THE IMPACT OF A PROBIOTIC MIXTURE (BIO-25 LRTM) ON SYMPTOMS AND INFLAMMATORY MARKERS IN DIARRHEA-PREDOMINANT IRRITABLE BOWEL SYNDROME: A DOUBLE-BLIND, PLACEBO-CONTROLLED CLINICAL TRIAL

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Background: Probiotic agents may have beneficial effects in irritable bowel syndrome (IBS), presumably via modulation of gut mucosal micro-inflammation. However, current evidence comes from small, poor quality studies. Bio-25, a probiotic mixture that contains 25 billion bacteria, was developed to treat IBS. Aim: To assess the effect of Bio-25 on symptoms and inflammatory markers in women with diarrhea-predominant IBS (IBS-D). Methods: A double-blind, placebo-controlled study conducted at the Tel Aviv Sourasky Medical Center between January 2014 and April 2015. Women fulfilling the Rome III diagnostic criteria for IBS-D were recruited prospectively. Patients with micro-inflammation at baseline, defined as high sensitivity CRP (hsCRP) 10 mg/l, were excluded. After a 2 week run-in period, 107 participants were allocated at random to receive a Bio-25 capsule twice daily for 8 weeks (treatment group, N=54) or placebo (control group, N=53). Stool consistency, frequency of loose stools, severity of abdominal pain, bloating, urgency and frequency were evaluated using the Bristol Stool Form Scale and visual analogue scales. To avoid recall bias patients reported their symptoms daily using an online secure system. Blood and stool samples were collected for hsCRP and fecal calprotectin (FC) levels at weeks 0 and 8. Data analysis was performed using the Wilcoxon and Mann Whitney tests, as appropriate. The institutional review board approved the study and participants signed informed consent. Results: Of the 107 patients who began the study 93 (49 from the treatment group and 44 from the control group) completed it. There were no differences between the groups in demographic characteristics, baseline symptoms, or inflammatory markers. All symptoms improved significantly, in both groups, at week 8 compared to baseline, but there was no statistically significant difference between the groups (Table 1). No significant change in
hsCRP or FC levels was noted at week 8 compared to baseline in either group (Table 2). FC measurements, performed post-hoc at the end of the study, identified 11 patients with elevated FC levels (100mcg/g) at baseline. Consequently, we performed another sub-analysis excluding these patients. With these patients excluded (N=48 in the treatment group and N=37 in the control group), the results were similar to those in the whole group analysis with no significant differences between the groups in either symptoms or inflammatory markers.

**Conclusions:** Eight weeks of treatment with Bio-25 led to significant improvement in symptoms in women with IBS-D. However, the size same effect was seen in the treatment and control groups. Moreover, Bio-25 showed no significant effect on inflammatory markers. More methodologically rigorous studies, such as the present one, are needed to delineate the role, if any, of probiotics in IBS.