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Diagnosis of Small Intestinal Bacterial Overgrowth by Lactulose Hydrogen Breath Test With Scintigraphic Oro-Caecal Transit Test: Methodological Validation of Diagnostic Criteria in Healthy Controls and Patients With Diarrhea Predominant Irritable Bowel Syndrome

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INTRODUCTION: The prevalence of small intestinal bacterial overgrowth (SIBO) in irritable bowel syndrome (IBS) patients remains contentious due to continuing uncertainty regarding diagnostic methodology. The lactulose hydrogen breath test (LHBT) is used to detect SIBO, however, recent papers have suggested that the results are confounded by wide variation of oro-caecal transit time. Combination with an independent, scintigraphic assessment of oro-cecal transit time (SOCTT) may address this problem with SIBO diagnosed when there is a rise in breath hydrogen before scintigraphic marker is seen in the caecum. AIM: To determine the most appropriate diagnostic criteria and clinical relevance of SIBO diagnosed using LHBT alone and combined HBT/SOCTT. SUBJECTS: 60 patients with diarrhea predominant irritable bowel syndrome (D-IBS) and 13 healthy controls. METHODS: A systematic analysis of the ability of six published diagnostic criteria to detect SIBO in D-IBS patients and controls was performed (Criteria 1: A H2 rise of ≥ 5ppm within 90 min; Criteria 2: A H2 rise of ≥ 20ppm within 90min within 90 min; Criteria 3: dual breath H2 peaks; Initial H2 rise, ≥ 5ppm (Criteria 4), 10ppm (Criteria 5) and 20ppm (Criteria 6) above baseline before the appearance of cecal contrast (Criteria 7): 0.001; R20ppm =0.860, p=0.003); however this association was lost in D-IBS patients (R5ppm =0.214, p=0.165). A H2 rise of ≥ 5ppm and 20ppm on LHBT and scintigraphic OCTT in health (R5ppm =0.896, p=0.005) or controls (R20ppm =0.437, p=0.003) were significantly elevated in both quiescent IBD having IBS-like and IBS, compared with quiescent IBD without IBS-like (p<0.01 respectively) or controls (p<0.01 respectively). Significant lower expression of ZO-1 and alpha catenin were found in both IBS and quiescent IBD having IBS-like, but not in IBS. Any change in histopathology was recorded. Improvement in symptoms was assessed by the symptoms’ diary completed by the patients. Improvement in quality of life was assessed by a validated IBS-QOL questionnaire administered pre- and post-treatment. Results: In the active drug group, there was a significant decrease in breath levels of pro-inflammatory cytokines IL-8 and TNF-α as judged by comparing mean improvement (p=0.000). There was an increase in anti-inflammatory cytokine IL-10 level (p=0.002). The tissue cytokine IL-8 level decreased (p=0.002), while IL-10 and IL-10/IL-12 ratio increased in the active drug group (p=0.006 & 0.008). Bowel related symptoms improved in each group without statistical differences except abdominal pain which was less severe at the end of treatment in the placebo group. There was an increase in 14 out of 34 parameters of QOL-IBS in patients who received the active drug (versus 6 parameters in placebo) while direct comparison of end of treatment questionnaire showed improvement in four in the active group and none in the placebo. The tissue cytokine profile showed a trend towards resolution at the end of treatment in patients with IBS-like symptoms. Improvement was noticed within the active drug group in the lymphoctic and neutrophil infiltrates (p=0.013, 0.011), epithelial mitosis (p=0.001), goblet cell depletion (p=0.035), and intracellular lymphocytes (p=0.005). However, direct comparison of post-treatment biopsies of both groups did not show any difference. Conclusion: Saccharomyces boulardi with Ispaghula husk was superior to placebo with Ispaghula husk in improving cytokine profile and quality of life in patients suffering from IBS-D.

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Functional Bowel Symptoms in Quiescent Inflammatory Bowel Disease: Role of Epithelial Barrier Disruption and Low Grade Inflammation


Objective: Determine the role of colonic barrier defects and low-grade inflammation to explain the presence of irritable bowel syndrome (IBS)-like in quiescent inflammatory bowel disease (IBD). Design: Cecal biopsies were collected in 51 IBS, 49 quiescent IBD (31 Crohn disease (CD) and 18 ulcerative colitis (UC)), and 27 healthy controls. IBS was assessed using Rome III criteria and IBS severity score. The integrity of epithelial barrier was evaluated by measuring paracellular permeability in biopsies mounted in Ussing chambers and mRNA expression of tight junction proteins (ZO-1, alpha catenin, occludin) Low-grade inflammation was appreciated evaluating mucosal intraphlethelial lymphocytes (IELs) and mast cells (MCs) counts and mRNA expression of IL-6, IL-8, IL-10 and TNF-alpha. IBS-like symptoms were defined as a 38% of CD and UC patients respectively. Paracellular permeability was significantly increased in both quiescent IBD having IBS-like and IBS, compared with quiescent IBD without IBS-like (p<0.01 respectively) or controls (p<0.01 respectively). Significant lower expression of ZO-1 and alpha catenin were found in both IBS and quiescent IBD having IBS-like. IELs and MCs were significantly higher in quiescent IBD having IBS-like, but not in IBS. Optimization of anti-inflammatory therapy may be considered in quiescent IBD having IBS-like.

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Cytokine and Clinical Response to Saccharomyces Boulardii Therapy in Diarrhea-Dominant Irritable Bowel Syndrome: A Double-Blind Randomized, Placebo-Controlled Study

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Introduction: Saccharomyces boulardii is a probiotic yeast. Its effect on blood and tissue cytokine levels in patients with diarrhoea and irritable bowel syndrome has not been extensively investigated. We aimed to assess the efficacy of Saccharomyces boulardii to improve cytokine profile, symptoms, quality of life, and histology in patients with IBS-D. Methods: In a double-blind placebo-controlled, study we randomized 72 patients, who fulfilled Rome III criteria, to receive Saccharomyces boulardii 250 mg oral thrice a day for 6 weeks (n=37) or a placebo (n=35) with a 2 week pre-treatment phase and 2 week follow up. Both arms received Ispaghula husk once a day in the previous. Pre-treatment colonscopy and end of treatment sigmoidoscopy were done. Rectal biopsies and blood samples were taken pre- and post-treatment and evaluated by ELISA. IL-8, IL-10, IL-12, and TNF-α were measured. Any change in histopathology was recorded. Improvement in symptoms was assessed by the symptoms’ diary completed by the patients. Improvement in quality of life was assessed by a validated IBS-QOL questionnaire administered pre- and post-treatment. Results: In the active drug group, there was a significant decrease in blood levels of pro-inflammatory cytokines IL-8 and TNF-α as judged by comparing mean improvement (p=0.000). There was an increase in anti-inflammatory cytokine IL-10 level (p=0.002). The tissue cytokine IL-8 level decreased (p=0.002), while IL-10 and IL-10/IL-12 ratio increased in the active drug group (p=0.006 & 0.008). Bowel related symptoms improved in each group without statistical differences except abdominal pain which was less severe at the end of treatment in the placebo group. There was an improvement in 14 out of 34 parameters of QOL-IBS in patients who received the active drug (versus 6 parameters in placebo) while direct comparison of end of treatment questionnaire showed improvement in four in the active group and none in the placebo. Though baseline histological findings were mild, improvement was noticed within the active drug group in the lymphoctic and neutrophil infiltrates (p=0.013, 0.011), epithelial mitosis (p=0.001), goblet cell depletion (p=0.035), and intraphlelial lymphocytes (p=0.005). However, direct comparison of post-treatment biopsies of both groups did not show any difference. Conclusion: Saccharomyces boulardi with Ispaghula husk was superior to placebo with Ispaghula husk in improving cytokine profile and quality of life in patients suffering from IBS-D.

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Effects of a Fermented Milk-Containing Klyuyveromyces Marxiannus B0399 and Bifidobacterium Lactis BB12 in Patients With Irritable Bowel Syndrome: A New Effective Agent

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Aim: To evaluate the effects on IBS symptoms induced by a new probiotic mixture compared to a standard formulation. Methods: 120 prospectively enrolled Rome III IBS patients (44M, 76F; age 37 ± 13) were randomized to either a fermented milk ("active preparation") containing Klyuyveromyces marxiannus fragilis B0399, Bifidobacterium lactis BB12, Lacticabolus bulgaricus and Streptococcus thermophiles, a "standard preparation" (i.e., Bifidobacteria lactis BB12, Lactobacillus bulgaricus and Streptococcus thermophiles) or placebo(milk drink). The study design was composed by a 2-week run-in period, a 4-week treatment period and a 2-week wash-out period. During each period, IBS cardinal symptoms (abdominal pain, bloating and bowel movement disturbances, VAS 0-10) and a composite IBS score, calculated as the sum of the three symptoms indicated above (VAS 0-30), were recorded on a daily basis. Bowel movement and stool consistency were also recorded. The global self-assessment was collected at the end of treatment and wash-out period, using a 4-point Likert scale. All data were analyzed using SPSS package. Results: For all symptoms those randomized for "active" and "standard" treatments experienced a greater significant reduction in symptoms in comparison to the placebo group. Both active and standard treatment were able to