View Abstract

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CURRENT CATEGORY: Immunology, Microbiology & Inflammatory Bowel Diseases
CURRENT SUBCATEGORY/DESCRIPTORS: IBD: Disease Activity Assessment
PRESENTATION TYPE: AGA Institute Poster
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Abstract

TITLE: FECAL CALPROTECTIN (FCAL) MONITORING IN ASYMPTOMATIC IBD PATIENTS, CALCULATING THE OPTIMAL CUT-OFF FOR MUCOSAL HEALING IN OUR POPULATION

AUTHORS (LAST NAME, FIRST NAME): Sambuelli, Alicia M.[1]; Gil, Anibal H.[1]; Negreira, Silvia[1]; Huernos, Sergio P.[1]; Chavero, Paula[1]; Tirado, Pablo[1]; Goncalves, Silvina A.[1]; Goldberg, Gisela[1]; Litwin, Nestor[2]

INSTITUTIONS (ALL): 1. Medicine, IBD Section - Bonorino Udaondo Hospital, CABA, Argentina.
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ABSTRACT BODY:

Abstract Body: BACKGROUND: FCal emerged as a useful tool for IBD management, but different assay methods, cut-offs, scenarios, phenotypes and populations may influence usefulness. AIMS**:** Two substudies were designed for the IBD population from a Latin-American center: **1)** To investigate the value of FCal in mucosal healing (MH) prediction (optimal cut-off, specificity, sensitivity, PPV, NPV) and thresholds for clinical activity and phenotypes, **2)** To evaluate the ability of FCal monitoring in IBD in remission to predict relapse.**MATERIAL and METHODS:** FCal was determined with Bühlmann fCAL®ELISA. **Substudy-1 (MH prediction and activity/pattern of IBD):** Included 100 IBD pts (44 UC 56 CD) who underwent routine colonoscopy (VCC) with categorization by IBSEN score (Frøslie KF, Gastroenterol 2007): "MH"(scores 0-1) and "non-MH", collecting FCal samples within previous wk. Optimal FCal cut-off for "MH"prediction (opt-MH cut-off) was calculated (ROC analysis). **Substudy-2 (Prediction of relapse):** included 50 UC and 50 CD in clinical remission (≥3 mo.), FCal: basal, ≥biannual (n 380; 3.8 per patient), VCC basal/final. Analysis: Kaplan Meier survival analysis for FCal levels above and below opt-MH cut-off. Mean follow-up 23.0±11.8 mo. Global definitions of clinical activity/relapse: P.Mayo (UC), HBI (CD), Location/Extent (Montreal). **RESULTS:Substudy-1:** FCal levels (Mean±SD) in pts with "MH" were significant lower vs. "Non-MH": UC 25/19 (191.3±174.6 vs. 621.1±368.3, p=0.0001) and CD 30/26 (237.0±196.9 vs. 618.5±319,3 p<0.0001) Kruskal-Wallis. Opt-MH cut-off was 242µg/g, AUC 0.84 (95% CI 0.753-0.906) p=0.0001, sensitivity: 76.4%, specificity: 84.5%, PPV: 85.7%, NPV: 74.5%. By clinical criteria FCal was lower (p<0.0001) in remission vs activity in UC (165.7±14.1 vs. 630.3±349.6) and CD (276.4±250.1 vs. 662.1±289.9), but FCal cut-off was higher (284 µg/g) than opt-MH cut-off. In endoscopically active CD pts, FCal levels in colonic CD (851.9±232.0) were higher vs. other locations (544.4±313.3) p=0.04. **Substudy-2:** Cumulative probabilities of clinical relapse at 6, 12, 18, 24 mo. of pts with FCal≥242 µg/g (n 34) were 20.6%, 38.2%, 44.7%, 51.6%, and with FCal under cut-off (n 66) rates were 1.5%, 3.1%, 5.1% and 7.9% respectively, HR: 14.22 (95% CI 6.18 to 32.72), p<0.0001, sensitivity: 85%, specificity 82.7%, PPV: 67.7%, NPV: 93.9%. Globally, relapsed 15 (30%) of UC and 12 (24%) of CD (NS). Clinical relapses with FCal≥242 were 67.7% vs 6.1% under cut-off, endoscopic relapses (available in 91 pts) with FCal ≥242: 75% vs. 6.8%, both p<0.00001. **CONCLUSIONS: 1)** The optimal cut off for mucosal healing in our IBD population was 242 µg/g, **2)** FCal values were significantly lower in remission vs. activity, either in UC and CD, but in endoscopically active colonic CD, FCal was higher vs. other CD locations, **3)** FCal showed to be an efficient tool to predict relapse for levels above opt-MH cut-off

HOW ARE CELIAC DISEASE PATIENTS FOLLOWED UP? RESULTS FROM A MULTICENTER CROSS-SECTIONAL STUDY FROM ARGENTINA

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BACKGROUND: Treatment with gluten-free diet as well as regular visits to a physician for symptom and nutritional control as well as analyses to determine persistence of intestinal inflammatory activity are recommended for celiac disease patients. It has been suggested that celiac patients are not adequately followed up; the determinants of such a phenomenon have not been clarified.

AIM: To describe the proportion of celiac disease patients that comply with follow up recommendations and to describe variables potentially associated with lack of adequate follow up

MATERIALS AND METHODS: A cross-sectional study was undertook in two referral centers in the Buenos Aires. Adult patients who were diagnosed with celiac disease for at least a year were identified from the endoscopic databases of both institutions and were invited to complete an anonymous survey. The following variables were collected: year of diagnosis, year of symptom onset, symptoms at presentation, family history of celiac disease, demographic data, symptom relapse if exposed to gluten, satisfaction with gastroenterologist care, financial assistance by health insurance providers for gluten-free diet-related costs. Self-reported Gluten-free diet adherence was assessed by means of the validated score by Biagi et al. Inadequate follow up was defined as the presence of any of the following: lack of regular follow-up by a gastroenterologist(annual or shorter-term if indicated by the physician) or lack of evaluation by a trained nutrition specialist or lack of follow-up analyses. A univariate analysis followed by a multivariate analysis using a logistic regression model was performed to determine the variables significantly associated with inadequate follow up.

RESULTS: Overall, 194 patients were enrolled. Median age was 40 years (range 18-74) and 79.89% were female. Median time from diagnosis was 4 years (1-58; 11.86% were asymptomatic on diagnosis. The most common symptom at the moment of diagnosis were diarrhea (41.24%) and abdominal pain/bloating (69.59). Self-reported gluten-free diet adherence was inadequate in 14.94% of patients. We found that 44.84% of patients were not adequately followed up: 41.24% do not attend regularly to follow-up visits, 17.23% of those patients who are followed up by a physician do not undertake any serological or endoscopic examination and 48.45% have never been evaluated by a trained nutrition specialist. On both univariate and multivariate analyses, satisfaction with gastroenterologist care on diagnosis [OR 1.61 (1.1-13.56)] and financial assistance for gluten-free diet-related costs [2.1 (1.3-25.65)] were related to adequate follow-up.

CONCLUSION: A significant proportion of celiac patients are not adequately followed up. Inadequate follow-up was not associated with self-reported lack of adherence to gluten-free diet. Both patient-related and medical-related factors may be subject to modification to improve follow-up of these patients.

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FINAL ID:

TITLE: CAPSULE ENDOSCOPY IMPACT ON THERAPEUTIC DECISIONS IN PATIENTS WITH CROHN'S DISEASE: A REAL-WORLD EXPERIENCE

AUTHORS (FIRST NAME, LAST NAME): Raquel González[1], Estanislao J. Gómez[1], Lisandro Pereyra[1], José M. Mella[1], Nicolas Panigadi[1], Carolina Fischer[1], Mariela Roel[1], Andres Mora Nuñez[1], Federico E. Bentolila[1], Cristian Ahumada[1], Daniel G. Cimmino[1], Silvia C. Pedreira[1], Luis A. Boerr[1]

ABSTRACT BODY:

Abstract Body: BACKGROUND. Small bowel (SB) evaluation in known Crohn's disease (kCD) is of paramount importance for planning therapy strategies. However, the utility of CE in helping physicians to make decisions in kCD is not currently well established.

AIMS. To investigate clinical utility of CE to assess activity and extension of kCD and also to evaluate whether the results of CE modify the subsequent therapeutic decisions.

METHODS. We conducted a single center retrospective cohort study. All consecutive adult's patients submitted to CE for kCD were included from Nov-2012 to Nov-2018. Data on demography, previous research, medications for IBD and follow-up were analyzed. Univariate analysis was carried out to identify CE features associated with changes in therapeutic management. A p value <0.05 was considered statistically significant.

RESULTS. A total of 345 CE protocols were performed, of which 90 were in IBD adult's patients. We included in the analysis 27 CEs submitted for kCD. The mean age was 35 years (range 15–75), 17 (63%) were males and median disease duration was 8 years. The CE reached the cecum in 26 cases (96%) and retention was observed in only one patient (4%) without necessity of surgical removal. At the time of CE, 5 patients (18%) had abnormal inflammatory biomarkers (C-reactive protein and/or faecal calprotectin), anaemia in 4 (15%), abdominal pain in 18 (67%), diarrhea in 16 (59%) and weight loss in 4 (15%). Thirteen of 27 patients (48%) had CE findings consistent with mucosal activity of CD. The lesions identified by CE included ulcers 11 (41%), erythema and villous edema 10 (37%), erosions 2 (7%), stenosis 2 (7%) and were distributed mainly in the distal part of the SB (3rd tertile) in 12 (44%), but in 4 (15%) the proximal SB (1st and 2nd tertile) was also affected. The mean Lewis Score (LS) was 784 (8–5392). Significant inflammatory activity (LS ≥ 135) was detected in 9 (33%) and was moderate or severe (LS > 790) in 2 (7%). CE has changed Montreal classification in 4 (15%) of patients and in 14 (52%) SB mucosal activity was ruled out. Indeed, CE has changed therapeutic management in 14 (52%) of patients within 3 months after the CE, as follows: 8 patients were started new biological therapy, 3 were optimized biological therapy, 2 were started on budesonide and 1 suspended azathioprine. Proximal SB affected, as compared to only distal SB affected, were more frequently associate with changes in therapeutic management (100% vs. 43%, p: 0.04). Significant inflammatory activity (LS ≥ 135), as compared to LS < 135, were also more frequently associate with changes in therapeutic management (82% vs. 25%, p: 0.004).

CONCLUSIONS. In our cohort, CE in patients with kCD added valuable clinical information and had a great impact on therapeutic decisions. Whether this approach will improve outcomes in kCD will require further investigation.

EFFICACY AND SAFETY OF *SACCHAROMYCES BOULARDII CNCM I-745 FOR THE TREATMENT OF DIARRHEA PREDOMINANT IRRITABLE BOWEL SYNDROME SIBO POSITIVE, AND ITS IMPACT ON MICROBIOTA COMPOSITION: A PILOT STUDY*

BACKGROUND: It has been suggested that both intestinal microbiota composition and function are associated with the development of diarrhea-predominant Irritable Bowel Syndrome (IBS-D). Furthermore, therapeutic alternatives which potentially modify microbiota such as antibiotics and probiotics have been proposed as valid options for the treatment of IBS-D. There is very little evidence on the efficacy of probiotics such as *S. boulardii*. Additionally, few evidence describe the modifications on intestinal microbiota produced by *S. boulardii* and its potential associations with clinical outcomes.

AIM: To evaluate the comparative efficacy for symptomatic improvement on SIBO positive, IBS-D patients between *S. boulardii* plus dietary treatment versus dietary treatment alone. To describe the composition of intestinal microbiota changes with both treatments and its potential association with clinical improvement.

MATERIALS AND METHODS: Adult patients with a diagnosis of IBS-D according to Rome III criteria from two referral centers located in Buenos Aires, Argentina were consecutively enrolled. Patients were asked to collect one fecal sample for microbiota and mycobiota study. Furthermore, patients fulfilled a previously-validated symptom severity questionnaire (IBS-SSS) and undertook a lactulose breath test; only those patients with a lactulose breath test compatible with small intestinal bacterial overgrowth (SIBO) were eligible for randomization. Clustered randomization was centrally generated; eligible patients were randomized in a 1:1 fashion to receive either *S. boulardii* 250 ug B.I.D. plus dietary advice (group 1) or dietary advice alone (group 2) for fifteen days. After treatment completion, patients were asked to perform another lactulose breath test and to collect another fecal sample. Demographic features as well as stool consistency at enrolment – defined by the Bristol Stool Scale – were also assessed. Genomic DNA from fecal samples were extracted and purified using previously described techniques. Analysis of bacterial composition was based on the V3 –V4 region of 16s rDNA; sequencing of the ITS2 region was used for fungal composition analysis. Data was processed according to QIIME v1 pipelinel; each sequence obtained was assigned to an Operational Taxonomic Unit (OTU). Additionally, qPCR analysis was performed for quantifying the abundance of the following species: *Faecalibacterium prausnitzii, Methanobrevibacter smithii, Bacteroides thetaiotaomicron* and *Pseudomona aeruginosa.* Correlation between microbial and fungal abundance and the above-mentioned clinical features was performed using Pearson correlation test.

RESULTS: Overall, 54 patients were randomized – 28 patients to group 1 and 26 to group 2. No significant differences in terms of demographic features, symptom severity or stool consistency were found between groups. Five patients group 2 and 1 patient in group 1 dropped out prematurely during the clinical trial. No major adverse events were observed in both groups during or after treatment interventions. Combined treatment with *S. boulardii* plus dietary advice led to a significant decrease in hydrogen excretion on lactulose breath test compared to baseline than dietary advice alone [-1800 (-3595 - -53), p=0.04]. Even though it did not reach statistical significance, a tendency towards a greater clinical improvement was observed in group 1. At day 15, a trend to a higher proportion of patients

having normal stool consistency was observed in group 1 (70.4% versus 47.6%, p=0.07). From a phylogenetic point of view, no major differences were found in terms of intestinal microbiota composition between groups. Only 2 genera (Lachnospiraceae_uncultured_bacterium and Ruminococcaceae_UCG 011) were correlated to SIBO on lactulose breath tests. Symptom severity was positively correlated to g-Gardenerella abundance (r=0.3, p=0.05) and negatively to g_[Eubacterium] coprostanoligenes group (r=-0.33, p=0.05). When comparing the differences in terms of microbiota composition after treatments, Decreases in abundances of c_Coriobacteriia (-67%), c_Deltaproteobacteria (-77.6%) and g_Hungatella (-74.9%) were found among group 1 patients, whereas decreases in abundances of c_Erysipelotrichia (-63%), c_Gammaproteobacteria (-77%), c_Lentisphaeria (-50%), c_Synergistia (-98.6%) and g_Enterobacter (-98.4%) were noticed in group 2. Interestingly, qPCR quantification revealed that *F. prausnitzii* were more abundant (+120%) in samples from patients treated with *S. boulardii plus* dietwith no more diarrhea than in patients still with diarrhea. *B.thetaiomicron* were more abundant (+219%) in group 1 patients with diarrhea than in patients with no more diarrhea in group 2. Furthermore, an increased abundance of *F. prausnitzii* (+400%) was found after *S. boulardii* + diet treatment in SIBO negative and IBS improved patient when compared to SIBO negative but no improved IBS.An increased abundance of *F. prausnitzii* (+76.5%) was found in samples from patients with an improvement of their abdominal pain scores when compared to non abdominal improved patient after treatment with *S. boulardii* + diet.

CONCLUSION: A tendency towards a lower hydrogen excretion and symptom improvement was observed among patients treated with *S. boulardii* and dietary advice. Moreover, addition of *S. boulardii* produced modifications in intestinal microbiota when compared to diet alone. The increase on *F. prausnitzii* abundance observed in patients with symptom resolution after treatment with *S. boulardii* merits further research as a potential benefitial therapeutic endpoint in these patients.

DDW 2019

View Abstract

FINAL ID:

TITLE: REAL LIFE PATTERNS OF GLUTEN-FREE DIET ADHERENCE IN CELIAC PATIENTS USING GIP EXCRETION.

AUTHORS (FIRST NAME, LAST NAME): Juan P. Stefanolo[1], Martín Tálamo[1], Samanta Dodds[1], Emilia Sugai[1], Paz Temprano[1], Ana Costa[1], María Laura Moreno[1], María Inés Pinto Sanchez[2], Edgardo Smecuol[1], Horacio Vázquez[1], Andrea F. Gonzalez[1], Sonia I. Niveloni[1], Elena F. Verdu[2], Eduardo Mauriño[1], Julio C. Bai[1, 3]

ABSTRACT BODY:

Abstract Body: Background/aim: Patients with celiac disease (CeD) treated with a gluten-free diet (GFD) are often exposed to gluten contamination. However, the frequency of such transgressions in a real life scenario is unclear. Therefore, we explored the pattern of fecal and urinary excretion of gluten immunogenic peptide (GIP) during a 4-week period in CeD patients on long-term GFD.

Methods: This descriptive and prospective study enrolled consecutive series of adult CeD patients on a GFD for more than two years. At baseline, patients completed a celiac symptom index (CSI) questionnaire to determine presence of symptoms. Patients collected stool and urine samples for 4 weeks. The collection protocol was designed to ensure coverage of gluten excretion during week-days and week-ends. Thus, the last stool on Fridays, and two urine samples during Sunday morning and evening, were collected. Urine samples were pooled in one single week-end assay.ELISA test for stool (iVYLISA GIP-S®, Biomedal S.L. Spain) and point-of-care tests (GlutenDetect®; Biomedal S.L., Spain) for urine were used for GIP detection.

Results: We enrolled 23 patients who were on a GFD for a median time of 7 yrs. Stool and urine samples were collected at all pre-established time points (n=92 for each type of excretion). GIP excretion in week-end urine samples was positive in 21/23 patients (91.3%), while GIP in stools collected during week-days was detected in 11/23 patients (47.8%) (*Fisher's Exact test*: $p<0.004$). Of all samples collected, while 41/92 GIP determinations in urine (44.6%) were positive, GIP was detected in 24/92 (26.0%)(*Chi square* test: $p<0.02$). Frequency of GIP excretion for each of the 4 weeks, progressively increased as the study progressed (1st vs. 4th week GIP excretion in either stool and/or urine: $p<0.05$) (Figure 1). No differences were observed comparing symptomatic (CSI scores >35 points) vs. asymptomatic patients.

Conclusions: The study shows evidence of a high frequency of dietary indiscretions in CeD patients on long-term treatment with GFD, independently of the presence of symptoms or not. Ingestion of gluten was notably more frequent during week-end than during week-days. We show that excretion of GIP (as a surrogate marker of gluten intake) increase along the 4-week study, likely due to a relaxation of dietary control by patients.

DDW 2019

View Abstract

FINAL ID:

TITLE: THERAPEUTIC RESPONSE TO SMALL INTESTINAL BACTERIAL OVERGROWTH (SIBO) IN IRRITABLE BOWEL SYNDROME (IBS). IS IT USEFUL TO TEST FOR?

AUTHORS (FIRST NAME, LAST NAME): Juan P. Stefanolo[1], Adriana Tevez[1], María M. Manresa[1], Tatiana Uehara[1], Maria Piskorz[1], Juan A. Sorda[1], Jorge A. Olmos[1]

ABSTRACT BODY:

Abstract Body: Background: IBS is known to be a multifactorial disorder with altered gut-brain interactions, frequently accompanied by psychiatric comorbidities. SIBO is present in some IBS patients. It is thought to be cause or a consequence because of changes in microbiota, provided by probiotics or antibiotics use, could render symptomatic relief.

Aims: To evaluate if there is symptomatic clinical, anxiety-depression and somatization response to rifaximin administration in diarrhea and mixed bowel movements pattern-subtype IBS patients (D-IBS and M-IBS) in positive vs negative SIBO patients.

Methods: We conducted a prospective experimental-comparative study. Adults patients were included if they met ROME IV criteria and organic cause was excluded. They were tested for SIBO by glucose-breath test (BT) Gastrolyzer (Bedfont) and treated with rifaximin 550 mg tid for 14 days regardless BT result.

To stablish symptomatic response we compared median/mean values of different specific scores (clinical: IBS severity scale, Anxiety-Depression: HAD score and somatization: PHQ 15 score) at one (first control) and three months (second control) after treatment.

Results: 100 D-IBS and M-IBS patients (Female=84) were enrolled. SIBO was found in 14 patients (14% [11% D-IBS and 3% M-IBS]). There was a 144 (median) points reduction (IQR 33-230) in negative SIBO patients (NSP) and 182 points reduction (IQR 76-290) in positive SIBO patients (PSP) after one month treatment (*p=NS*); and 119.5(IQR -2-210) and 139 (IQR 76-290) points reduction in NSP and PSP three months after treatment, in IBS severity scale, respectively (*p=NS*). We found a mean 1 (95% CI 0-3) and 3.5 (95% CI 2-6) points reduction in HAD score, for anxiety, (*p=0.006*) and 0 (95% CI -1-3) and 4.5 (95% CI 2-8) points reduction (*p=0.0004*) for NSP and PSP at one and three months after treatment respectively (Figures 1 and 2). Depression score was only statistically significant reduced (p=0.04) after three months treatment in PSP (mean: 2, 95% CI: 0-4) (figure 3). PSP had better response in PHQ 15 score either first (7.5[95% CI: 1-11] vs 1[0-5] *p=0.01*) or third month after treatment (4.5 [95% CI: 2-10] vs 2 [-1-5] *p=0.0015*) (figures 4 and 5).

Conclusion: PSP had better clinical response in IBS symptoms, although not statistically significant. Otherwise PSP had better anxiety and somatization improvement one month after treatment and it was even greater at three months. PSP had also depression improvement at three months compared with NSP.

DDW 2019

View Abstract

CONTROL ID: 3156538

CURRENT CATEGORY: Pancreatic Disorders

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PRESENTATION TYPE: AGA Institute Oral or Poster

PRESENTER: Maria I Vaccaro

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Abstract

TITLE: THE AUTOPHAGY-RELATED-PROTEIN VMP1 IS SECRETED IN EXOSOMES FROM PANCREATIC TUMOR CELLS

AUTHORS (LAST NAME, FIRST NAME): Garcia, Maria N.[1]; Sepúlveda-Acuña, Paula[1]; Renna, Felipe[1]; Orquera, Tamara[1]; Vaccaro, Maria I.[1]

INSTITUTIONS (ALL): 1. Institute of Biochemistry and Molecular Medicine, CONICET, School of Pharmacy and Biochemistry, University of Buenos Aires, Buenos Aires, Argentina.

ABSTRACT BODY:

Abstract Body: Different from degradative autophagy, *secretory autophagy* is thus a newly recognized mechanism of increasing relevance to explain the secretion of some molecules of critical biological importance. VMP1 is an autophagy-related transmembrane protein essential for autophagosome biogenesis. VMP1 is induced in pancreas by pancreatic diseases such as pancreatitis and pancreatic ductal adenocarcinoma. Exosomes are small vesicles (40-120 nm) which are released to extracellular medium by secretory autophagy. Here we demonstrate that VMP1 is involved in secretory autophagy and it is released from pancreatic cells as a membrane protein of the exosomes. Setting up two exosome purification protocols, by ultracentrifugation and by isolation with magnetic beads fussed to anti-VMP1 antibodies, we identified the presence of *VMP1-exosomes*, labeled with CD63, in supernatant of different pancreatic cancer cell lines. We confirmed the secretion of VMP1-exosomes by electron microscopy, western blot and flow cytometry and using other markers of exosomes, such as CD81, CD9 and Alix. By means of the induction of autophagy with starvation, rapamycin treatment or overexpression of VMP1 and the autophagy inhibition by shATG5, shVMP1, 3-MA and chloroquine, we confirmed that VMP1-exosome secretion depends on autophagosome formation. Using VMP1-exosome fraction secreted by cell lines expressing CD63-GFP, we demonstrated that VMP1-exosomes are able to be up-taken by other cell lines, suggesting that VMP1-exosomes might be able to mediate remote communication between cells. Finally, using three different antibodies, we detected VMP1 in human serum from donors (N=20) and we purified exosomes from human serum using magnetic beads fussed to anti-VMP1 antibodies. In conclusion, we detected for the first time, an autophagic protein secreted to the cellular environment, which is able to be up-taken by other cells. Further, the demonstration of VMP1-exosomes in human serum is of high potential as a relevant molecule for diagnosis, treatment and monitoring diseases such as pancreatitis and pancreatic ductal adenocarcinoma.

(No Table Selected)

(No Image Selected)

DISCLOSURE

The following authors have completed their 2019 DDW disclosure: Maria Garcia: No Answer. | Paula Sepúlveda-Acuña: No Answer. | Felipe Renna: No Answer. | Tamara Orquera: No Answer. | Maria Vaccaro: Disclosure completed

COLONIC BIOPSY PRACTICE IN PATIENTS WITH CHRONIC DIARRHEA AND NORMAL ENDOSCOPIC FINDINGS

Juan Lasa; Silvina Paz; Astrid Rausch; Ignacio Zubiaurre

Gastroenterology Department. Hospital Britanico. Buenos Aires, Argentina

BACKGROUND: Chronic diarrhea may sometimes be a challenging diagnostic dilemma. In patients without a clear cause and normal endoscopic findings, microscopic colitis may be a possible diagnosis that should be excluded. Consecutive colonic biopsies are hence recommended. Determinants of the compliance of such a recommendation have not been extensively assessed.

AIM: To describe the proportion of patients with chronic diarrhea and normal endoscopic findings that had colonic biopsies taken and the potential variables that are associated with the compliance of such a practice.

MATERIALS AND METHODS: Endoscopic database of our institution was reviewed from January 2013 to July 2018 to identify adult subjects referred for endoscopy due to chronic diarrhea who did not show any macroscopic finding that could explain their symptoms. The proportion of patients that had colonic biopsies taken was estimated; also, the following variables were also retrieved: gender, age, endoscopist's specialty, identification of any colonic polyp, number of biopsy samples taken, proportion of patients with a diagnosis of microscopic colitis. A univariate analysis was performed followed by a multivariate analysis using a logistic regression model to determine the variables significantly associated with the collection of colon mucosa specimens.

RESULTS: Overall, we reviewed 8422 colonoscopies and identified 403 patients referred for chronic diarrhea with normal endoscopic findings; 300 (74.44%) had colonic biopsies taken. We found no differences in terms of gender between patients with and without colonic biopsies; however, the former were significantly younger [median age 59 (57-61) vs 67 (64-70) respectively, p=0.0001]. We found a significantly smaller proportion of patients with colonic biopsies who had at least one colonic polyp identified (33.33% vs 86.41%, p=0.001) and also a significantly higher proportion of gastroenterologist operator among patients with colonic biopsies (26.21% vs 11%, p=0.001). On multivariate analysis, the aforementioned variables were significantly associated with the odds of colonic sample obtention [OR 0.97 (0.96-0.99), 0.26 (0.18-0.37) and 0.2 (0.15-0.48) respectively]. Mean number of colonic samples taken by gastroenterologists was significantly higher than those taken by non-gastroenterologists (7.36±5.3 vs 3.2±3.43, p=0.001). Prevalence of microscopic colitis was 1.99% (2.66% among patients with colonic biopsies); 62.5% were catalogued as lymphocytic colitis. On multivariate analysis, both age and the number of biopsies taken were significantly associated with the diagnosis of microscopic colitis [OR 1.04 (1.01-1.1) and 1.18 (1.02-1.36), respectively), whereas no significant association was found with gender, celiac disease diagnosis and colorectal polyp finding.

CONCLUSION: A non-neglectable proportion of patients with chronic diarrhea and normal endoscopic findings do not have colonic biopsies taken. This could have a significant impact on the prevalence of diagnosis of conditions such as microscopic colitis.

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FINAL ID:

TITLE: EFFECT OF *BIFIDOBACTERIUM INFANTIS* NSL SUPER STRAIN IN HIGHLY SYMPTOMATIC CELIAC DISEASE PATIENTS ON LONG-TERM GLUTEN-FREE DIET. A PILOT STUDY

AUTHORS (FIRST NAME, LAST NAME): Edgardo Smecuol[1], Paz Temprano[1], Ana Costa[1], Emilia Sugai[1], María Laura Moreno[1], María Inés Pinto Sanchez[2], Horacio Vázquez[1], Juan P. Stefanolo[1], Andrea F. Gonzalez[1], Christopher R. D'Adamo[3], Sonia I. Niveloni[1], Elena F. Verdu[2], Eduardo Mauriño[1], Julio C. Bai[1, 4]

ABSTRACT BODY:

Abstract Body: Background: A strict gluten-free diet (GFD) is currently the only recommended treatment for celiac disease (CeD). Despite apparent compliance with the diet, 30-50% of treated patients have gastrointestinal (GI) symptoms. A recent DBPC trial showed that oral administration of *Bifidobacterium infantis* NLS super strain (*B. infantis* NSL-SS) alleviated symptoms in newly diagnosed CeD patients consuming gluten[1], and that this effect could be attributed to the modulation of innate immunity[2].

Aim: We explore the effect of a three-week course of *B. infantis* NSL-SS on persistent symptoms in patients with CeD following a long-term GFD.

Methods: We conducted a prospective, randomized, cross-over, double-blind, placebo-controlled trial. Adult patients were enrolled if they were on a GFD for at least two years and were symptomatic at screening according to the GI symptom rate score (GSRS) (>3 points in the mean global score or >2 for any individual syndromes). Patients voluntarily consuming gluten, with complications, other treatments that might have affected results, or limitations for following protocol or collecting stool or urine samples were excluded. After a one-week run-in period, patients were randomized to receive *B. infantis* NSL-SS (Natren LIFE START 2 ® Natren Inc. CA.) (2 capsules 3 t.i.d.; 2 x 10^9CFU/capsule) or placebo for 3 weeks. After a 2-week wash-out period, patients switched treatment for the next 3 weeks. Outcome was assessed based on changes (Δ) in the celiac symptoms index (CSI) for each treatment. Stool and urine samples were also collected at the end of each period for detection of gluten immunogenic peptide (GIP) excretion.

Results: Eighteen patients were enrolled; 2 were excluded due to intentional transgressions and 4 due to inconsistences in symptoms questionnaire reports. In the per protocol analysis (n=12), there were no significant changes in the CSI total score and subscales comparing probiotics vs. placebo. However, there was a significant improvement of specific CeD symptoms in *B. infantis* treatment compared to placebo (median Δ [range]: 5.0 points [0 to 9] vs. 2.5 [-7 to 4], respectively; $p<0.03$; Mann-Whitney) when this analysis was restricted to patients with total CSI scores above the median (Figure 1). There was a significant placebo effect in general health subscale ($p<0.04$). Globally, we observed a non-significant carryover effect when probiotics was the first treatment. GIP excretion in stools and urine was similar in both treatments. No side effects were detected in either intervention.

Conclusions: This exploratory study suggests that *B. infantis* NSL-SS may improve specific CeD symptoms in a subgroup of GFD treated patients with higher symptomatic burden despite adherence to the diet. These findings require confirmation in larger studies.

1- J Clin Gastroenterol 2013; 47:139-47

2- J Clin Gastroenterol 2017; 51: 814-7

Characteristics and outcomes of patients with Inflammatory Bowel Disease followed at a tertiary care university hospital in Buenos Aires

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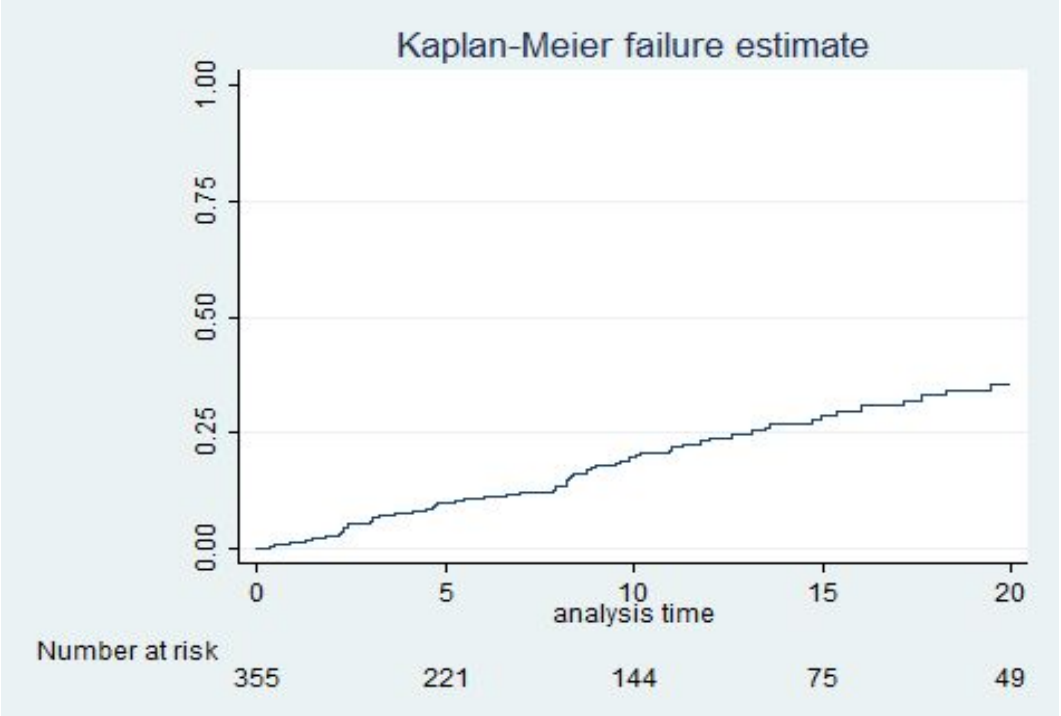
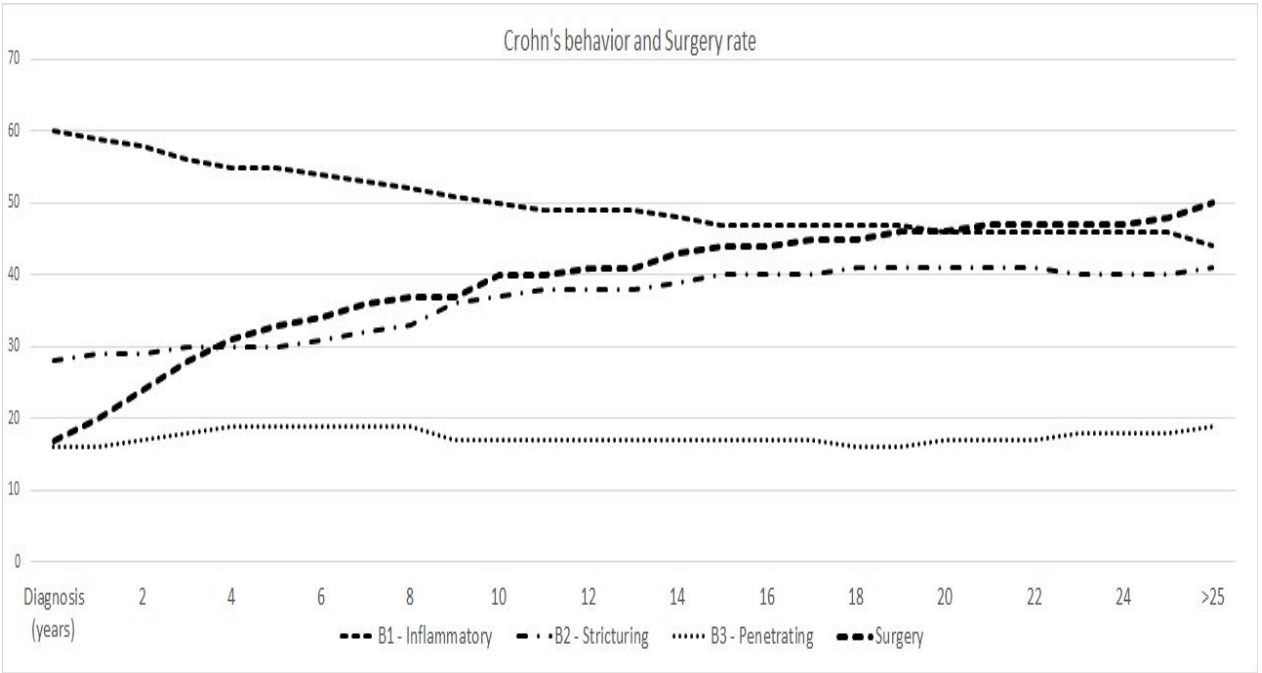
Introduction: Clinical expression of inflammatory bowel disease (IBD) varies between regions as well as between ethnic groups. In our country, little information is available on the clinical course of these disorders.
Objective: Describe severity and extent of IBD at time of diagnosis and during the course of disease. Also, behavior of the disease, steroid-dependence/resistance (SDR), immunosuppressant-biologics requirements, need for surgery and dysplasia/colorectal cancer (D-CRC) progression in adult patients attending a referral center in Latin America.
Design: Retrospective observational cohort study of adults with IBD, over the age of 18, followed at the Gastroenterology Department of a tertiary care university referral center in Argentine between Jan-02 and Jan-17.
Results: Seven hundred and twenty three patients with IBD diagnosis were reviewed, of which 461 were included. Fifty four percent were women (n=251) and age at diagnosis was 48±8 years. Diagnosis was Ulcerative Colitis (UC) in 80% of patients (n=369) and Crohn's Disease (CD) in 20% (n=92). In 20 patients with UC diagnosis was changed to CD during 10.6±9.6 years of follow-up, and in 6 from CD to UC during 12.5 ±9.9 years.
Among UC patients, 22% required hospitalization at onset and 34% at some point during the course of disease. In the case of CD patients, 48% were hospitalized at diagnosis and 50% during follow-up.
In UC, extension was left-sided at diagnosis in 46% and extensive in 47% by the end of follow-up; 12% progressed during the study period (graph 1). In CD, 42% of patients showed ileocolonic involvement, 33% ileal, 22% colonic and 3% upper GI tract, remaining mostly stable during follow-up.
The majority of CD patients presented an inflammatory pattern at onset, with increasing rates of fistulae and stenosis (graph 2).
Sixteen percent of patients with UC needed a coloproctectomy, 69% of these during early disease stages. In CD, 48% of patients required surgery during the study period (graph 2).
Concerning medical therapy, 45% of UC and 40% of CD patients presented SDR. Up to 87% of CD and 39% of UC patients required thiopurines.
One biological therapy was prescribed in 18% of UC cases and 2 biologics or more in 32%; in CD, 50% of patients received one biologic drug and 2 or more in 33%.
Progression to D-CRC was detected in 10% of UC patients (6% of these linked to the IBD) and D-CRC was diagnosed in 5% of CD cases (only 1% linked to the IBD).
Discussion: These results show that in the last 15 years, despite increased use of potent therapies, rates of hospitalization, steroid dependence/resistance and surgery remain high. As previously described, in UC, progression and disease extension occurred in 12%. Our results confirm that most CD patients present a benign inflammatory phenotype at time of diagnosis with increased rates of complications with time.

Graph 1. Likelihood of ulcerative colitis progression (disease extension)



1 year	3%	0.97 (CI 0.95-0.99)
5 years	11%	0.89 (CI 0.85-0.92)
10 years	22%	0.79 (CI 0.73-0.83)

Graph 2. Change in disease pattern and need for surgery in Crohn´s Disease



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Abstract

TITLE: **NON-VARICEAL UPPER GASTROINTESTINAL BLEEDING IN PATIENTS WITH LIVER CIRRHOSIS: CLINICAL FEATURES, ENDOSCOPIC FINDINGS AND MORTALITY**

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ABSTRACT BODY:

Background: Variceal bleeding in chronic liver disease has been studied extensively (1, 2), however 30-40% of upper digestive hemorrhages in cirrhotic patients are non-variceal (NVUGIB) and clinical features and endoscopic findings of this population have rarely been reported (3, 4). The aim of this study was to identify the outcomes and predictors of rebleeding and mortality in cirrhotic patients with NVUGIB.

Materials and Methods: Patients with chronic liver disease who presented clinical manifestation of bleeding (melena, hematemesis, and hematochezia) without bleeding of variceal origin were included within a retrospective cohort. They were followed until liver transplantation, transjugular portosystemic shunt placement (TIPS) or death. Clinical features, endoscopic findings, treatment, rebleeding and mortality were analyzed. Predictors of rebleeding and mortality were defined by a multivariate COX analysis.

Results: Forty three patients were included in the analysis. The mean age was 52 years old with women predominance. The most prevalent causes of chronic liver disease were autoimmune cirrhosis (20.9%), hepatitis C (16.3%), and alcoholic hepatitis, with Child-Pugh B-C status (74.41%). The most frequent clinical presentation was melena and peptic ulcer was the most common cause of bleeding. Eight patients (19%) required endoscopic treatment. The rebleeding rate was 11.4% (n: 5/43) and 10 patients (23%) died during hospitalization. The most frequent cause of death was septic shock. MELD score > 20 was statistically significant as a mortality predictor in crude and multivariate analysis (adjusted HR 6.12, 95% CI 1.52-42.21, P <0.01). Transfusions received and albumin levels were rebleeding predictors in univariate analysis (crude HR 7.88, 95% CI 1-62, p0.05 and crude HR 0.31, 95% CI 0.11-0, 87, p0.03, respectively).

Conclusions: The most common cause of non-variceal bleeding in chronic liver disease patients was peptic ulcer, coinciding with previous published reports. Mortality and rebleeding rates were influenced by the fact that most of the patients had advanced liver disease (Child Pugh C and MELD score> 20). The most important cause of death was septic shock.