

## LONG-TERM PROSPECTIVE ASSESSMENT OF QUALITY OF LIFE IN CELIAC DISEASE PATIENTS. DETERIORATION AT FOUR-YEARS ON TREATMENT

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**Background:** The gluten-free diet (GFD) produces a positive short-term impact on quality of life (QoL) of patients with celiac disease (CD). However, a concern about the long-term outcome has been raised by cross-sectional studies.

**Aim:** Our objective in this prospective study was to assess QoL of patients for long-term after the initiation of treatment.

**Patients/methods:** We evaluated 34 newly diagnosed adult CD patients (median age: 39 yr; 32 females) and 70 sex-and age-matched healthy controls using a multidimensional approach based on self-administered questionnaires: the Short Form 36 Health Survey (SF-36), the Gastrointestinal Symptoms Rating Scale (GSRS) and the Beck Depression Inventory (BDI) at diagnosis, and at one-year and more than four-years (median: 53 months) after commencing treatment.

**Results:** At diagnosis, patients exhibited a significant alteration of all items of the three questionnaires compared with controls ( $p < 0.01$  to  $p < 0.0001$ ). One-year treatment produced a substantial improvement of most outcome measures ( $p < 0.04$  to  $p < 0.0001$ ), attaining comparable scores to healthy subjects ( $p = NS$ ). Compared to the one-year assessment for the overall population, the SF-36 questionnaire performed at four-years evidenced a deterioration of some items such as: social function ( $p < 0.0002$ ), role emotional ( $p < 0.005$ ), role physical ( $p < 0.002$ ),

vitality ( $p < 0.0003$ ), mental health ( $p < 0.002$ ) and general health perception ( $p < 0.002$ ). Interestingly, most of them remain significantly higher than at diagnosis ( $p < 0.03$  to  $p < 0.0005$ ). While BDI scores impaired at four years ( $p < 0.002$ ) compared to the one-year assessment, no changes were detected in the most common GI symptoms assessed by the GSRS ( $p = NS$ ). Despite the long-term deterioration of BDI, the final score remained significantly better than those registered at diagnosis ( $p < 0.0006$ ). The long-term impairment of the patients' perception of QoL was mainly related to the deterioration of some parameters in patients non compliant with the treatment. In this context, social function ( $p < 0.02$ ), physical role ( $p < 0.04$ ), emotional role ( $p < 0.04$ ), general health perception ( $p < 0.002$ ), perception of diarrhea ( $p < 0.02$ ) and indigestion ( $p < 0.01$ ) and the BDI score ( $p < 0.002$ ) were significantly deteriorated in non compliant patients.

**Conclusions:** Our prospective multidimensional long-term assessment of QoL evidenced a deterioration of some outcome measures after the initial one-year normalization. The study suggests that the deterioration seems to be primarily associated to the effect of the degree of compliance with the GFD on the social sphere, the behavioral dimension of patients and some symptoms.

## SODA WATER TEST IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE

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**Introduction:** The absence of a protective gastroesophageal barrier in gastroesophageal reflux disease (GERD) pathophysiology could be either a permanent defect or the more common and accepted mechanism of transient lower esophageal sphincter relaxation. In both cases, the belching mechanism is facilitated, thus evidencing impaired gastric air retention capacity.

In order to analyze the relationship between gastric air retention capacity and GERD, a simple soda water test (SWT), with proved reproducibility, was performed. Subjects with and without typical symptoms of heartburn and/or regurgitation were included.

**Aim:** To assess the sensitivity and specificity of SWT in subjects with and without symptoms of GERD, in relationship with the 24-hour pH measurement.

**Material and methods:** A prospective cross-sectional descriptive study consisting of 43 subjects (21 females), mean age 48 ( $\pm 15$  years) was designed. The volume of soda water intake inducing the first belch episode noticed by the patient was measured before 24-hour esophageal ambulatory pH measurement. The subjects were divided into two groups: 22 normal pH study subjects (12 females, mean age 46 $\pm 15$ ) and 21 pathological pH study subjects (9 females, mean age 48 $\pm 16$ ). Volumes were calculated with a measuring container. Patients were asked to swallow every

five seconds small amounts of sparkling water while seated. They were asked to stop drinking as soon as they noticed the first belch episode. Then, the minimum volume for inducing belching was measured.

Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratio (LR+) and negative likelihood ratio (LR-) were estimated for the following volumes: 50, 100, 200, 300 and 400 ml.

### Results:

Volume	Sensitivity	Specificity	PPV	NPV	LR+	LR-
50 (95% CI)	0.306 (0.144- 0.536)	0.981 (0.840- 0.998)	0.917 (0.517- 0.991)	0.671 (0.512- 0.799)	15.889 (0.93- 269.79)	0.708 (0.519- 0.966)
100 (95% CI)	0.313 (0.142- 0.556)	0.800 (0.609- 0.911)	0.500 (0.237- 0.763)	0.645 (0.489- 0.789)	1.563 (0.536- 4.551)	0.859 (0.585- 1.262)
200 (95% CI)	0.625 (0.386- 0.815)	0.520 (0.335- 0.700)	0.455 (0.259- 0.653)	0.684 (0.460- 0.846)	1.302 (0.746- 2.273)	0.721 (0.345- 1.506)
300 (95% CI)	0.813 (0.570- 0.934)	0.400 (0.234- 0.593)	0.464 (0.295- 0.642)	0.769 (0.497- 0.918)	1.354 (0.910- 2.015)	0.469 (0.152- 1.447)
400 (95% CI)	0.875 (0.640- 0.965)	0.320 (0.172- 0.516)	0.452 (0.292- 0.622)	0.800 (0.490- 0.943)	1.287 (0.928- 1.784)	0.391 (0.095- 1.611)

**Conclusions:** Acceptable sensitivity and specificity were obtained with volumes of 300 ml and 100 ml, respectively. This simple and inexpensive method, albeit not perfect, could be useful for ambulatory evaluation of patients with GERD symptoms.

## PREVALENCE OF INFLAMMATORY BOWEL DISEASE IN A UNIVERSITY HOSPITAL HEALTH MAINTENANCE ORGANIZATION

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**Introduction:** The estimated prevalence of inflammatory bowel disease (IBD) in Europe and U.S. is approximately 100 to 200 per 100,000 for ulcerative colitis (UC) and 50 to 100 per 100,000 for Crohns disease (CD). Currently in Argentina there are no national registries for IBD.

**Objective:** To determine the prevalence of IBD in a population belonging to a health maintenance organization (HMO) and describe its characteristics.

**Materials and methods:** A retrospective, descriptive, cross sectional study was carried out. The electronic medical records from an HMO with a population mainly composed by urban middle class individuals were searched. Different keywords were used to select the group with greater chance of having IBD. The records were reviewed in order to confirm the diagnosis according to clinical findings and complementary studies and to describe the evolution and characteristics of the disease.

**Results:** Among 147,109 individuals enrolled in the HMO, 687 were identified using the keywords. The diagnosis of IBD was established in 143 (M/F: 68/75), with an estimated prevalence of 97.2 per 100,000 (95% CI, 82.5–114.5). The prevalence of UC and CD was 76.1 (95% CI 63.2–91.6) and 15.0 (95% CI 9.8–22.7) per 100,000, respectively. Nine patients

were diagnosed as indeterminate colitis with an estimated prevalence of 6,1 per 100,000 (95% CI 3.18-11.76). Among patients with UC (M/F: 52/60), the median age at the moment of diagnosis was 37.5 (r: 3-78) and 56.5% were between 10 to 40 years at onset. The most frequent clinical presentation was pancolitis (43%) and 31% of these patients underwent colectomy. The prevalence of primary sclerosing cholangitis was 6%. Among patients with CD (M/F: 13/9), the median age at the moment of diagnosis was 37.0 (r: 11-81) and 53% were between 10 to 40 years at onset. The most frequently affected region was the terminal ileum. Nine patients underwent surgical procedures (41%). Patients with indeterminate colitis account for 6% of all IBD, with a median age at diagnosis of 63 (r: 28-83). The affected areas were rectum in 55% and left colon in 45%.

**Conclusion:** The estimated prevalence of UC in an HMO population from Argentina is similar to previous reports from Europe and the U.S., although the estimated prevalence of CD is lower. Even though the study population is not a random sample and represents only a small percentage of Argentine inhabitants, the data we obtained may allow a better understanding of the epidemiology of IBD in Argentina.

## SPECTRUM OF ENDOSCOPIC FINDINGS IN PATIENTS WITH SYMPTOMS RELATED TO GASTROESOPHAGEAL REFLUX DISEASE (GERD) IN ARGENTINA: NATIONWIDE EPIDEMIOLOGICAL STUDY

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**Introduction:** GERD is classified by endoscopy in non-erosive reflux disease (NERD), erosive esophagitis (EE) and Barrett esophagus (BE). There are no published nationwide epidemiological studies in Latin America regarding endoscopic findings of patients with GERD symptoms.

**Aim:** 1) Estimate the prevalence of NERD, EE and BE in patients with GERD symptoms, in Argentina. 2) Evaluate the association of endoscopic findings with clinical characteristics and the impact in health related quality of life.

**Methods:** Were included patients from 14 geographical areas of Argentina, of both sex between 18-65 years of age with typical symptoms of GERD (at least 2 times a week). Exclusion criteria were patients on H2RA or PPI treatment between 1 month prior to the study, gastric surgery and AIDS. All of the patients underwent endoscopic studies. The endoscopic findings of EE were classified by Los Angeles (LA) classification. BE patients were classified by Praga classification. The following clinical characteristics were evaluated: age, sex, smoking, BMI, alcohol, coffee and yerba-mate consumption and the presence of hiatal hernia. All patients were asked to complete a symptom questionnaire and a health related quality of life questionnaire (Velanovich specific test). Prevalence was estimated by IC 95% for each group. Univariate analysis and multi factor analysis by

Cumulative Logistic Model (analysis for order category) were used to evaluate the association of endoscopic findings with clinical characteristics and health related quality of life (HRQL).

**Results:** 397 patients (mean age 46±15 years, male 41%, female:59%) were included. The prevalence of NERD was 60.2% (IC: 55,2-65,5%), EE 35.5% (IC:30,8-40,5%), (LA:A: 47%; LA:B: 33%; LA:C: 14%; LA:D: 6%). BE was observed in 4.3% of the population studied, 71% were long and 29% short Barrett's esophagus, the inflammatory component was found in 53%. The findings of circumferential, tongues and mixed patterns of BE were 24%, 35% and 41% respectively. The predictive model to analyze the association between clinical characteristics and endoscopic findings used a discriminate capacity of 70-80 measured by an AUC=0.77. The clinical variables associated with severe mucosal injury (BE>EE>NERD) were age (OR 1.3), male sex (OR 4.9), BMI>25 (OR 1.9) and nocturnal symptoms (OR 2.5). No association was found between HRQL and endoscopic findings.

**Conclusions:** 1) the prevalence of endoscopic findings in GERD patients from Argentina is comparable to developed countries data. 2) overweight/obesity, older age, male sex and nocturnal symptoms were the most potent predictor of endoscopic severity. 3) HRQL is similar in all groups.

## EFFECTIVIDAD COMPARATIVA DE UN PROBIÓTICO VS. UN ANTIBIÓTICO EN LA RESPUESTA TERAPÉUTICA DE PACIENTES CON SOBRECRECIMIENTO BACTERIANO DEL INTESTINO Y DISTENSIÓN ABDOMINAL CRÓNICA FUNCIONAL

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**Introducción:** Habitualmente los pacientes con sobrecrecimiento bacteriano del intestino son tratados con el empleo de diversos antibióticos. Actualmente existen evidencias de que determinados probióticos presentan efectividad en la respuesta clínica en pacientes con distensión abdominal con o sin intestino irritable.

**Objetivo:** Establecer la efectividad clínica comparativa a corto plazo del metronidazol vs. Probiótico en pacientes con sobrecrecimiento bacteriano del intestino y distensión abdominal crónica funcional

**Sujetos y método:** Se trata de un estudio piloto prospectivo y aleatorizado. 50 pacientes con distensión abdominal crónica (criterios Roma III) y diagnóstico mediante test de lactulosa H2 en aire espirado, de sobrecrecimiento bacteriano del intestino (criterios de Pimentel y col), en forma consecutiva fueron aleatorizados (método computarizado) a recibir: 25 sujetos (23 mujeres, edad: 49±19) Metronidazol .500mg dos veces por día durante 5 días y otros 25 sujetos (20 mujeres, edad 58±19) un Probiótico conteniendo: *Lactobacillus casei* (3,3X10<sup>7</sup>U.F.C), *Lactobacillus plantarum* (3,3X10<sup>7</sup> U.F.C) *estreptococcus faecalis* (3,3x10<sup>7</sup> U.F.C) y *Bifidobacterium Brevis* (1,0x10<sup>6</sup> U.F.C) 5ml dos veces por día durante 5 días. Todos efectuaron por

igual una dieta con restricción de Alcohol, legumbres, lácteos y verduras de hoja. La respuesta al tratamiento fue evaluada por un interrogador independiente a los 15 días de terminado el tratamiento, mediante un cuestionario de respuesta global de 5 niveles (mucho mejor, mejor, igual, peor y mucho peor). Mejor y mucho mejor, fueron consideradas respuestas positivas.

**Resultados:** 13/25 (52%) de los sujetos que recibieron Metronidazol, refirieron mejoría con este tratamiento. La mejoría clínica con el probiótico fue de 20/25 (82%)

Se constataron diferencias estadísticamente significativas a favor del probiótico empleado. P:0,036 (Pearson chi cuadrado). Todos los pacientes evaluados completaron el tratamiento propuesto sin manifestar efectos adversos que les obligara a suspender el mismo.

**Conclusiones:** En base a esta prueba piloto podemos considerar al probiótico empleado de mayor efectividad que el Metronidazol en la respuesta clínica precoz de pacientes con distensión abdominal crónica y sobrecrecimiento bacteriano del intestino.

Los autores desean aclarar que no han recibido ningún tipo de apoyo ni subsidio de la industria farmacéutica para la realización de este trabajo.

## CURRENT CLINICAL SPECTRUM OF CELIAC DISEASE IN AN ADULT HOSPITAL-BASED POPULATION IN ARGENTINA. IMPROVEMENT OF AWARENESS OF EXTRAINTESTINAL PRESENTATION

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Celiac Disease (CD) is a systemic disease no longer considered to be restricted to the intestinal tract. Various clinical forms have been increasingly recognized including those in which G.I. or abdominal symptoms are absent. The changing clinical spectrum of CD prompted us to analyze our adult hospital-based population.

**Aim:** (1) To evaluate the clinical presentation which triggered the medical work-up leading to diagnosis of CD. (2) To identify the current contribution of Hospital Departments (excluding Pediatrics) to CD diagnosis. (3) To assess recent changes in the awareness of CD.

**Materials and methods:** Out of 222 cases with a confirmed diagnosis of CD (serologic test (tTGA & EMA) + intestinal histology; 2002 through 2007), 15 failed a blinded review of diagnostic biopsy, 63 lacked clinical information, and in 72 the reason for serologic testing was unavailable and were thus excluded. We analyzed, the signs/symptoms prompting specific CD diagnosis work-up in 72 patients, female: 3.2:1, age x: 45y range: 17-75y. The referring clinical Department responsible for CD suspicion was recorded. The change in awareness of CD was explored through the number of performed serologic tests/y and the ratio between n of serologic tests/y corrected by

n consultations/y (NT/NC).

**Results:** Symptoms leading to suspicion of CD (n=116) were diarrhea /abdominal pain in 44, anemia 27, autoimmune disease 15, skin manifestation 6, osteoporosis 6, chronic fatigue 5, elevated ALT 5, family history of CD 4, other 4

Diagnosis according to referring Department (%): Gastroenterology 50, Endocrinology 21, Internal medicine 18, Hematology 8, Dermatology 1, Rheumatology 1, Gynecology 1, Neurology 1. The n of serologic tests for CD/y increased from 793 on 2003 to 1627 on 2007, a 205% increase (p:<0.05). NT/NC increased 70% from 0.63 on 2003 to 1.08 on 2007.

**Conclusions:** 1. Anemia, diarrhea and abdominal pain were the leading symptoms arising suspicion of CD. 2. Regarding the Medical Departments involved in CD diagnosis, Gastroenterology was still responsible for 50% of cases. However, Internal Medicine, Hematology and Endocrinology generated a almost similar n of CD diagnoses (47%) probably reflecting an increased awareness of the multiple forms of CD. 3. The ratio relating number of serologic test per number of consultations per year, increased by 70% from 2003 through 2007 confirming a true increase in awareness of CD

## ROLE OF ANTIBODIES IN THE LONG TERM FOLLOW UP OF PATIENTS WITH CELIAC DISEASE TO PREDICT THE ADHERENCE TO GLUTEN-FREE DIET

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**Introduction:** The Celiac Disease (CD) is characterized by a permanent sensitivity to gluten. The treatment for this disease is the life-long strict compliance with a gluten-free diet (GFD). The average of compliance with GFD ranges between 15 and 80%. Antibodies' role in the follow up of these patients regarding the adherence to the GFD is not well established.

**Aims:** To determine the relation between the antibodies for celiac disease and the adherence to the GFD in patients with over a year of treatment.

**Materials and methods:** Patients with celiac disease with a minimum of 1 year of gluten-free diet (GFD) were prospectively included. They were asked to complete a self-survey regarding the compliance to the GFD and a level of adherence was determined: low (no compliance or more than 2 gluten intakes per week); medium (1 or 2 gluten intakes per week, or 2 or 3 gluten intakes per month); or high (1 gluten intake per month, or less than 3 intakes per year). The follow up was performed by their general practitioners. From 1 year of GFD onwards, the results of the available antibodies at the time of the last follow up were assessed: anti-gliadine IgA and IgG (AGA-IgA, AGA-IgG), anti-endomysium IgA and IgG (EMA-IgA, EMA-IgG), anti-transglutaminase (ATG), and deaminated peptides

of gliadine IgA and IgG; considering them positive or negative. Through univariate analysis, the above-mentioned antibodies were correlated (independent variables) in order to identify predicting factors of high and low adherence to the GFD (dependent variables).

**Results:** 90 patients were analyzed; age  $43.6 \pm 15.3$  years old, 89% women, 58% classic celiacs. The average time of GFD was 7.9 years. 63% had been on a GFD for over 3 years. 71% (CI 69-80) showed high adherence to the GFD, and 6.7% (CI 2-13) showed low adherence. GFDs of less than 3 years were a determining factor for low adherence, RR 2.41 (CI 1.2-2.89). The predictive antibodies for GFD high adherence were: 1) Negative EMA-IgA, RR 1.27 (CI 1.03-1.54); 2) negative ATG, RR 1.62 (CI 1.12-2.47); 3) all negative requested ones, RR 1.60 (CI 1.17-2.18). The predictive antibodies for GFD low adherence were: 1) Positive AGA-IgA, RR 15.5 (CI 2.29-105); 2) positive EMA-IgA, RR 10.2 (CI 2.19-47.7); 3) positive ATG, RR 9.63 (CI 1.53-63.4).

**Conclusion:** After 1 year of treatment, the negativity of EMA-IgA or ATG antibodies was significantly correlated with the high adherence to GFD; and the positivity of AGA-IgA, EMA-IgA or ATG antibodies was significantly correlated with a low adherence.

## PEDIATRIC INFLAMMATORY BOWEL DISEASE IN A LATIN-AMERICAN POPULATION FROM BUENOS AIRES. MULTICENTER STUDY

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**Introduction:** Inflammatory Bowel Disease (IBD) occurs in 10-15% of pediatric population. In this last decade, pediatric IBD has increased in the developed world, but there are no published data on what has occurred with pediatric IBD in Latin America.

**Aim:** To describe the clinical behaviour and course of pediatric IBD in a latin-american population from Buenos Aires in the last 20 years.

**Material and methods:** From June 2006 to June 2007, a retrospective, descriptive, multicenter study was conducted in 3 referral centers (One private community and two public pediatric hospitals). We included 424 patients: 263 ulcerative colitis (UC) (62%), 103 Crohn's disease (CD) (24.3%) and 58 Indetermined Colitis (13.7%), who were diagnosed from 1988 to 2007. Mean age at diagnosis was 10.03 ys ( $r$  0.28-21.27), with a male/female rate of 1.7:1. Diagnosis was established by clinical features, radiology, endoscopy and histology. Statistical analysis: independent-samples t test and ANOVA procedure.

**Results:** The mean age at onset was 8.8 years ( $r$  0.02-21) with an average diagnostic delay of 14 months ( $r$  0-14.66 years) and mean follow-up of 4 years (0-23). The most frequent clinical presentation was abdominal pain (72.2%), chronic diarrhea (67.8%) and weight loss (58.9%) in CD; and bloody diarrhea

(81.8%) in UC. According to anatomic location and extent of CD, ileocolonic involvement was seen in 47/103 (46%), followed by colonic (32/103, 31%), ileal-ileocecum (13%) and gastroduodenal (11%) compromises. CD's biologic behaviour was inflammatory (77%), fistulizing (18%) and fibrostenosing (5%). Anatomic classification in UC showed pancolitis in 202/263 (77%), left colitis (17%) and rectitis (6%). UC was mild in 30%, moderate in 56% and severe in 14%. At least one extraintestinal manifestation was seen in 125/424 patients (29.5%), being hepatobiliary compromise (19.3%) and peripheral arthritis (8.5%) the most frequent ones. We observed an incidence of 14 new cases per year in the 1988-1999 period, that contrasts with 32 new annual cases in the next decade ( $p$  0.0001), being the UC:CD relation 3.9:1 and 2:1 respectively.

**Conclusions:** In this first multicenter study in Buenos Aires a significant increase of IBD was registered in this last decade, particularly with Crohn's, similar to reports in industrialized countries, although in this area ulcerative colitis is still predominant. Other multicenter studies from Latin America are necessary to estimate the real incidence of pediatric IBD in this region. The results obtained may help understand if the environment or local habits play a role in the persistent increase and in the different distribution throughout the world.

## GASTRIC ACID SUPPRESSION WITH A NEW ORAL POWDER OMEPRAZOLE SUSPENSION FOR INFANTS WITH GERD. PILOT STUDY

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**Background:** Gastroesophageal reflux disease (GERD) has a prevalence of 10 to 20 % in the pediatric population. The 24-hour pHmetry (24hr pH) is still considered the "gold standard" for its correct diagnosis. A double channel catheter with a sensor in the stomach enables the evaluation of the acid suppressive capacity of proton pump inhibitors. Omeprazole is the elective drug for a proper treatment because it is safe, effective and well tolerated. Unfortunately, there are no adequate pharmaceutical presentation forms (capsules, tablets, granules) for infants.

**Aim:** To assess the acid suppression capacity of a new pharmaceutical association of omeprazole with sodium bicarbonate and sodium alginate (OBA)\*, powder for oral suspension, to be used in small infants with GERD. **Material and methods:** A prospective pilot study in 9 full-term infants with no congenital nor associated anomalies under 12 months of age with GERD was conducted since January 2008 to April 2009. A written informed consent was obtained from parents before the beginning of the diagnostic pHmetry. The response was measured according to the gastric variations of pH after a 3-day treatment with OBA in relation to the diagnostic study. Two double channel pHmetry with gastric sensor were performed on different days in the same patient. The first one to establish the diagnosis (day 0) and the second one (day 3) after receiving omeprazole (OBA) at 1,5 mg/kg/day in a twice/dose/day (BID). By each 10 mg of omeprazole the association contains 840 mg of sodium bicarbonate and 125.04 mg of sodium alginate.

**Statistical analysis:** For data comparison, non-parametric Wilcoxon test, was performed to compare the average time at which gastric pH was < 4 pre and post OBA.

All the values were expressed as mean ± standard deviations.

**Results:** No adverse events were observed in infants and the suspension

flavor was palatable. Time with gastric pH < 4 in each patient, is showed in Table 1.

The comparison between the first and the second gastric pH-metry showed a significant reduction in gastric acidity (Table 2).

The non-parametric Wilcoxon test used to compare the average time at with gastric pH

was < 4 pre and post OBA, showed significant statistical values,  $p < 0.01$ .

**Conclusions:** The results of this study show that this oral powder combination induces significant and intensive acid gastric suppression in small infants with GERD. These results would make OBA a therapeutic option, employing an adequate pharmaceutical presentation form for infants.

This study was sponsored by Laboratorios Bagó S.A. Buenos Aires, Argentina.

\*Ulcozol, powder for oral suspension. Laboratorios Bagó S.A. Buenos Aires, Argentina.

**Table 1.** Time with gastric pH < 4 (percentage and hours) in each patient.

Patient	Time with gastric pH was < 4 (percentage and hours)			
	Basal		Post-OBA	
	Percentage	Hours	Percentage	Hours
1	46.94	11.27	0.75	0.18
2	52.44	12.59	0	0
3	10.97	2.63	0	0
4	31.81	7.63	0	0
5	53.31	12.8	0	0
6	52.84	12.68	2.23	0.53
7	43.03	10.33	0	0
8	29.24	7.02	0.07	0.01
9	63.21	15.17	0	0

**Table 2.** Mean ± Standard Deviations time (expressed in percentage and hours) at which gastric pH was < 4.

	Percentage	Hours
Basal	42.64 ± 16.03	10.24 ± 3.85
Post-OBA	0.34 ± 0.75	0.75 ± 0.18

## P-GLYCOPROTEIN 170 (P-GP) FUNCTIONAL ACTIVITY IN PERIPHERAL BLOOD LYMPHOCYTES (PBL) ACCORDING THERAPEUTIC RESPONSE IN ULCERATIVE COLITIS (UC)

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**Background:** P-gp, encoded by MDR-1 gene, is a transmembrane efflux pump described overexpressed in cancer refractoriness by pumping treatment drugs out of cells. It is expressed in PBL, other haematopoietic cells, apical superficial epithelium of colon, ileum and other tissues with barrier function. It is an interesting and controversial candidate for UC therapeutic response and pathogenesis. Increased expression has been reported associated with steroid UC refractoriness. Conversely, deficient P-gp function has been postulated as UC susceptibility/severity factor.

**Aim:** to investigate the role of MDR1 gene in the therapeutic response of UC by studying the P-gp functionality in PBL.

**Methods:** P-gp functional activity was evaluated in PBL of 27 patients (15 M, 12 F) median age 30 (16-71) yrs with active UC (Mayo score: severe n 9, moderate n 9, mild n 9) categorized in: S-REFR (steroid-refractory, n 16) and S-RESP (steroid-responders, n 11); healthy controls (HC, n 68): similar age/gender. Rhodamine123 (a fluorescent P-gp substrate) efflux was studied by flow cytometry, (FACS Calibur, Becton-Dickinson) in absence and presence of P-gp modulators: Verapamil 100 µM, Valspodar 1µM reassessment. Data were expressed evaluating the behaviour of two markers (M1, M2) defined based on % of cells with different fluorescence levels. M1 (high fluorescence,

low P-gp pump activity) and M2 (low fluorescence, high activity) were compared in the three groups. After inhibition, it should be expected that Rhodamine123 remain in the intracellular leading to an increase of % of cells in M1 vs. M2.

**Results:** ( $X \pm SD$ ) Significant differences were observed in absence and presence of verapamil inhibition, showing increased P-gp functional activity in S-REFR vs. S-RESP ( $p < 0.01$ ) and HC ( $p < 0.001$ ), but not between S-RESP and HC (ANOVA and Student-Newman-Keuls post-test)(Tabla) Results were not influenced by cumulative steroids. Three out of 4 severe patients showing M2>M1 in the assay with verapamil required surgery. Clinical disease activity correlated with M2 (with inhibitor=  $r:0.57$ ,  $p=0.000056$ , Spearman). Interestingly, S-REFR showed a shift (M2 to M1) in an early new assay when some newly added drug reached effectiveness (6-MP n:4, infliximab n:1).

**Conclusion:** our results suggest: 1) a relevant role of P-gp in UC treatment response 2) a possible usefulness of P-gp functional assay in the early detection of individual therapeutic response.

	WITHOUT INHIBITOR		WITH INHIBITOR	
	M1	M2	M1	M2
CONTROLS	47±12	50±12	82±8	14±9
S-RESP	48±10	49±10	88±6	10±5
S-REFR	34±13	63±14	62±22	35±22

## AUTOPHAGY MEDIATED BY TRANSGENIC PANCREAS EXPRESSION OF VMP1 PREVENTS THE SEVERE EFFECTS OF ACUTE PANCREATITIS IN MICE

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Autophagy is an evolutionarily preserved degradation process of cytoplasmic cellular constituents, which has been known for its role in protecting cells against stresses such as starvation. The pancreatitis-induced vacuole membrane protein 1 (VMP1) triggers autophagy in mammalian cells. VMP1 is early expressed and localizes in autophagosomal membranes in pancreas acinar cells from rats with acute pancreatitis. Our aim was to study the role of VMP1 mediated autophagy during acute pancreatitis. We used transgenic mice in which the pancreas acinar-cell-specific elastase promoter drives VMP1-EGFP expression. Pancreatitis was induced by seven intraperitoneal injections of caerulein (50 µg/kg) given at 1h interval; mice were killed by decapitation 6 and 12 hours after the first injection and pancreases were removed. Wild type mice developed acute pancreatitis with high amylase and lipase levels in serum, while enzyme levels in transgenic mice were significantly reduced. Histological analysis revealed high degree of necrosis in wild type mice as well as a markedly infiltration, expressed as number of inflammatory cells per 100 pancreatic acini and MPO activity. In contrast, almost none inflammation was seen in treated transgenic mice, without necrosis evidence either. In order

to understand the process by which VMP1 expressing mice do not develop necrotizing pancreatitis, we analyzed levels of autophagy, trypsin activity and cell death in pancreas tissue. While autophagy was evident in transgenic mice, immunostaining and western blot analysis of LC3 and VMP1 showed that autophagy and VMP1 expression were poor or not detectable in wild type mice undergoing experimental pancreatitis. Moreover, trypsin activity measured by hydrolysis of a synthetic substrate was significantly reduced in pancreas from VMP1 transgenic mice comparing to wild type mice undergoing acute pancreatitis.

Surprisingly, cleaved caspase-3 western blot analysis and TUNEL assay revealed a significant increase of apoptosis levels in pancreas acinar cells from VMP1 transgenic mice comparing to that of wild type mice treated with caerulein. Our results indicate that autophagy induction prevents trypsinogen activation and favors the development of apoptosis, with a remarkable reduction in the local inflammatory response. We conclude that VMP1-triggered autophagic pathway in acinar cell prevents the severe effects of acute pancreatitis in mice.

## FUNDIC GLAND POLYPS AND ASSOCIATION WITH PROTON PUMP INHIBITOR INTAKE: A PROSPECTIVE STUDY IN 1,780 UPPER GASTRODUODENAL ENDOSCOPIES

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**Background:** Fundic gland polyps (FGP) are incidentally found when an upper gastroduodenal endoscopy is performed for a non-related indication. Prevalences ranging between 0.1 % and 1.9 % have been reported in several publications and some authors suggested a relationship with proton pump inhibitor (PPI) intake and middle-aged women.

**Objectives:** We aimed to determine the prevalence of FGP and its association with PPI intake.

**Material and methods:** We prospectively studied the 1,780 patients who underwent an upper gastroduodenal endoscopy at our center between June 2007 and August 2008. Polyps were classified according to their histology and FGP were specially considered. PPI intake during a period of at least 12 months, female sex and age were assessed as risk factors for the presence of FGP. PPI intake and sex were statistically evaluated by a  $\chi^2$  test and age by an unpaired t test. Then, a multiple logistic regression analysis was applied to these variables. A P value lower than 0.05 was considered as significant and odds ratio (OR), with its 95 % confidence interval (CI), was used as measure of association.

**Results:** Gastric polyps were found in 129 patients (7.2 %): FGP 77 (4.33 %), pseudopolypoid foveolar hyperplasia 26

(1.46 %), chronic gastritis 12 (0.67 %), hyperplastic polyps 8 (0.45 %) and carcinoid polyp 1 (0.06 %). In 5 cases histology was not available. Patients without histological diagnosis were excluded for the assessment of risk factors. PPI intake was detected in 49 patients with FGP (63.6 %) and 264 without FGP (15.5 %) ( $P < 0.0001$ ). Fifty-nine patients with FGP (76.7 %) and 987 without FGP (58.13 %) were women ( $P < 0.001$ ). The mean age was  $58.91 \pm 11.82$  in patients with FGP and  $50.34 \pm 15.04$  in patients without FGP, with a difference of 8.57 years (95 % CI 5.13-12.00) ( $P < 0.0001$ ). The three variables maintained their significance in the multiple model: PPI intake:  $P < 0.0001$ , OR 9.00 (95% CI 5.44-14.89); female sex:  $P = 0.0001$ , OR 2.95 (95% CI 1.69-5.15); and age:  $P = 0.001$ , OR 1.03 (95% CI 1.01-1.05). The goodness of fit of the model, measured as area under the curve, was 81.3 %, indicating a very good discrimination.

**Conclusions:** In our population, FGP had a higher prevalence than that reported previously, representing 62 % of gastric polyps with histologically confirmed diagnosis. Although female sex and age were also significant, PPI intake was the strongest risk factor associated with the presence of FGP.

## PHYSICIANS' COMPLIANCE TO THEIR OWN COLORECTAL CANCER SCREENING: WHAT IS THE FULFILLMENT OF THIS STRATEGY AMONG THEM?

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**Introduction:** Colorectal Cancer (CRC) is the second leading cause of death from cancer in western countries. Screening is strongly recommended as early diagnosis improves survival and reduces mortality in 20%.

However, its fulfillment in general population is about 50%. Physicians' compliance to their own screening is low, being Gastroenterologists, surgeons and radiologists the most compliant. Colonoscopy is the chosen method. Considering that Physicians' attitudes about their habits and own health exert strong influence in their patients recommendations, it is necessary to improve education to perform this strategy.

**Objectives:** 1. Estimate the percentage of physicians that had a screening test done. 2. Estimate the frequency distribution of tests used among professionals.

**Method:** We conducted an anonymous survey among 269 physicians of 50 years or older from four hospitals and four national and international scientific conventions between March and November, 2008. The survey, validated from Spanish into English, included demography, and nine questions about specialty, family history of CRC, compliance to screening, signs or symptoms at the moment of screening, age and tests used, reasons for having or not done the screening

and the results of the test.

**Statistical Analysis:** SPSS Medcalc 9.1 and VCCstat 2.0.

**Results:** 242 data surveys were included (response rate 90%); 83% of the participants were male; average age was 58 +6 years, and 98% were in current practice. Specialties were grouped as follows: Internal Medicine 72%, Surgical 18% and others 9%. 100 physicians had a test done (41% IC 95% 35-47%). The test most frequently used was colonoscopy in 70% (IC 95% 60-78%) followed by Barium Enema 10% (IC 95% 5-18%). Out of the whole screened physicians, 36% of them had family history of CRC, 63% didn't and 1% was unaware of this fact. A half of screened physicians were between 50 and 55 years. Internal Medicine specialists were the most compliant. Health care providers' recommendation was the main reason reported for screening. 59% of the professionals didn't screen; the reasons for this were personal decision, fear of procedure, and insufficient knowledge of guidelines on screening and lack of time.

**Conclusions:** Physicians own compliance to CRC screening is suboptimal. The barriers mentioned would be a challenge to implement strategies in order to achieve healthy habits and compliance to preventive care programs among physicians.

## TRANSVAGINAL NOTES CHOLECYSTECTOMY: POSTOPERATIVE GYNECOLOGICAL EVALUATION

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**Background:** the development of NOTES procedures raise issues regarding new ways of access to the abdominal cavity. The transvaginal access through posterior colpotomy has been widely used by gynecologists for the treatment of several conditions and has many advantages over other access (transgastric, transrectal and trans-vesical).

**Objective:** assessment of the postoperative gynecological impact, both anatomical and functional, after transvaginal NOTES cholecystectomy.

**Patients and method:** 22 female patients were operated between August 2007 and September 2008. All patients fulfilled the following requirements: a) symptomatic gallbladder stones, b) previous pregnancy, c) absence of common bile duct obstruction d) negative pregnancy tests, e) normal mini-mental test. The gynecologic screening evaluation included: interrogation, examination including colposcopy and pelvic-transvaginal ultrasound. A transvaginal NOTES cholecystectomy was attempted in the 22 patients with a hybrid technique: with laparoscopic control via a 5 mm umbilical trocar, a 2 way trocar was inserted through the right posterior vaginal cul de sac which allowed the insertion of a videogastroscope, forceps and diverse instruments. Once cholecystectomy was performed it was removed through the vagina and closure was attained with

a running suture of absorbable vycril 2/0. The postoperative follow up included gynecologic assessment at postoperative days 7, 30 and 60 and included guided questionnaire (patients satisfaction with the procedure, restart of sexual activity, spontaneous pain, dyspareunia), physical examination and colposcopy to assess healing, presence of anatomical injuries, vaginal secretion and other alterations.

**Results:** the operation with the NOTES hybrid technique could be completed in 21 of the 22 patients (95 %). In the remaining case the operation had to be performed laparoscopically due to pelvic adhesions (5 previous cesarean sections). One case required a minilaparotomy through a previous Pfannestiel incision for checking hemostasis of the vaginal cul de sac. The systematic assessment prove adequate healing of the vaginal access with no local complications. Two patients restarted sexual relations before the 30 days prescribed, and the rest followed compliance with the indications. None of the patients refer dyspareunia. Two patients got pregnant after the procedure and one underwent a normal birth delivery without complications.

**Conclusions:** the transvaginal NOTES access proves to be safe, with excellent outcomes, no complications and void of negative impact in the gynecologic and sexual aspects.

## COVERED VS. UNCOVERED SELF-EXPANDABLE METALLIC STENTS (SEMS) FOR MALIGNANT DISTAL BILIARY OBSTRUCTION (MDBO)

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**Background:** The palliation of unresectable MDBO by uncovered SEMS (uSEMS) and its advantages over plastic stents are well studied. However, recurrent jaundice and cholangitis can occur as a result of tumor ingrowth and occlusion of uSEMS. On the other hand, covered SEMS (cSEMS) were designed to overcome these problems, but have been reported to be associated to higher migration and cholecystitis rate.

**Aim:** To compare the efficacy, patency and complications rate of cSEMS and uSEMS in the palliation of MDBO.

**Patients and methods:** We conducted a retrospective cohort analysis of patients with unresectable MDBO who underwent ERCP and placement of cSEMS or uSEMS for biliary drainage at our institution. From July 2001 to March 2008, 62 patients received wallstents for unresectable MDBO. Under general anesthesia, endoscopic sphincterotomy was performed to all patients followed by the deployment of a wallstent. The procedure related morbidity, stent patency, stent related morbidity and overall patient survival after stent placement was determined. Patients were evaluated monthly on an outpatient basis.

**Results:** 52 patients (84%) were followed and included in this analysis. They underwent a total of 58 wallstent placement (31[53%] uSEMS, and 27[47%] cSEMS). 28 (54%) patients were male, and mean patient age was  $69 \pm 13$  (33-97). The underlying malignancy was pancreatic cancer 41 (79%), ampu-

llary cancer 5 (10%), cholangiocarcinoma 4 (8%), biliary papillomatosis in 1, and metastatic lymph node in 1 patient. There were two ERCP related complications (booth in uSEMS group). The median follow-up between stent placement and occlusion or patient death with patent stent was 170 days (4-1240). For cSEMS, median follow-up was 189 days (5-1162), and for uSEMS, it was 140 days (4-1240). In the cSEMS group, stent dysfunction occur in 8 (30%) patients versus 7 (23%,  $p=0,31$ ) in the uSEMS group. Median time to occlusion was 270 days (interquartile range 229) in cSEMS, and 129 days (IQR 95,  $p=0,055$ ) in uSEMS. The stenting period complications were: Migration (6[23%] cSEMS, 0 uSEMS,  $p=0.006$ ). Occlusion (2[8%] overgrowth in cSEMS vs 0 uSEMS,  $p=0.204$ ; and 0 ingrowth in cSEMS vs 7[23%] in uSEMS  $p=0,012$ ). Cumulative stent patency rate to 170 days was 0.82 (0.58–0.94, [95% CI]) for the cSEMS group and 0.64 (0.4–0.82 [95%CI]) in the uSEMS group ( $p=0.2$  [Cox-mantel test]). The estimated survival to 270 days was 0.48 (0.29–0.68 [95%CI]) in cSEMS and 0.37 (0.22–0.56 [95%CI]) in uSEMS group ( $p=0.92$ ).

**Conclusions:** We found no significant difference in stent patencies, survival or total complications between uSEMS and cSEMS. However, migration was more frequent with cSEMS and ingrowth in uSEMS.

## COLONOSCOPY IN THE ELDERLY. DO THEY REALLY NEED IT?

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**Background:** As demographics shifts towards an aging population, the use of endoscopy in the elderly is increasing every year. Furthermore, most of the elderly presents symptoms such as abdominal pain or constipation due to disorders related to age. However, the clinical benefits of performing colonoscopy in the elderly remain unclear.

**Aim:** To assess whether colonoscopy in the elderly has clinical benefits.

**Patients and methods:** Cross sectional survey of consecutive patients over 75 years of age referred to our endoscopic center to perform colonoscopy in a two-year period. Patients with hematochezia, anemia, positive fecal occult blood test, weight loss and those with personal or family history of colorectal polyps or cancer were considered as high-risk group. Patients with abdominal pain, constipation, diarrhea, change in bowel habits or those who underwent screening colonoscopy were considered as low-risk group. Findings were classified as positive when patients' treatment and prognosis change (colorectal polyps, colorectal cancer, inflammatory bowel disease, ischemic colitis) and as negative when treatment and prognosis do not change (normal colonoscopy, diverticula). Colonic angiodys-

plasia was considered as a positive finding in the high-risk group and as a negative finding in the low-risk group because no treatment is recommended in the absence of anemia and gastrointestinal bleeding. Variables were analyzed using the chi-square Test.

**Results:** Of a total of 2,400 colonoscopies, 320 (13.3%) were performed in patients over 75 years, of which 186 belonged to the high-risk group and 134 to the low-risk group. Positive findings were evidenced in 82 patients (41 had colorectal polyps, 27 colorectal cancer, 2 inflammatory bowel disease and 12 colonic angiodysplasia) of the high-risk group and in 28 patients (22 had colorectal polyps, 3 colorectal cancer, 1 inflammatory bowel disease and 2 ischemic colitis) of the low-risk group (44% vs 20%,  $p<0.05$ )

**Conclusion:** In this study, colonoscopy has a high diagnostic yield in the elderly patients of the high-risk group. In contrast, the clinical benefits of performing colonoscopy in the elderly patients of the low-risk group seem to be low. As the elderly population continues to grow, further studies evaluating the usefulness of advanced endoscopic procedures will be needed.