, analyzed by means of the Cochran Mantel/Haenszel method. RESULTS: 128 patients each were enrolled either into the panto group or into the rani group, of which 109 (panto) and 113 (rani)