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Effect of oral supplementation of the probiotic capsule UB-01BV in the treatment of patients with bacterial vaginosis

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Abstract

Bacterial vaginosis (BV) is a common condition affecting millions of women annually and is characterised by a reduction in native lactobacilli. Antimicrobial therapy used to cure the disease is often found to be ineffective. We postulate that the potential probiotic capsule UB-01BV might be efficient in the treatment of BV. In the present study, 30 Indian women diagnosed with BV presenting symptoms such as white discharge, pH greater than 4.7, increased discharge, odour, colour of discharge and pruritus were included. All subjects were assigned to receive two potential probiotic capsules UB-01BV a day for 7 days. At the end of the treatment all subjects showed significant (P<0.001) positive response as revealed by a reduction in vaginosis symptoms. Therefore, the results of the present study provide the first preliminary evidence that the potential probiotic capsule UB-01BV can exert a significant reduction in vaginal infection.

Keywords: probiotics, bacterial vaginosis, lactic acid bacteria

1. Introduction

Bacterial vaginosis (BV) is a term used to describe disorders that cause infection or inflammation of the vagina. BV is quite a complex disease, characterised by the substitution of native lactobacilli either by facultative anaerobic bacteria such as *Atopobium*, *Gardnerella* and *Mobiluncus* (Fredricks *et al.*, 2005; Hillier, 2005), *Mycoplasma* (French *et al.*, 2006) or aerobic bacteria such as pathogenic *Escherichia coli* and/or *Enterococcus* (Donder *et al.*, 2002). The net result is an increase in pH, production of sialidase by colonising pathogenic microbes (Cauci *et al.*, 2002) or amine production by them resulting in white discharge and a fishy odour (Hapsari *et al.*, 2006). Vaginal infections can have symptoms like itching, burning, and vaginal discharge (Falagas *et al.*, 2007). If vaginosis is left untreated, it can lead to other complications like pelvic inflammatory disease (Ness *et al.*, 2006), infertility, pre-term birth, low birth weight, etc. (Anukam *et al.*, 2006). Hence, vaginitis is considered to be a warning symptom to prevent the occurrence of such complications and should be treated in time. Classical treatment for BV comprises either oral or vaginal antibiotic supplements, such as metronidazole or clindamycin. However, the cure rate is low and recurrences are often found (Bradshaw *et al.*, 2006). The recurrence is due to failure in establishing a normal microbiota following antibiotic therapy (Hillier *et al.*, 1993). This has led to considering the use of long-term, low-dose suppressive therapy for BV. Other studies also suggest that the incidence of BV increases the risk of sexually transmitted diseases (Myer *et al.*, 2005), making it essential to develop new approaches to the preservation of a healthy vagina, particularly therapies which can be readily available, more affordable and with a higher efficacy in terms of reducing recurrence of the disease.

Probiotic bacteria are considered an alternative treatment choice for BV prevention due to their ability to produce antimicrobial compounds, including bacteriocins, lactic and/or acetic acid and hydrogen peroxide (Ya *et al.*, 2010).

Oral supplementations of probiotic capsules are particularly alluring because of their ease of use and high satisfaction versus the use of creams and gels. The aim of the present study was to determine the efficacy of oral supplementation of a potential probiotic capsule UB-01BV in the treatment of BV.

2. Materials and methods

Selection of patients for clinical study

Thirty women registered at the out-patient department in Government Medical College and Hospital, Aurangabad, India, with symptoms of BV were examined. The study was approved by the Institutional Ethics Committee (ref no: ICE/09/09) and all subjects gave written consent before any research activity was initiated. The inclusion criteria for the subjects was based on the following symptoms: positive for whiff test, vaginal pH greater than 4.7 (normal pH between 3.8-4.5), along with other symptoms like increased discharge, odour and pruritus. Subjects were excluded if they were diagnosed as pregnant, suffered from diseases like insulin-dependent diabetes mellitus, hypothyroidism, severe obesity or liver disease, or diseases which may affect pH of the body and subjects receiving any systemic antibacterial agents 30 days prior to enrolment. Patients who had taken systemic or vaginal antibiotics, probiotics, systemic or vaginal anti-fungal agents or systemic corticosteroids in the previous 30 days were also excluded from the study.

Bacterial strains and treatment

The potential probiotic capsule UB-01BV (Provinorm) consists of several strains of *Lactobacillus* and one strain of *Bifidobacterium bifidum*, manufactured at Unique Biotech Limited, Hyderabad, India, under the WHO good manufacturing practices. Each capsule contained 10^9 viable cells of each strain (Table 1). These strains exhibit potential probiotic properties and antimicrobial activity under *in vitro* analysis hence were selected for the treatment of BV.

Table 1. Composition of the probiotic capsule UB-01BV.

Strain	Quantity (10^9 cfu/capsule)
Lactobacillus acidophilus strain UBLA-34	2.0
Lactobacillus rhamnosus strain UBLR-58	2.0
Lactobacillus reuteri strain UBLRu-87	2.0
Lactobacillus plantarum strain UBLP-40	1.0
Lactobacillus casei strain UBLC-42	1.0
Lactobacillus fermentum strain UBLF-31	1.0
Bifidobacterium bifidum strain UBBB-55	1.0

The study subjects were not blinded to the treatment they received. All subjects were asked to use two capsules of UB-01BV a day for 7 days.

Data collection and diagnosis

For efficacy

The diagnosis of BV was assessed based on Amsel's criteria for the presence/severity of the following symptoms, whiff test (2 = positive; 1 = negative), vaginal swab examination for pH, increased discharge (3 = severe; 2 = moderate; 1 = mild; 0 = absent), colour of discharge (3 = greyish white, 2 = white, 1 = colourless), odour (3 = severe; 2 = moderate; 1 = mild; 0 = absent) and pruritus (3 = severe; 2 = moderate; 1 = mild; 0 = absent) during the treatment. Subjects were asked to return for follow-up during the 2, 4, 7 and 15th day of treatment. Analysis took place on day 2, 4, 7 and was also included to assess recurrences and safety parameters.

For safety

Safety assessment was carried out on screening (day 1) and at last visit (day 15). The following tests were done on entry and on completion of the study: (1) haematology (haemoglobin, haematocrit, red cell count, leukocyte count with differential and platelet count); (2) SGPT/alanine amino transferase; and (3) serum creatinine.

Statistical analysis

Data was analysed using SPSS/PC+10.0 statistical packages (IBM, Armonk, NY, USA). Descriptive statistics were given as mean±SD with n as the number of observations. Student's paired t-tests were applied to compare basal and final values. Friedman (non-parametric 2-way ANOVA) tests were applied to detect overall change during treatment considering all time points. Descriptive statistics were calculated per protocol population (completed patients). All the tests were two-tailed and the level of significance was taken as $P>0.05$.

3. Results

In the present study the 30 subjects at Government Medical College and Hospital, Aurangabad, India enrolled to participate had symptoms and signs of BV. The condition of the subjects at the beginning of the study is mentioned in Table 2. Patients did not report any side effects with probiotic treatment. All subjects tested positive for the whiff test (30/30) and they differed as regards the severity of other symptoms such as increase in discharge, colour of discharge, odour and pruritus.

Table 2. Comparative analysis of vaginosis symptoms initially and during the course of treatment.

Variable	Baseline	Day 2	Day 4	Day 7	Day 15	Friedman value, significance[1] and *P*-value
pH	NA[1]	6.23±0.57	NA	6.00±0.00	NA	NA
Whiff (amine) test	NA	2=30 (100%)	NA	NA	1=30 (100%)	NA
Colour of discharge	2.86±0.43	2.9±0.40	2.9±0.365	1.06±0.36	1±0	109, S, *P*<0.001
Odour	2.80±0.48	2.83±0.38	2.47±0.63	1.53±0.63	0.40±0.67	102, S, *P*<0.001
Increased discharge	2.77±0.43	2.80±0.41	2.40±0.56	1.63±0.61	0.60±0.56	98, S, *P*<0.001
Pruritus	2.67±0.48	2.70±0.47	2.37±0.61	1.37±0.61	0.33±0.56	101, S, *P*<0.001

[1] NA: not analysed; S = significant.

Efficacy

Among the 30 patients who enrolled for the study, all returned for follow-up at day 2, 4, 7 and 15. All subjects were negative for amine (whiff) test at the end of the treatment (day 15).

In most of the subjects colour of discharge (greyish white, 2.89±0.43) observed on day 1 changed gradually during day 4 and had disappeared significantly on day 7 of treatment (from 2.89±0.43 on day 1 to 1.06±0.36 on day 7) followed by complete disappearance in colour of discharge (1.0±0.0, $P<0.001$) at the end of follow-up (day 15). Similarly, severity of increase in discharge (2.77±0.43), odour (2.80±0.48) and pruritus (2.67±0.43) observed at the beginning of treatment was found to be unchanged till day 4 of treatment, whereas on day 7 a significant reduction in the severity of these symptoms was observed. At the end of treatment (day 15) most of the subjects recovered significantly ($P<0.001$) as regards increased discharge (0.60±0.56), odour (0.40±0.67) and pruritus (0.33±0.56) (Table 2).

Safety

The patients did not report any adverse effects during the course of the study. All haematological parameters did not differ significantly at the beginning and end of the treatment ($P>0.1$) (Table 3).

4. Discussion

The role of probiotics in conferring health benefits to the host is being increasingly realised (Reid *et al.*, 2001) and species of *Lactobacillus* are studied extensively for vaginosis treatment, due to their non-pathogenic character, their ability to produce lactic and/or acetic acid (thereby maintaining a vaginal pH of around 4.2), to convert H_2O_2 and to produce bacteriocins. (Falagas *et al.*, 2007). Recent studies have highlighted the persistent problem of BV and suggested long-term antibiotic therapy for the prevention recurrences (Sobel *et al.*, 2006). Oral supplementation of probiotics is also effective as most of the urogenital bacterial microbiota originate from the gastrointestinal

Table 3. Haematological parameters of patients upon consumption of the probiotic capsule UB-01BV.

Parameters	Day 1	Day 15	t-value, significance[1], *P*-value
Haemoglobin (g/dl)	11.08±1.56	11.00±0.86	0.1, NS, *P*=0.9
Total red blood cells (10^6/µl)	4.48±0.35	4.47±0.33	0.1, NS, *P*=0.9
Total white blood cells (cells/mm^3)	6,826.67±1120.94	6,773.33±1223.04	0.9, NS, *P*=0.4
Eosinophil (%)	2.73±3.34	2.44±4.21	0.3, NS, *P*=0.7
Neutrophil (%)	62.37±4.71	63.37±4.94	0.7, NS, *P*=0.4
Monocytes (%)	0.00±0.00	0.00±0.00	0.0, NS, *P*=1.0
Lymphocytes (%)	34.30±4.84	33.50±5.21	0.8, NS, *P*=0.5
Serum creatinine (mg/dl)	0.63±0.20	0.68±0.25	0.2, NS, *P*=0.8
SGPT[2] (U/l)	9.73±2.86	9.73±4.28	0.0, NS, *P*=1.0

[1] NS = not significant.
[2] SGPT = serum glutamate pyruvate transaminase.

tract (Tannock *et al.*, 1990). The intestinal passage of these probiotic strains leads to a beneficial impact on the vaginal microbiota. This might have occurred due to the strains themselves ascending to the vagina from the rectal area or altering the ability of the pathogens to transfer to this niche (Reid *et al.*, 2001).

Studies also demonstrate that the vaginal microbiota changes constantly and particularly during the menstrual cycle it can be dominated by BV pathogens in the absence of *Lactobacillus* sp. (Keane *et al.*, 1997; Schwebke *et al.*, 1999). Hence supplementation with probiotic bacteria or *Lactobacillus* strains reduces the risk of infection several-fold (Reid *et al.*, 2003).

The present study demonstrates that 7-day oral consumption of the potential probiotic capsule UB-01BV is safe and reduces BV symptoms. All the subjects noted significant relief in symptoms during the 7-day treatment. Similarly, Anukam *et al.* (2006) reported that a 6-day treatment duration with *Lactobacillus* strains GR-1 and RC-14 significantly alleviated the symptoms of BV.

Reid *et al.* (2003) have reported that oral administration of *Lactobacillus rhamnosus* GR-1 and *Lactobacillus fermentum* RC-14 for 2 months was found to be effective in preventing recurrences of BV. Another trial proved that consumption of yoghurt containing *Lactobacillus acidophilus* was found to be more effective in the treatment of BV compared to pasteurised yoghurt (Shalev *et al.*, 1996).

5. Conclusions

This study concludes that the potential probiotic capsule UB-01BV is safe and quite effective in minimising the vaginal infections and consequent symptoms such as increased discharge, odour, colour of discharge and pruritus. Hence, oral supplementation of the probiotic capsule UB-01BV could be a solution for the efficient treatment of BV. This study, however, had limitations because it was preliminary with a small number of patients. Further studies are needed to establish a significant effect in larger numbers of patients before it can be accepted as an alternative mode of treatment for patients with BV symptoms.

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