

HIGH RATE OF MISINTERPRETATION OF HISTOLOGICAL DIAGNOSIS OF CELIAC DISEASE IN THE CLINICAL PRACTICE. Inés Pinto, Edgardo Smecuol, Roberto Mazure, Ana Cabanne, Sonia Niveloni, Eduardo Mautiño, Julio C. Bai. Small Bowel disorder Section, Department of Medicine. “Dr. C. Bonorino Udaondo” Gastroenterology Hospital, Buenos Aires, Argentina.

BACKGROUND/AIM: The histological analysis of small bowel mucosa is considered the gold standard for diagnosing celiac disease (CD). However, misinterpretation of specimens maybe source of potential pitfalls in clinical practice. Thus, poor sample quality, inadequate orientation and cutting could determine over- or under- interpretation of intestinal morphology. Our aim in the present study was to analyze the histological diagnostic performance in clinical practice reviewing a series of intestinal biopsies studied by general pathologists. **MATERIAL AND METHODS:** We performed a retrospective analysis of 186 consecutive specimens from patients referred for a second opinion to a tertiary center from September 2003 to October 2006. Original pathologic reports produced by many different clinical pathologists were retrieved. Characterization of CD by the expert reviewer was based on morphological grounds (Marsh’s type II or greater enteropathy). According to original reports, 129 samples had been considered as compatible with CD and 57 as having normal histology. Agreement was also established according to the Cohen’s kappa statistics for dichotomy variables. **RESULTS:** According to the expert review, 12 samples (6.4%) were not valuable at all because bad or poor quality of specimens. Both, original pathological reports and the review agreed diagnosis in 120 samples (64.5%). This included 77 specimens identified as CD and 43 having normal histology. Respect to original reports, 54 specimens (29.0%) had a divergent diagnosis by the expert pathologist (final diagnosis was CD in 11 and normal histology in 43). Using the kappa statistic, inter-observer agreement was 0.38. Based on the final diagnosis, misinterpretation was mainly produced by an over-diagnosis as CD of normal histological samples (40% vs. 25%; OR 0.48, 95% CI 0.24-0.97; $p < 0.05$). **CONCLUSIONS:** Our study detected major differences in the histopathological assessment of small intestinal biopsies between non-experienced and expert pathologists. Overall, misinterpretation by general pathologists was produced in 35.5% of specimens. These pitfalls in clinical practice may have profound negative implications for patients.

HYPNOSIS AND SATIETY IN HEALTHY VOLUNTEERS

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Background: There is now good evidence that hypnotherapy can modify several gastrointestinal functions (e.g. gastric acid secretion, orocecal transit time, rectal sensitivity) and it is useful in the management of gastrointestinal functional disorders (e.g. irritable bowel syndrome, dyspepsia, non-cardiac chest pain).

Aim: To assess if hypnosis can modify satiety in healthy volunteers (HV).

Design: prospective, open, randomized, pilot study, with a crossover design for hypnotic procedure.

Material and methods: A total of 19 HV, 11 females, aged 22-55 years (mean: 29,4) and 8 males, aged 23-34 years (mean: 27,37) fulfilling hypnotic susceptibility according to a validated questionnaire (Absorption Scale) were evaluated. Mean weight in females was 62,69 Kg (52-84,5) and in males 83,1Kg (62-112,7). Satiety drink test (SDT) was performed using a balanced energetic drink (1,5 Kcal/ml) administered at 15 ml/min and expressed as the maximum Kcal tolerated per individual. All subjects attended for 3 sessions at weekly intervals and gave their written informed consent before entering in the study.

After a SDT at baseline, all subjects were randomized to 2 groups before performing the SDT: Group 1 receiving only induction (I) of the hypnotic state and Group 2 receiving induction plus a direct suggestion satiety oriented (I+S). At the third session, subjects in Group 1 received (I+S) and conversely, subjects in Group 2 (I+S) were put on (I) before performing the SDT.

Results: In women, mean maximum Kcal tolerated was at basal 560,45 (mean SE 30,25) vs 638,18 (mean SE 45,13) after (I) and vs 482,68 (mean SE 38,53) post (I+S), showing a significant difference ($p < 0.01$) in satiety after (I+S) compared to basal satiety. It is interest to note that a significant difference ($p < 0.01$) was also observed when comparing mean maximum Kcal tolerated after (I) alone vs (I+S).

No difference in satiety (SDT) was found in men between basal compared to (I) and vs (I+S), being mean maximum Kcal tolerated at basal 717,13 (mean SE 102,21) vs 767,81 (mean SE 68,22) after (I) vs 776,38 (mean SE 93,44) after (I+S).

Conclusion:

Satiety can be significantly modified by hypnosis in female healthy volunteers.

Mechanisms why women are more prone than men to achieve a significant difference in satiety after hypnosis are not completely understood.

An advance in the categorization of Crohn's disease (CD): genetic, serologic and environmental factors correlate with Montreal classification (MC) . Sambuelli, Alicia M.¹; Crusius, Jacob B. A.,² Negreira, Silvia M.¹; Gil, Anibal H.¹; Huernos, Sergio P.¹; Czech, Andrea¹; Goncalves, Silvina¹; Toro, Martin A.¹, Tirado, Pablo¹; Cabanne, Ana¹; Pena, Amado S.²

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2. Pathology, VU University Medical Center, Amsterdam, Netherlands. **BACKGROUND:** An International Working Party (2005 Montreal WCG) modified the CD classification, to improve its applicability for clinical and research proposals. Its benefit must be validated worldwide with the future aim of an integrated clinical molecular and serological classification. **AIM:** To investigate associations between MC categories, genetic and serologic markers, and smoking status. **MATERIAL AND METHODS:** 143 unrelated CD (fulfilled data: 123) were categorized by MC in: Behavior: *nonstricturing nonpenetrating* (**B1:** n 58), *stricturing* (**B2:** n 38), *penetrating* (**B3:** n 27 internal fistulas), *perianal disease modifier* (**p:** n 50), Location: **L1:** n 25 (*ileal*), **L2:** n 55 (*colonic*), **L3:** n 36 (*ileocolonic*), **L4:** n 7 (*upper GI disease, isolated or associated with L1, L2, L3*), Age at diagnosis (yrs) **A1:** n16 (\square 16) **A2:** n 76 (17-40) **A3:** n 32 >40). Smoking stratification: *current smokers* (heavy: 15 cigarettes daily-5 yrs) *ex-smokers, non-smokers*. Disease duration: \square 5 yrs (B2 except. with postsurgical death: N1) Median 10 yrs (2 - 57) from CD onset. Genetic studies: 3020insC (SNP13), Gly908Arg (SNP12) and Arg702trp (SNP8) NOD2/CARD15 mutations by PCR. Serologic determinations: IgA/IgG ASCA, Anti- E. coli outer membrane porin (OmpC) IgG (ELISA, INOVA, CA), pANCA by IFI (INOVA, CA). Statistics: multiple logistic regression and survival analysis.

RESULTS:

Behavioral positive independent associations:

B2: with SNP13 (OR 5.5, CI 95%: 1.6-19.4, p=0.007) and heavy smoking (OR 3.8, CI:1.4-10.5, p=0.007).

B3: with SNP12 (OR:9.9, CI:1.8-55.6 p=0.009) and ASCA (OR 5.6, CI 1.8-17.2, p=0.002).

Shift B2-B3 subset : (N 15) with SNP8 (OR 7.7, 95% CI 1.30-45.1, p<0.05), ASCA (OR 7.4 CI:1.4-39.8, p=0.02) and OmpC (OR: 8.5, CI: 0.7-41.8, p=0.009).

Perianal disease: with ASCA (p<0.05).

Location positive associations:

L1: with smoking (OR 6.2, CI 2.2-17.4, p=0.0005). Smoking, SNP13 and ASCA reached significance if S.bowel is categorized irrespective of site.

L3: with SNP12 isolated (OR 23.9, CI 2.8-203.9, p=0.004) or L4 combined.

Negative associations suggesting a protective role: perianal disease with SNP13.

L2: (similarly to B1) associated with ASCA and smoking (SNP13 as trend).

L4 isolated: small sample.

A1,A2,A3: did not shown associations.

Log-rank test showed significant probabilities to develop complications for same variables described in logistic regression.

CONCLUSIONS: We found diverse associations with prognostic connotations between MC, genetic and serologic markers and smoking, some of them not feasible to detect by Vienna Classification subsets. MC seems to be a progress toward an integrated clinical, molecular and serological classification of CD.

Efficacy of 6-mercaptopurine (6-mp) in the treatment of ulcerative colitis (UC):
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BACKGROUND: 6-mp is a purine analogue extensively used in Crohn's disease management; however, there is limited information concerning its use in UC. **AIM:** to evaluate efficacy and safety of 6-mp UC treatment. **MATERIAL AND METHODS:** records of UC patients receiving 6-mp from Jan 2000 to Dec 2006 attending a single center were reviewed to assess clinical response, mucosal healing, steroid discontinuation, colectomy rates, and safety. Indication was steroid-dependent UC defined as difficulty to withdraw steroids during previous 6 mo. with two discontinuation attempts. We included 80 patients (40 males), mean age 31 yrs (range 13-68), extensive UC: 39 patients, left-sided: 36, distal: 5, mean time from UC onset until 6-mp treatment 6.8 yrs (6mo-28 yrs). Tentative 6-mp dose was 1 mg/kg. An 8 wk course of meprednisone started at 40 mg/d was used as a bridge. Efficacy was categorized as global response (Mayo score \leq 3 with rectal bleeding subscore \leq 1, endoscopic improvement and steroid free intervals $>$ 1 yr) and remission (Mayo score \leq 2 with mucosal healing as defined by a Mayo endoscopic subscore \leq 1, plus sustained steroid discontinuation). **RESULTS:** Global response rates at 6 mo, 1, 2, 3 yrs were 89% (n=72), 82% (n=69), 76% (n=51), 71 % (n=40) and remission rates 89%, 80%, 68%, 59%. Surgical requirement at the same times was 7%, 12%, 15%, 17% (Kaplan Meier Life Table); 44% of colectomized were 6-mp intolerant. Steroids were discontinued in 4.7 \pm 0.4 mo., 12% of cases needed sporadic courses. Mean 6-mp dose for achieving efficacy was 0.94 \pm 0.03 mg/kg. A significant increase in mean cell volume in responders vs. no responders (p<0.00001, Wilcoxon signed test) was observed. Responders had lower final mean WBC values, although significant difference compared with non-responders was not reached. WBC helped select non-responder patients to treat with higher dose (>1mg/kg) to achieve efficacy (11% of cases). Side effects, observed in 30% of patients, were: raised liver enzymes (10%) is normalized by stopping 6-mp, 3 of them continued with lower dose), leucopenia (7.5%, 2/3 of them reverted by decreasing dose), fever (2.7%), pancreatitis (2.5%), nausea (2.5%) and infections (6.3%: pneumonia, varicella, herpes zoster). Thirteen (16%) patients discontinued 6-mp. Hospitalization was only required in non-responders. **CONCLUSION:** 6-mp has shown to be effective in steroid dependent UC treatment, exhibiting a suitable rate of endoscopic response and low rate of colectomy in long-term follow up. Routine analyses were useful in monitoring safety and to improve efficacy. Benefits of 6-mp seem to outweigh potential risks of other therapies and surgical procedures.