Prophylaxis of Pouchitis Onset With Probiotic Therapy: A Double-Blind, Placebo-Controlled Trial

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See editorial on page 1535.

Background & Aims: We have recently documented the efficacy of a highly concentrated probiotic preparation (VSL#3) in the prevention of flare-up in patients with chronic pouchitis. The aim of this study was to compare probiotic therapy with VSL#3 versus placebo in the ability to prevent the onset of acute pouchitis during the first year after ileal pouch-anal anastomosis. Methods: Forty consecutive patients who underwent ileal pouch-anal anastomosis for ulcerative colitis were randomized to receive either VSL#3 (1 packet containing 900 billion bacteria/day) (n = 20) or an identical placebo (n = 20) immediately after ileostomy closure for 1 year. The patients were assessed clinically, endoscopically, and histologically after 1, 3, 6, 9, and 12 months. Health-related quality of life was assessed using the Inflammatory Bowel Disease Questionnaire. Results: Two of the 20 patients (10%) treated with VSL#3 had an episode of acute pouchitis compared with 8 of the 20 patients (40%) treated with placebo (log-rank test, z = 2.273; P < 0.05). Treatment with VSL#3 determined a significant improvement in Inflammatory Bowel Disease Questionnaire score, whereas this was not the case with placebo. Conclusions: Treatment with VSL#3 is effective in the prevention of the onset of acute pouchitis and improves quality of life of patients with ileal pouch-anal anastomosis.

Total proctocolectomy with ileal pouch-anal anastomosis (IPAA) has emerged over the past 15 years as the surgical procedure of choice for the management of ulcerative colitis (UC). Pouchitis, a nonspecific, idiopathic inflammation of the ileal reservoir, is the most frequent long-term complication following pouch surgery for UC.1 The reported incidence of pouchitis is largely variable because of the difference in the nature and duration of follow-up and particularly because a myriad of diagnostic criteria have been used to define this syndrome.2–7 Most patients who develop acute pouchitis do so within the first year after surgery, but some experience their first attack years later.4 The cause is still unknown, but it seems that both a history of UC and increased bacterial concentration are main factors.1,8 The role of bacteria is further emphasized by the evident efficacy of antibiotics.9–11 This syndrome is clinically characterized by variable symptoms, including increased stool frequency and fluidity, rectal bleeding, abdominal cramping, urgency and tenesmus, incontinence, fever, and extraintestinal manifestations.8 A clinical diagnosis should be confirmed by endoscopy and histology. The endoscopic features of pouchitis include mucosal erythema, edema, friability, petechiae, granularity, loss of vascular pattern, erosions, and superficial ulceration. Histologic examination shows an acute inflammatory infiltrate with crypt abscesses and ulceration in addition to chronic inflammation, including villous atrophy and crypt hyperplasia, which is almost universal and probably represents an adaptive response of the pouch mucosa to fecal stasis.12 The absence of clear and universally accepted criteria for the diagnosis, classification, and definition of activity of pouchitis has led to great variability in the reported incidence of pouchitis and assessment of therapy. To overcome this problem, Sandborn et al. developed a Pouchitis Disease Activity Index (PDAI).13 This 18-point index is based on clinical symptoms and endoscopic appearance as well as acute histologic findings and represents an objective and reproducible scoring system for pouchitis. Active pouchitis is defined as a score ≥7, and remission is defined as a score <7.

Probiotics are defined as living microorganisms that, on ingestion in adequate amounts, exert health effects

Abbreviations used in this paper: CFU, colony-forming units; IBDQ, Inflammatory Bowel Disease Questionnaire; IPAA, ileal pouch-anal anastomosis; PDAI, Pouchitis Disease Activity Index.
beyond inherent basic nutrition. Bacteria associated with probiotic activity are most commonly lactobacilli, bifidobacteria, and streptococci; however, other non-pathogenic bacteria such as some strains of *Escherichia coli* and nonbacterial organisms such as the yeast *Saccharomyces boulardii* have been used. The rationale for using Saccharomyces and nonbacterial organisms such as the yeast *E. coli* beyond inherent basic nutrition is based on convincing evidence implicating intestinal bacteria in the pathogenesis of Crohn’s disease, ulcerative colitis, and pouchitis.

Promising results have been obtained with probiotic therapy in experimental colitis and in maintenance treatment of UC. We have recently used a probiotic preparation (VSL#3) characterized by a high bacterial concentration (300 billion/g of live microorganism) and the presence of a cocktail of 8 different bacterial species. This probiotic preparation has been shown to be effective in maintenance treatment of chronic pouchitis in a double-blind, placebo-controlled trial, in maintenance treatment of UC, and in preventing postoperative recurrence of Crohn’s disease. More recently, VSL#3 has been shown to be effective as primary therapy in interleukin 10 gene–deficient mice and to have a direct effect on epithelial barrier function.

The aim of this study was to compare the efficacy of VSL#3 with placebo in the prevention of onset of pouchitis during the first year after restoration of the fecal stream.

### Materials and Methods

This study was performed in accordance with the Declaration of Helsinki and was approved by the ethical committee of our hospital; written informed consent was obtained from the patients. Eligible patients were between 18 and 65 years old who underwent protective ileostomy closure after IPAA for UC. Patients with known Crohn’s disease, undergoing IPAA without ileostomy, or with perianal disease (including abscess, fissure, stricture, or anal sphincter weakness) as well as pregnant or lactating women were excluded. No other concurrent treatment was allowed.

The primary end point of the study was the occurrence of pouchitis. Secondary end points were quality-of-life assessment (Inflammatory Bowel Disease Questionnaire [IBDQ]) and comparisons of fecal concentrations of bacteria before and after treatment. Post-hoc exploratory analysis included comparison of stool frequency between treatment groups.

### Study Medication

VSL#3 (VSL Pharmaceuticals, Inc., Ft. Lauderdale, FL) was provided in packets, each of which contained 900 billion viable lyophilized bacteria of 4 strains of *Lactobacillus* (*L. casei*, *L. plantarum*, *L. acidophilus*, and *L. delbrueckii* subsp. *bulgaricus*), 3 strains of *Bifidobacterium* (*B. longum*, *B. breve*, and *B. infantis*), and 1 strain of *Streptococcus salivarius* subsp. *thermophilus* (designated hereafter as *S. thermophilus*). Maize starch was included as filler. Placebo was provided in identical bags containing 3 g of maize starch. VSL#3 and placebo were administered once each night. The taste and smell of the active drugs were not readily identifiable.

### Study Design

This was a randomized, double-blind, placebo-controlled study. Within 1 week after ileostomy closure, patients were randomized to receive 1 packet/day of VSL#3 or placebo for 12 months. Assignment to therapy or placebo was determined according to a computer-generated randomization scheme. Randomization was performed by the clinical trial pharmacist, who kept the codes until completion of the study. None of the staff or patients had access to the randomization codes during the study. The medications were dispensed by the investigator at each visit; compliance was assessed by counting returned bags and questioning the patients.

### Evaluation and Scheduling

Demographics and risk factors for pouchitis (recent cessation of tobacco use, sclerosing cholangitis, extraintestinal manifestations, pancolitis) were assessed at baseline. Assessment of symptoms (stool frequency, rectal bleeding, fecal urgency, abdominal cramps, fever), endoscopic examination of the ileal pouch and the ileum for a few centimeters proximal to the pouch (with mucosal biopsy specimens), and histologic assessment of biopsy specimens were performed at baseline and after 1, 3, 6, 9, and 12 months according to the PDAI.

Based on the criteria of Sandborn et al., patients with a total PDAI ≥7 were classified as having active pouchitis. Patients had to have histologic and endoscopic acute inflammation as well as clinical symptoms to be diagnosed with active pouchitis.

Health-related quality of life was assessed at baseline and after 1, 3, 6, 9, and 12 months by using the IBDQ, which considers bowel, systemic, and emotional symptoms as well as social function. IBDQ scores range from 32 (worst quality of life) to 224 (best quality of life).

### Safety Assessment

All unfavorable, unexpected symptoms were recorded in the diary kept by patients during the study. Laboratory studies, including a complete blood count and blood chemistry measurements, were performed at baseline and at the end of treatment.

### Microbiologic Determinations

Fecal sample collection. Fecal samples were examined before starting treatment (T0) and after 6 months of treatment (T1). The specimens were collected with sterile plastic containers, immediately stored at −20°C, and analyzed within 10 days to evaluate their bacterial microflora composition.
Isolation and enumeration of fecal bacterial groups. Anaerobic culture techniques, isolation procedures, and identification methods were performed as previously described.\textsuperscript{32} One gram of each fecal sample was homogenized in 99 mL of preduced half-strength Wilkins Chalgren Anaerobic Broth (Oxoid, Basingstoke, England) and serially diluted in an anaerobic cabinet (Anoabic System, model 2028; Forma Scientific Co., Marietta, OH). The dilutions were spread onto plates containing the following agar media: LAMVAB\textsuperscript{33} for Lactobacillus; RBB\textsuperscript{34} for Bifidobacterium; Schaedler anaerobe (Oxoid) plus defibrinated horse blood (50 g/L), mendadine (5 mg/L), vancomycin (28 mg/L), and kanamycin (100 mg/L) for Bacteroides; and O.P.S.P. (Oxoid) for Clostridium perfringens. Plates were anaerobically incubated in triplicate at 37°C for 24–48 hours. The same dilutions were removed from the anaerobic glove box and used to inoculate the following media: azide maltose (Biolife, Milan, Italy) for enterococci; MacConkey (Merck, Darmstadt, Germany) for coliforms; and ST agar\textsuperscript{35} slightly modified by adding bromocresole purple (30 mg/L), bromocresol green (100 mg/L), and nalidixic acid (30 mg/L) for S. thermophilus. Plates were aerobically incubated in triplicate at 37°C for 24–36 hours. The lower limit of detection was 1000 microorganisms/g feces, and bacterial concentrations were expressed as colony-forming units (CFU) per gram of dry feces. Representative colonies of each selective medium were identified to genus level by standard bacteriologic procedures such as Gram stain reaction, colonial and cellular morphology, and biochemical reactions.

Polymerase chain reaction detection of S. thermophilus and Bifidobacterium. Amplification reactions were performed in a Biometra Thermal Cycler II (Biometra, Goettingen, Germany). Dynazyme II (Celbio, Milan, Italy) was used as thermostable polymerase in the condition suggested by the supplier. The total volume of each reaction mixture was 25 μL. For each sample, the quantification of the specific bacterial group or strain was performed by direct amplification of 30–50 colonies selected from the highest dilution plates. Cells from plate colonies were used as a template without isolation of chromosomal DNA. The ratio between the number of colonies analyzed by polymerase chain reaction and the total number of colonies grown on the highest dilution plate, presenting at least 30 colonies, was calculated. The 16S–23S ribosomal RNA primer set ThI/ThII,\textsuperscript{36} species specific for S. thermophilus, was used for polymerase chain reaction detection and quantification of this microorganism during the trial, because ST-modified medium was not selective enough to discriminate S. thermophilus from other streptococci and enterococci. The reaction mixture consisted of 200 μmol/L of each deoxynucleoside triphosphate, 1 μmol/L of ThI and ThII primer, and 1 U of Dynazyme II. The amplification profile was at 95°C for 1 minute, 55°C for 30 seconds, and 72°C for 1 minute. This was repeated for 40 cycles. The program also included a preincubation at 95°C for 5 minutes before the first cycle and a final incubation at 72°C for 5 minutes. Bifidobacteria amplification using the primer sets Bif164/Bif662,\textsuperscript{37} InfY-BV.L/R, and BreY-BV.R/L,\textsuperscript{38} specific for the genus Bifidobacterium and for the VSL#3 strains B. infantis and B. breve, respectively, was accomplished under the following experimental conditions. The polymerase chain reaction mixture was composed of 200 μmol/L of each deoxynucleoside triphosphate, 0.5 μmol/L of each primer, and 1 U of Dynazyme II. The thermocycle program consisted of the following time and temperature profile: (1) 95°C for 5 minutes; (2) 40 cycles of 1 minute at 95°C, 30 seconds at a specific annealing temperature, and 1 minute at 72°C; and (3) 5 minutes at 72°C. The annealing temperature was 55°C for the primer sets Bif164/Bif662 and InfY-BV.L/R and 64°C for the primer set BreY-BV.R/L.

Enumeration of S. thermophilus and VSL#3 strains B. infantis and B. breve was performed by direct amplification of 30–50 colonies, randomly selected from the highest dilutions of ST-modified and RB agar plates. Aliquots (5–10 μL) of the amplified products were subjected to gel electrophoresis in 2% agarose gels and visualized by ethidium bromide staining.

Statistical Analysis

Baseline characteristics of patients after randomization into the 2 groups were compared using the χ² test corrected by Yates or the Student t test for independent samples as appropriate. Values of P < 0.05 were considered statistically significant. Survival analysis was used to analyze the data set with respect to first onset of pouchitis. The Kaplan–Meier method was used to estimate the survivor function, and comparison of cumulative rates of pouchitis between treatment groups was tested using the log-rank test. Wilcoxon signed rank test for paired data was used to compare the PDAI score at each visit with the basal visit score after adjustment of data using the last-observation-carried-forward method. The Mann–Whitney U test for unpaired data was used for the comparison of PDAI score at each visit between the 2 treatments. Comparison of IBDQ score at each time between treatment groups and at each visit versus the basal score for each treatment group was performed using the Mann–Whitney U test for unpaired data and the Wilcoxon signed rank test for paired data, respectively. Comparison of stool frequency at each time between treatment groups and at each visit versus the basal value was performed using the Student t test. Comparison of fecal concentration of bacteria before treatment and after 6 months was performed using the Student t test.

Results

Patient Characteristics

Forty-five patients were screened, and 40 were eligible and participated in this trial. Twenty were randomly assigned to receive VSL#3 and 20 to receive placebo. Five patients were ineligible or declined participation; 3 patients were excluded because they refused consent, 1 patient did not accept the endoscopic and histologic examination at baseline, and 1 patient was
being treated with corticosteroids for another medical condition.

The characteristics of the patients are shown in Table 1. The study groups were well matched with respect to age, sex, smoking habits, extension of colitis, and presence of extraintestinal manifestations before surgery.

The basal median PDAI score was 0 (range, 0–0) in both groups, median stool frequency was 9 in both groups (range, 5–12 in the VSL#3 group and 6–11 in the placebo group), and basal median IBDQ score was 100.5 (range, 74–166) in the placebo group and 102.5 (range, 84–159) in the VSL#3 group (P = NS).

### Clinical Results

Figure 1 shows the clinical outcome of the patients. Of the 20 patients who received placebo, 8 (40%) had an episode of acute pouchitis during follow-up (3 within 3 months, 4 within 6 months, and 1 within 9 months). Of the 20 patients treated with VSL#3, only 2 (10%) had an episode of acute pouchitis (after 9 and 11 months). Figure 2 shows the life-table analysis of the cumulative rates of pouchitis in the 2 groups (log-rank test, z = 2.273; P < 0.05).

Figure 3 shows the median total PDAI score over time in all patients studied using the last-observation-carried-forward method. There was a significant increase starting from the third month in the placebo group (P < 0.001), but this was not the case in the VSL#3 group. The difference between the 2 treatments was significant at all time visits starting from the 3-month visit (P < 0.01).

Table 2 shows the total PDAI score and the score of each component of the PDAI at the different intervals in all patients. The median total PDAI score of the 8 patients who had pouchitis in the placebo group was 10 (range, 8–13); this score was the result of a significant increase in clinical (median, 3; range, 2–4; P < 0.01), endoscopic (median, 4; range, 3–5; P < 0.01), and histologic (median, 3; range, 2–5; P < 0.01) scores of the PDAI. In the VSL#3 group, the 2 patients who had acute pouchitis had a median total PDAI score of 9 (range, 8–10; P < 0.01), with a median clinical portion score of 3 (range, 2–4; P < 0.01), median endoscopic portion score of 3 (range, 3–3; P < 0.01), and median histologic portion score of 3 (range, 3–3; P < 0.01). The patients with pouchitis in the placebo group tended to have a slightly more active inflammation compared with the 2 patients who developed pouchitis in the VSL#3 group.
However, all of these patients were successfully treated with a 15-day course of an antibiotic (ciprofloxacin or metronidazole).

The 12 patients in the placebo group and the 18 patients in the VSL#3 group who remained in remission had a median total PDAI score of 1 (range, 0–2) and 0 (range, 0–1), respectively. Median stool frequency significantly and progressively decreased only in those patients treated with VSL#3; the significant difference was already evident after 3 months (Figure 4). Median stool frequency in these patients at the end of the trial was 8 (range, 6–12) in the placebo group and 5 (range, 3–9) in the VSL#3 group (P < 0.001).

The median IBDQ score was not significantly improved at the end of the trial in the placebo group compared with baseline (104.5 [range, 78–179] vs. 100.5 [range, 74–166], respectively; P = NS). In the VSL#3 group, the median IBDQ score at the end of the trial was significantly improved compared with baseline (175 [range, 86–220] vs. 102.5 [range, 84–159], respectively; P < 0.001) and was significantly superior to the score obtained in the placebo group (P < 0.001) (Figure 5). This significant difference was already evident after 1 month of treatment; in fact, the IBDQ score increased gradually during the study only in patients treated with VSL#3. The increase in IBDQ score was global and randomly distributed across the instrument. In patients who remained in remission in the VSL#3 group, the median IBDQ score was 195 (range, 178–220) and was significantly superior to that of patients who remained in remission in the placebo group (150.5 [range, 120–179]; P < 0.01).

Results of Microbiologic Studies

In patients treated with VSL#3, no significant changes were registered for concentrations of Bacteroides, coliforms, clostridia, and enterococci compared with their basal levels. On the contrary, fecal concentrations of lactobacilli, bifidobacteria, and S. thermophilus were significantly increased after 6 months of treatment compared with concentrations at baseline (Table 3) (P < 0.001). In the placebo group, fecal concentrations of all species evaluated remained similar to that before starting treatment.

Polymerase chain reaction analysis showed that, after administration of VSL#3, S. thermophilus was detected at high levels in all patients treated (4.8 × 10^7 CFU/g; P < 0.02), whereas only 20% and 37% of patients, respectively, harbored S. thermophilus before probiotic treatment (1.5 × 10^3 CFU/g) and after receiving placebo (1.7 ×

**Table 2.** Score of Total PDAI and of Each Component in All Patients

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<th>PDAI score</th>
<th>Treatment</th>
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<th>3</th>
<th>6</th>
<th>9</th>
<th>12</th>
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<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–0)</td>
<td>0 (0–4)</td>
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NOTE. Data expressed as median and range.

![Figure 4](image_url) Median stool frequency in patients who did not develop pouchitis during treatment at the different intervals with (A) VSL#3 or (B) placebo. *Placebo significantly superior to VSL#3 (P < 0.01); **placebo significantly superior to VSL#3 (P < 0.001).

![Figure 5](image_url) Median IBDQ score over time in patients treated with (A) VSL#3 and (B) placebo. *VSL#3 significantly superior to placebo (P < 0.01); **VSL#3 significantly superior to placebo (P < 0.001).
The availability of the 16S–23S ribosomal RNA–targeted primers InfY-BV.L and BreY-BV.R, strain specific for VSL#3 *B. infantis* and *B. breve*, respectively, made it possible to study the fate of these strains through the gastrointestinal tract. For each fecal sample, collected at different times of the trial (T0 and T1), bifidobacterial colonies were directly amplified with the 16S–23S ribosomal RNA strain-specific primers and the titer variations of VSL#3 *B. infantis* and *B. breve* strains were studied. VSL#3 *B. infantis*– and *B. breve*–specific polymerase chain reaction signals could be detected only after the consumption of VSL#3, whereas no amplicon was obtained amplifying colonies from feces recovered from patients receiving placebo. In patients treated with the probiotic preparation, the VSL#3 bifidobacteria *B. infantis* and *B. breve* were found in 50% and 70% of patients treated with VSL#3 at a mean concentration of 2.2 × 10^9 and 5.1 × 10^9 CFU/g feces, respectively. A simultaneous transient presence of both VSL#3 *B. infantis* and *B. breve* was observed in the fecal population of 20% of patients treated with VSL#3.

### Safety

No side effects or significant changes from baseline values in any of the laboratory parameters examined were registered in either group of patients.

### Discussion

In this controlled trial, oral administration of the probiotic preparation VSL#3 was effective in the prevention of onset of pouchitis in patients who underwent IPAA for UC. Patients treated with VSL#3 had a significantly lower incidence of pouchitis compared with placebo. Moreover, treatment with this probiotic preparation determined a significant improvement in quality of life that was not noted with placebo. Interestingly, among patients who did not develop pouchitis, treatment with VSL#3 was associated with a significant increase in IBDQ score and a significantly lower stool frequency compared with placebo. The efficacy of this new probiotic preparation may be related to the increased concentration of protective bacteria, as shown by the microbiologic data. Further, variations in intestinal β-galactosidase and urease activity as a result of changes in the microflora induced by administration of VSL#3 have been described recently.39

The cause of pouchitis is still unknown and is likely to be multifactorial; however, the immediate response to antibiotic treatment suggests a pathogenic role for the microflora, and pouchitis was associated with a decreased ratio of anaerobic to aerobic bacteria, reduced fecal concentrations of lactobacilli and bifidobacteria, and an increase in luminal pH.40 Treatment of pouchitis is largely empiric, and only a few small placebo-controlled trials have been performed. Antibiotics are the mainstay of treatment; metronidazole and ciprofloxacin are the common initial therapeutic approach, and most patients have a dramatic response within a few days.9–11

The onset of pouchitis is most likely observed during the first year after pouch surgery. We reported a 40% incidence of pouchitis in the group treated with placebo; this higher rate of pouchitis compared with that previously reported is probably the result of the very aggressive follow-up we adopted; in fact, most of the patients who developed pouchitis in our study exhibited mild disease that probably would not be identified using only clinical criteria, as was done in most previous studies. Moreover, the cumulative risk of developing pouchitis at 12 months has been reported to be 37% in 2 recent studies.4,7

Recent studies have supported the potential therapeutic role of probiotics in inflammatory bowel disease. Encouraging results have been obtained with probiotic therapy in experimental colitis. Administration of *Lactobacillus reuteri* was shown to significantly reduce inflammation in acetic acid– and methotrexate-induced colitis in rats.17,18 More recently, *Lactobacillus* was shown to be able to prevent the development of spontaneous colitis in interleukin 10–deficient mice,19 and continuous feeding with *L. plantarum* could attenuate an established colitis in the same knockout model.20 A strain of *Lactobacillus salivarius* subsp. *salivarius* reduced the rate of progression from inflammation through dysplasia and colonic cancer in interleukin 10–deficient mice,21 and a novel strain of *B. longum* was able to attenuate inflammation in a lymphocyte transfer model using severe combined immunodeficient mice.22 In 3 controlled studies, capsules containing a nonpathogenic strain of *E. coli*, the Nissle 1917,
were shown to be similarly effective to mesalamine in maintenance treatment of UC.23–25

In an open study, VSL#3 was shown to be effective in the prevention of relapses in patients with UC who were intolerant or allergic to sulfasalazine or 5-aminosalicylic acid.27 More recently, we have shown in a double-blind study that VSL#3 was significantly superior to placebo in maintaining remission in patients with chronic pouchitis.26

In regard to the mechanisms of action, recent studies have shown that treatment with VSL#3 leads to a significant increase in tissue levels of the anti-inflammatory cytokine interleukin 10, together with a significant decrease in tissue levels of the proinflammatory cytokines interleukin 1, tumor necrosis factor α, and interferon gamma; a reduction in matrix metalloproteinase activity; and a normalization of colonic barrier function.29,41 Microbiologic studies have shown that administration of VSL#3 was able to determine a significant increase in fecal concentrations of bifidobacteria, lactobacilli, and S. thermophilus as previously shown,26,27 not modifying the fecal concentration of Bacteroides, clostridia, coliforms, and enterococci, suggesting that the beneficial effect was not mediated by the suppression of the endogenous flora.

The use of a molecular method to distinguish between endogenous and exogenous ingested bifidobacteria confirmed that the bifidobacteria strains administered with VSL#3 were able to survive the gastric acid and bile and to influence the gut flora composition. Furthermore, the specific detection of VSL#3 strains B. infantis and B. breve only in feces of patients treated with VSL#3 confirmed that the increase in the total fecal bifidobacteria population after probiotic consumption was due to the presence of VSL#3 bifidobacteria strains. The different colonization behavior, in terms of size and frequency of detection, of the exogenous bifidobacterial strains in the patients treated with VSL#3 emphasizes the complexity of the relationships between exogenous bacteria and the human host.

In conclusion, the results of this study indicate that the use of a highly concentrated mixture of probiotic bacterial strains is effective in the prevention of onset of pouchitis during the first year after pouch surgery and significantly improves the quality of life of patients with IPAA. These results further support the potential role for probiotics in therapy of inflammatory bowel diseases.

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