

Effect of supplementation of standard antibiotic therapy with oral probiotics for bacterial vaginosis

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ABSTRACT

Background: Bacterial vaginosis is a common cause of vaginal infection worldwide in women of child bearing age. It can be asymptomatic or mild infection but can lead to many complications especially during pregnancy. Recurrence is also frequently seen in women suffering from bacterial vaginosis. This infection usually occurs when normal lactobacillus flora in vagina is disrupted and replaced by pathogens. Administration of probiotics will restore normal vaginal flora and maintain normal pH and it could prove to be a reliable alternative to antibiotics in future.

Objective: To assess the effect of supplementation of standard antibiotic therapy with oral probiotics (*Lactobacillus*) for treatment of bacterial vaginosis.

Material methods: It was an open labeled prospective study in which 100 women diagnosed with bacterial vaginosis were randomly divided into two groups. Diagnosis was made using Amsel's criteria and Nugent scoring was done. Group A was given Oral Metronidazole, 400 mg BD for 7 days along with oral probiotic tablet containing *Lactobacillus rhamnosus* BD for 6 weeks whereas Group B was administered Oral Metronidazole, 400 mg BD for 7 days. Patients were assessed at 7 days for symptomatic improvement and again at the end of 6 weeks using Nugent scores. Results obtained were then compared.

Results: Out of all patients 2 patients in Group A and 5 patients in Group B could not complete the study. At the end of 7 days, there was improvement in symptoms

ie decrease in itching, odour and discharge. There was a significant difference in mean Nugent score before and after treatment between group A and group B at the end of 6 weeks.

Conclusion: This study concluded that improvement in patients taking probiotics along with standard antibiotic therapy was significantly more as compared to antibiotics alone.

Keywords: Nugent score, metronidazole, amsels criteria, prebiotics, vaginal infections

Introduction

Vaginosis is the most common infection in women of child bearing age. The commonest organisms causing vaginosis are anaerobic gram negative rods such as *Prevotella bivia*, *Prevotella intermedia*, *Bacteroides* species, anaerobic gram positive rods, anaerobic gram positive cocci and facultative anaerobic bacteria.^[1] Normally lactobacilli flora inhibit growth of other microorganisms through certain properties such as adhesive ability, production of acids, bacterocins, hydrogen peroxide, biosurfactants and competition to mannose and glycoprotein receptors. Bacterial vaginosis occurs when its normal lactobacillus flora in vagina is disrupted and replaced by pathogenic bacteria.^[2] Recurrent infections are common in BV infections and difficult to treat. The standard therapy for BV is oral metronidazole, vaginal clindamycin cream or metronidazole gel^[3] whereas targeted therapy is given according to antibiotic resistance. But these

drugs are associated with their own set of adverse effects. Metronidazole causes gastrointestinal disturbances like nausea and vomiting and less commonly metallic taste in mouth, paraesthesias and leucopenia^[4] whereas Clindamycin causes sensitivity reactions like rash, gastrointestinal symptoms like anorexia, abdominal pain, nausea, vomiting, diarrhea and rarely neutropenia, leucopenia, jaundice and skeletal muscle paralysis.^[5] Most proposed non antibiotic therapies for BV are vaginal or oral probiotics which aim to restore the normal vaginal microbial flora.^[6] Efforts to artificially restore normal vaginal flora with use of probiotics could be a reliable alternative to antibiotic especially in recurrent cases in future. Domination of lactobacilli in healthy vaginal microflora and absence in bacterial vaginosis prompts for search of its role in alternative treatment. In vitro studies have suggested that

certain specific strains of lactobacilli are able to inhibit adherence of *Gardnerella vaginalis* to the vaginal epithelium and/or produce lactic acid thus decreasing vaginal pH and hydrogen peroxide which is toxic to other microorganisms and prevents their colonization in the vagina and/or bacteriocins, which also inhibits the growth of bacteria causing bacterial vaginosis.^[7,8] Also, probiotics can be used in patients for long duration without any adverse effects and may be helpful in patients of repeated infections. Therefore, this study was conducted to evaluate the effect of oral probiotics in addition to standard antibiotic therapy in patients of bacterial vaginosis.

Material and Methods

It was an open labelled, prospective, randomised study conducted in a tertiary care hospital in Punjab. A total of 100 women older than 18 years of age attending gynaecology clinic with complaints of vaginal discharge, itching, malodour and diagnosed with bacterial vaginosis were included in the study and randomly divided into two groups (A and B) of 50 each. Women with baseline score of 3-4 as per Amsel's criteria and Nugent's score more than 7 were included for study. Group A was given Oral Metronidazole, 400 mg BD for 7 days along with oral probiotic tablet containing *Lactobacillus rhamnosus* BD for 6 weeks whereas Group B was administered Oral Metronidazole, 400 mg BD for 7 days. Initial assessment was done on seventh day based on improvement of symptoms and again at the end of 6 weeks based on Nugent's scoring. The scoring at 6 weeks was compared between two groups using unpaired test. Any female who was pregnant, lactating or had associated other gynaecological problem was excluded from the

study. The project was approved by institutional ethics committee.

Diagnosis by Amsel's criteria^[9] includes presence of a homogenous vaginal discharge, pH of vagina more than 4.5, presence of clue cells in wet mount of vaginal discharge and a positive whiff test. According to Amsel, if 3 out of 4 criteria is positive, patient has bacterial vaginosis.

Diagnosis by Nugent criteria^[10] (Gold standard for diagnosis of Bacterial vaginosis) includes counting average number of bacteria in 10-20 oil immersion fields on gram stained microscopic slide of vaginal swab. Score was counted by assessing for presence of large gram positive rods (*Lactobacillus* morphotypes; decrease in *Lactobacillus* scored as 0-4), small gram variable and gram negative rods (*G. Vaginalis* and *Bacteroides* morphotypes; scored as 0-4) and curved gram/a.azaAaa variable rods (*Mobiluncus* spp. Morphotypes; scored as 0-2). After grading the amount of each morphotype detected on smear, the total score is calculated from 0-10.

- A score of 1-3 is considered normal
- A score of 4-6 is considered intermediate
- A score of 7-10 is consistent with Bacterial vaginosis

Data was analyzed statistically by using SPSS software version 19. Paired t test was applied to compare any significant difference in mean Nugent score within each group and Unpaired t test was applied to find any difference in mean Nugent score between both groups.

Results

Out of 50 patients in each group, 7 could not complete the follow up (2 in Group A and 5 in Group B). Average age of women in group A was 33 years and 34 years in group B.

Table 1: Mean Nugent Score in both groups before and after treatment

Group A N=48	Mean Nugent score		Group B N=45	Mean Nugent score	
	Before	After		Before	After
n=6	7	3	n=9	7	4
n=5	7	5	n=11	8	4
n=15	8	3	n=4	8	5
n=10	8	5	n=8	9	5
n=12	9	4	n=13	9	6

Table 2: Comparison of Nugent score before and after treatment in both groups

	Mean score before treatment	Mean Nugent score after 6 weeks	Mean difference	P value	Mean difference between two groups±SEM
Group A N=48	8.02±0.699	3.87±0.86	4.14±1.09	t=26.31, df=47, p<0.001	0.72±1.77
Group B N=45	8.26±0.78	4.84±0.85	3.42±0.499	t=45.96, df=44, p<0.001	

t=4.06, df=91, P <0.001

In both the groups, there was improvement of symptoms i.e decrease in itching, odour and discharge after seven days of treatment and there is decrease in nugent score in both the groups after treatment. (Table 1) In Group A mean nugent score before treatment was 8.02±0.699 which decreased to 3.87±0.86 after 6 weeks and was statistically significant. In Group B mean nugent score before treatment was 8.26±0.78 which decreased to 4.84±0.85 after 6 weeks and was statistically significant. (Table 2) Group A showed significant difference in mean Nugent score when compared with group B (Table 2). Eleven patients in Group A and three patients in Group B had recurrence of vaginosis within the study time period. No adverse event was recorded during the study period.

Discussion

Bacterial vaginosis is the most common cause of vaginal discharge among women of reproductive age group. It is an extremely common health problem for women, occurring in 35% of women attending sexually transmitted infections clinic, 15-20% of pregnant women and 5-15% of women attending gynaecology clinics.^[11] The number of lactobacilli in vagina of women with bacterial vaginosis is significantly lower than in healthy women. So, efforts have been made to normalise the vaginal flora by administration of oral or vaginal probiotics. This study aimed to study the effect of administration of oral probiotics in women diagnosed with bacterial vaginosis. Clinical trials have shown that intravaginal administration of *Lactobacillus acidophilus* for 6-12 days, or oral administration of *Lactobacillus*

acidophilus or *Lactobacillus rhamnosus* GR-1 and *Lactobacillus fermentum* RC-14 for 2 months, resulted in cure of BV (defined as 0-1 positive score according to Amsel's criteria) and/or reduced recurrence of BV, and/or caused an increase in vaginal lactobacilli and restoration of a normal vaginal microbiota, significantly more frequently than did a placebo, acetic acid or no treatment.^[12]

Results of this study found significant improvement in women taking oral probiotics along with antibiotics than group taking antibiotic alone. This was in concordance with study of G. Vujic et al that found restitution to balanced vaginal flora in 26.85% of BV patient on placebo in comparison to 61.62% of patients in probiotic group after follow up period of 6 weeks.^[13] In another study conducted by Heczko et al, data from 154 (probiotic n= 73, placebo n= 81) participants was analysed to determine the efficacy of oral probiotics. It concluded that probiotic lengthened the time to clinical relapse of bacterial vaginosis symptoms up to 51% compared to placebo. Probiotic use also reduced and maintained low vaginal pH and Nugent score and increased vaginal *Lactobacillus* counts following standard treatment.^[14] According to Marcone et al, the safe and effective long term vaginal administration of *Lactobacillus rhamnosus* appears to be a useful complementary approach in the management of bacterial vaginosis.^[2]

It was concluded from the study that there was significant improvement in patients of bacterial vaginosis who were supplemented with oral probiotic along with antibiotics as compared to antibiotics alone during 6 week study period.

More studies on larger number of patients will be required to assess the effect of probiotics for recurrence of BV and any associated adverse event.

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