

An RCT for Efficacy of Oral Probiotics in Treatment of Cases with Symptomatic White Discharge per Vagina in Rural Population

Kusuma Naik, Avinash, H Nusrat, L Krishna, Ravi Kumar

ABSTRACT

Objective: Determine the efficacy of probiotics in treating women with symptomatic white discharge per vagina (WDPV), role of oral probiotics in restoring the vaginal flora.

Results: This is a prospective randomized clinical study done on 50 women with symptomatic WDPV who are attending gynecology outpatient procedures, these patients underwent Grams stain, received antibiotics along with probiotics for a period of 1 week, again reviewed with repeat Grams stain, 50% were in the age group of 21 to 30 years, duration of symptoms was between 1 and 6 months. In 36% of patients, there was improvement in the lactobacilli count from pretreatment to post-treatment in 100% of cases, but the response in terms of symptomatic relief was seen in 82%. The improvement in the lactobacilli count was interpreted using Nugents scoring.

Conclusion: The combination of probiotic *L. rhamnosus* GR-1 and *L. fermentum* RC-14 is not only safe for daily use in healthy women, but it can reduce colonization of the vagina by potential pathogenic bacteria and yeast.

Keywords: Probiotics, Lactobacilli, WDPV.

How to cite this article: Naik K, Avinash, Nusrat H, Krishna L, Kumar R. An RCT for Efficacy of Oral Probiotics in Treatment of Cases with Symptomatic White Discharge per Vagina in Rural Population. J South Asian Feder Obst Gynae 2012;4(3):126-129.

Source of support: Nil

Conflict of interest: None declared

INTRODUCTION

Urogenital infections afflict an estimated few billion women in a year, the size of this problem and the increased prevalence of multidrug resistant pathogens make it imperative for alternate treatment. The microorganisms that colonize the vagina play a major role in maintenance of resistance against infestations from pathogenic organisms.

When this flora is dominated by lactobacilli or a commensal flora, the person is regarded as being healthy in terms of the urogenital tract, unless other specific disease traits are evident. When the vault is colonized primarily or solely by pathogenic bacteria, such as *Escherichia coli* or *Gardnerella vaginalis*¹⁻³ the patient is generally regarded as having an abnormal flora. Antimicrobial therapy has been reasonably effective at curing bacterial infections of the bladder and vagina, but mounting drug resistance and failure of antibiotics to change host receptivity to pathogen recurrences, plus a negative impact on patient quality of life, make it imperative that alternative therapeutics be found.⁴⁻⁷

Probiotics are regarded as 'Live microorganisms which when administered in adequate amounts confer a health benefit

on the host'.⁸ A recent Food and Agriculture Organization of the United Nations and the World Health Organization Working Group has developed guidelines for what constitutes a true 'probiotic', and very few so called health products currently meet these criteria because they have no published clinical studies showing a benefit of their strains on the host.⁹ Probiotic *Lactobacillus rhamnosus* GR-1 and *Lactobacillus fermentum* RC-14 have been shown in open studies to colonize the vagina following oral intake.^{10,11}

Bacterial vaginosis (BV) is the most common cause of abnormal vaginal discharge in women of childbearing age. The causative organisms for this condition are *Gardnerella vaginalis*, *Mycoplasma hominis* and anaerobic bacteria. It is thought that a shift to a symptomatic BV state may simply be due to a decline in the levels of 'beneficial' lactic acid and hydrogen peroxide-producing lactobacilli and/or an increase in the levels of Gram-negative anaerobes.

A variety of events can contribute to the development of BV in which a mixture of the organisms listed above is usually present in concentrations 100 to 1,000 times greater than in the healthy vagina.

The standard scoring system termed the 'Nugent score' is an accepted technique using microscopic examination of a Gram-stained smear of vaginal discharge for determining BV. Due to the wide variety of Gram smear results from vaginal samples that can be considered normal, specific bacterial types need not be reported, but may be listed as 'organisms resembling normal urogenital flora', Yeast should always be reported with an added comment, such as '*Candida* species are normal flora in the genital area of 30 to 40% of women. The presence of yeast must be correlated with the clinical picture'. Smear results that score >7 in the Nugent scoring system should be reported as 'consistent with bacterial vaginosis'. It is acceptable to not report cells, or bacteria, and only report presence or absence of yeast, and whether smear results are consistent with BV or not.¹²

Aim

This study is designed to:

1. Determine the efficacy of probiotics in treating women with symptomatic WDPV
2. Role of oral probiotics in restoring the vaginal flora.

MATERIALS AND METHODS

This is a prospective randomized clinical study done on women with symptomatic white discharge per vagina (WDPV) who are attending gynecology outpatient procedures at PESIMSR, Kuppam.

Laboratory examination of vaginal smears and the determination of the Nugent score						
N score—The sum of the scores for each bacterial morphotype listed below						
<i>Lactobacilli</i>	Score	<i>Gardnerella, Bacteroides</i>	Score	<i>Curved Gram-negative bacilli</i>	Score	Sum=*N score
30 or >	0	0	0	0	0	0
5-30	1	<1	1	<1	1	3
1-4	2	1-4	2	1-4	1	5
<1	3	5-30	3	5-30	2	8
0	4	30 or >	4	30 or >	2	10

Note: Number of organisms seen/100× objective

Interpretation of Nugent score	
N-score	Reports
0-3	Smear not consistent with BV
4-6	Clue cells not present
4-6	Clue cells are present
>7	Smear consistent with BV

Women were examined at their first visit—after detailed history and clinical examination, including local examination to see the amount, character of discharge and for presence of cervical movement tenderness. Routine investigations to rule out presence of anemia, diabetes and urinary infection are done along with Gram stain of the vaginal discharge to study the type of organism and the load of lactobacilli, which is defined using Nugent scoring. These patients receive a combination of antibiotics (Ofloxacin + Ornidazole + fluconazole) along with probiotics containing 2,500 million spores of *Lactobacilli rhamnosus* GR-1 and *L. fermentum* RC-14, for a period of 1 week.

These patients are called back after 1 week and examined by the same gynecologist, asked regarding symptom relief, examination findings are compared and Grams stain is repeated to look for treatment response and also for the restoration of vaginal flora.

RESULTS

In the present study, 50 women with history of WDPV received probiotics along with antibiotics. Fifty percent of patients were aged between 21 and 30 years indicating the increased incidence of RTI in reproductive age group. Thirty-six percent had history of pain abdomen along with WDPV and the duration was between 15 days and 6 months in 64% of them.

Among them 48% had received treatment before coming here and were not relieved of the symptoms. On examination, there was copious discharge in 56, 50% had cervical and vaginal congestion, 32% had erosion on the cervix.

Forty percent had hemoglobin levels between 8 and 10 gm% (mean ± SD: 10.73 ± 1.21), this shows the correlation between anemia and vaginal infections. Four percent had random blood sugars >160 mg/dl (mean ± SD: 87.19 ± 13.48), 15% of them had associated urinary tract infection.

Pretreatment Gram's stain is interpreted with respect to the lactobacilli score (Table 1) using one of the criteria's in Nugent's score.

Among patients in pretreatment group, 66% of them had <1 organism/100× objective, this showed the shift in vaginal flora, only 2% of them showed count between 5 and 30.

Forty-two percent of patients showed >30 organisms/100× in the post-treatment Grams stain. Fifty percent of patients showed counts between 5 and 30 among post-treatment.

Pap smear is done for all the patients, 66% of them showed inflammatory (Table 2).

Forty-one patients (82%) were relieved of symptoms, there was response even in terms of improved vaginal flora (Table 3).

Nine patients (18%) were not relieved of symptoms, even though there was improvement in vaginal flora in seven of these nonresponders, they were not relieved symptomatically. The cause among these patients were noninfective, i.e, chronic cervicitis in three patients, diabetes mellitus in two patients, CIN-2 and three in two patients, one patient had Cu-T *in situ* which had caused recurrent PID, one patient had history of immunocompromised status which caused recurrent pelvic inflammatory disease.

Table 1: Lactobacilli score—pre- and post-treatment

Lactobacilli score (number of organisms seen/100× objective)	Pretreatment (n = 50)	Post-treatment (n = 50)
0 (30 or >)	Nil	42%
1 (5-30)	2%	50%
2 (1-4)	12%	6%
3 (<1)	66%	2%
4 (0)	20%	Nil

Table 2: Pap smear

Pap smear	Number of patients (n = 50)	%
1. Inflammatory smear	33	66.0
2. Bacterial vaginosis	8	16.0
3. Cervical intraepithelial neoplasia	2	4.0
4. <i>Candida</i> positive	2	4.0
5. <i>Trichomonas vaginalis</i>	4	8.0

Table 3: Response

Response	Number of patients (n = 50)	%
Yes	41	82.0
No	9	18.0

Only 32% patients had side effects like nausea, vomiting in 26% , giddiness in 8% and pain abdomen in 2% of patients (Table 4). But these side effects cannot be completely attributed to use of probiotics only, as in the study they receive additional antibiotics also.

Table 4: Side effects

Side effects	Number of patients (n = 50)	%
Absent	34	68.0
Present	16	32.0
• Nausea and vomiting	13	26.0
• Giddiness	4	8.0
• Pain in abdomen	1	2.0

DISCUSSION

The therapy resulted in a significant improvement in the vaginal flora in terms of increased lactobacilli presence. The outcome was not designed to be mechanism-based, but the results indicate that intestinal passage of these probiotic strains led to a beneficial impact on the vaginal microflora. This may have occurred due to the strains themselves ascending to the vagina from the rectal area. It is feasible that the therapy caused an alteration in the mucosal immunity of the host (via the gut and/or vagina) and that this played a part in reducing pathogen counts.

The loss of vaginal lactobacilli appears to be the major factor in the cascade of changes leading to bacterial vaginosis and relapses are associated with failure to establish a healthy lactobacilli dominated vaginal flora.

The mode of action has not been elucidated but might comprise:

1. Increased ascension of probiotic and/or indigenous lactobacilli from the rectal skin to the vagina.
2. Reduced ascension of pathogens from the rectal skin to the vagina.
3. Enhancement of the intestinal mucosal immunity which affects vaginal immunity rendering the environment less receptive to bacterial vaginosis organisms.

In our present study, the lactobacilli score was improved with oral probiotics.

Among patients in pretreatment group, 66% of them had <1 organism/100× objective, this showed the shift in vaginal flora, only 2% of them showed count between 5 and 30.

Among post-treatment group 42% of patients showed >30 organisms/100×. Fifty percent of patients showed counts between 5 and 30 among post-treatment. This shows the improved vaginal flora following treatment with probiotics.

Nine patients (18%) were not relieved of symptoms, even though there was improvement in vaginal flora in 7 of these nonresponders, they were not relieved symptomatically. The cause among these patients were noninfective, i.e. chronic cervicitis in 3 patients, diabetes mellitus in 2 patients, CIN-2 and 3 in 2 patients, one patient had Cu-T *in situ* which had caused recurrent PID, one patient had history of immuno-compromised status which caused recurrent pelvic inflammatory disease. Therefore only the altered vaginal flora

leading to bacterial vaginosis should not be blamed on, as other predisposing factors has to be treated simultaneously.

SUMMARY

Probiotics in Vaginitis and Other Urogenital Infections

Although antimicrobial therapy is generally effective in eradicating urogenital infections, there is still a high incidence of recurrence. There is good clinical evidence to show that the intestinal and urogenital microbial flora have a central role in maintaining both the health and well-being of humans.

REFERENCES

1. Wasieleski M, Hanke W, Kalinka J. Association between abnormal microbiological flora of the lower genital tract in early pregnancy and socioeconomic, demographic and environmental risk factors *Med Sci Monit* 2001;7:1250-55.
2. Schwebke JR, Richey CM, Weiss HL. Correlation of behaviours with microbiological changes in vaginal flora. *J Infect Dis* 1999;180:1632-36.
3. Bruce AW, Chadwick P, Seddon JM, Vancott GF. The significance of perineal pathogens in women. *J Urol* 1974;112: 808-10.
4. Sewankambo N, Gray RH, Wawer MJ, et al. HIV-1 infection associated with abnormal vaginal flora morphology and bacterial vaginosis. *Lancet* 1997;350:546-50.
5. Reid G, Bruce AW, Beheshti M. Effect of antibiotic treatment on receptivity of uroepithelial cells to uropathogens. *Can J Microbiol* 1988;34:327-31.
6. Petrof EO, Schwartz DN, Quinn JP. Urinary tract infections and a multidrug-resistant *Escherichia coli* clonal group. *N Engl J Med* 2002;346:535-36.
7. Ellis AK, Verma S. Quality of life in women with urinary tract infections: Is benign disease a misnomer? *J Am Board Fam Pract* 2002;13:392-97.
8. FAO/WHO. Evaluation of health and nutritional properties of powder milk and live lactic acid bacteria. Food and Agriculture Organization of the United Nations and World Health Organization Report 2001.
9. FAO/WHO. Guidelines for the evaluation of probiotics in food. Report of a joint FAO/WHO Working Group 2002.
10. Reid G, Bruce AW, Fraser N, Heinemann C, Owen J, Henning B. Oral probiotics can resolve urogenital infections. *FEMS Immunol Med Microbiol* 2001;30:49-52.
11. Reid G, Beuerman D, Heinemann C, Bruce AW. Probiotic *Lactobacillus* dose required to restore and maintain a normal vaginal flora. *FEMS Immunol. Med Microbiol* 2001;32:37-41.
12. Clinical microbiology proficiency testing: Clinical bacteriology. www.cmpt.ca/pdf/.../nugent_score_interpretation_apr_09.pdf

ABOUT THE AUTHORS

Kusuma Naik

Assistant Professor, Department of Obstetrics and Gynecology, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh India

Correspondence Address: C-50, KPWD Quarters, Jeevan Bhima Nagar, Bengaluru-75, Karnataka, India, Phone: 9886391794 e-mail: kusumamv.naik@gmail.com

Avinash

Assistant Professor, Department of Obstetrics and Gynecology, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh India

H Nusrat

Assistant Professor, Department of Obstetrics and Gynecology, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh India

L Krishna

Professor, Department of Obstetrics and Gynecology, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh India

Ravi Kumar

Associate Professor, Department of Microbiology, PES Institute of Medical Sciences and Research, Kuppam, Andhra Pradesh India