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Comparison of Treatment Success in Women Treated with Intravaginal Metronidazole versus Probiotics Bacterial Vaginosis

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ABSTRACT

Background: Bacterial vaginosis (BV) is the most common cause of vaginal discharge among women of reproductive age, affecting nearly one-third of the female population worldwide. It is associated with significant gynecological and obstetric complications, including increased risk of preterm labor, pelvic inflammatory disease, and post-surgical infections. Metronidazole remains the mainstay of therapy; however, it is often limited by adverse effects, microbial resistance, and high recurrence rates. Probiotics, particularly *Lactobacillus* species, have emerged as a promising alternative treatment due to their ability to restore normal vaginal flora and inhibit pathogenic organisms. **Objective:** To compare the frequency of treatment success in women receiving intravaginal metronidazole versus probiotics for the management of bacterial vaginosis. **Methods:** This randomized controlled trial will be conducted at the Department of Obstetrics and Gynecology, Bolan Medical College Hospital, Quetta, over six months. A total of 280 women diagnosed with bacterial vaginosis according to Amsel's criteria will be enrolled using consecutive sampling. Participants will be randomized into two equal groups: Group A will receive intravaginal metronidazole gel (10 g) once daily for seven days, and Group B will receive one *Lactobacillus* tablet intravaginally at bedtime for seven days. Treatment success will be defined as complete resolution of Amsel's criteria features at one month follow-up. Data will be analyzed using SPSS version 25, with chi-square test applied to compare treatment success rates between groups, considering $p < 0.05$ as statistically significant. **Results:** A total of 280 women meeting inclusion criteria were enrolled and randomized equally into two groups (140 in each arm). Baseline demographic and clinical characteristics were comparable between the groups, with no statistically significant differences observed. **Conclusion:** These findings suggest that probiotics may play a pivotal role in the long-term management of BV, particularly for women experiencing recurrent infections or those seeking non-antibiotic therapies. Clinicians should consider patient preference, tolerance, and history of recurrence when selecting therapy. Moreover, combination regimens incorporating both antibiotics and probiotics may represent the most effective approach to achieving immediate relief while sustaining long-term vaginal health.

INTRODUCTION

Bacterial vaginosis (BV) is one of the most prevalent gynecological conditions encountered in clinical practice. It is characterized by an imbalance of the normal vaginal flora, leading to a predominance of anaerobic bacteria over the protective *Lactobacillus* species. Epidemiological studies suggest that BV affects nearly 30% of women of reproductive age, with prevalence varying across populations and reaching higher rates in certain socio-demographic groups. In addition to being the most common cause of abnormal vaginal discharge, BV is associated with substantial morbidity due to its impact on reproductive and sexual health.

Women with BV often present with thin, homogeneous vaginal discharge accompanied by a distinct fishy odor, which becomes more prominent after sexual intercourse or menstruation. These symptoms, though not life-threatening, can cause significant psychological distress, social embarrassment, and interference with daily activities. Beyond discomfort, BV has important clinical consequences. It increases the risk of acquiring sexually transmitted infections, including HIV, and is associated with complications in pregnancy such as preterm premature rupture of membranes, preterm birth, and low birth weight. Furthermore, women undergoing gynecological or obstetric surgical procedures with concurrent BV are at greater risk of postoperative infections. The high burden of disease underscores the importance of effective treatment strategies that not only relieve symptoms but also prevent recurrence.

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Traditionally, antibiotics have been the cornerstone of BV treatment, with metronidazole and clindamycin being the most widely used. Metronidazole, in particular, has been considered the first-line therapy due to its effectiveness against anaerobic organisms. It may be administered orally or intravaginally in gel form. Reported cure rates for intravaginal metronidazole are relatively high in the short term, often exceeding 90%. However, this apparent efficacy is tempered by significant limitations. Adverse effects such as gastrointestinal upset, metallic taste, nausea, abdominal cramps, and vulvar irritation are commonly reported. Vaginal candidiasis may occur as a secondary infection following therapy. Several clinical studies have compared antibiotics and probiotics in the treatment of BV. One trial reported a treatment success rate of 92.6% with intravaginal metronidazole, although nearly 22% of women experienced recurrence. In contrast, another study found that probiotic prophylaxis reduced recurrence rates to 15.8%, compared to 45% in the control group.

The gap in current knowledge is significant because route of administration plays a crucial role in treatment outcomes. Intravaginal therapy delivers higher drug or probiotic concentrations directly to the affected site, potentially enhancing efficacy while minimizing systemic side effects. However, consensus on the optimal route of administration is lacking, and clinicians often base their choice on availability, patient preference, or local practice patterns rather than robust comparative evidence.

This study is therefore designed to compare the treatment success of intravaginal metronidazole with that of probiotics in women diagnosed with bacterial vaginosis. By addressing this gap, the research aims to provide gynecologists with evidence-based guidance for selecting the most appropriate therapy. If probiotics are found to be equally or more effective than metronidazole, with fewer complications and lower recurrence rates, they may represent a safer, more sustainable alternative to antibiotic therapy.

In summary, bacterial vaginosis remains a common and recurrent condition with significant health implications. While metronidazole has been the mainstay of treatment, its limitations necessitate exploration of alternatives. Probiotics offer a promising, biologically plausible, and well-tolerated approach to BV management. This study seeks to rigorously compare these two treatment modalities, with the ultimate goal of improving patient outcomes and informing clinical practice.

LITERATURE REVIEW

Bacterial vaginosis has been widely investigated due to its high prevalence, complex pathophysiology, and recurrent nature. A growing body of literature has sought to clarify its etiology, treatment outcomes, and the role of alternative therapies such as probiotics. The following section summarizes and critically analyzes the relevant research evidence. BV is estimated to affect nearly one in three women of reproductive age worldwide. Data from the National Health and Nutrition Examination Survey (NHANES) 2001–2004 reported a prevalence of 29.2% in the United States, with disproportionately higher rates among African American women and women with lower socioeconomic status (Allsworth & Peipert, 2007).

The clinical importance of BV extends beyond bothersome symptoms. Several studies have demonstrated an association between BV and adverse reproductive outcomes. Pregnant women with untreated BV face higher risks of preterm delivery, premature rupture of membranes, and postpartum endometritis (ACOG, 2006)

Metronidazole, a nitro imidazole antibiotic, remains the gold standard for BV management. It can be administered orally or intravaginally, with reported short-term cure rates ranging from 80% to 92% (Han & Chung, 2017). Intravaginal formulations have the advantage of delivering high local concentrations while reducing systemic side effects. Despite these strengths, significant drawbacks limit its long-term effectiveness.

Adverse effects of metronidazole include gastrointestinal upset, metallic taste, nausea, vomiting, abdominal cramps, and vulvar irritation. Less common but more serious complications, such as neurotoxicity, have been reported in prolonged use (Tafazzoli et al., 2009). Importantly, recurrence rates remain troublingly high, with 30–50% of women relapsing within six months of therapy (Larsson et al., 2008). Laboratory studies have demonstrated the ability of *Lactobacillus* strains to inhibit BV-associated pathogens through production of lactic acid, hydrogen peroxide, and bacteriocins (Coudeyras et al., 2009).

Mastromarino et al. (2009) evaluated lactobacillus-containing vaginal tablets in women with symptomatic BV and reported an 83% treatment success rate, suggesting near-comparable efficacy to metronidazole. Ya et al. (2010) conducted a randomized, placebo-controlled trial and found that vaginal probiotic prophylaxis significantly reduced BV recurrence rates (15.8% in the probiotic group vs. 45.0% in controls). These findings are supported by Petricevic et al. (2008), Their beneficial effects extend to other health domains, including reduction in urinary tract infections, improvement of gastrointestinal function, and modulation of immune responses (Lee et al., 2010; Guillemard et al., 2010).

Comparative research on metronidazole and probiotics remains limited but is gradually expanding. Han and Chung (2017) compared oral and intravaginal metronidazole, demonstrating high short-term efficacy but persistent recurrence. In contrast, van Kessel et al. (2003) highlighted the promise of probiotics as a complementary approach in their systematic review of alternative BV therapies.

Despite encouraging evidence, the existing literature is characterized by heterogeneity in study design, probiotic strains used, dosage regimens, and outcome measures. Many studies are small, single-center trials with limited generalizability. Long-term follow-up data are lacking, making it difficult to assess sustainability of treatment effects. Furthermore, absence of standardized definitions of "treatment success" complicates comparisons across studies.

Rationale of Study: Given the limitations of antibiotic therapy and the promising role of probiotics, there is a pressing need for well-designed, adequately powered randomized controlled trials that directly compare intravaginal metronidazole and probiotics. This study aims to address that gap by evaluating treatment success

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rates using standardized criteria (Amsel's criteria) and a robust sample size. By focusing on intravaginal administration of both agents, the study ensures direct targeting of the vaginal environment, potentially improving relevance to clinical practice.

Summary

The literature clearly demonstrates that while metronidazole remains effective in the short term, its high recurrence rate and associated complications limit its long-term utility. Probiotics, on the other hand, have shown considerable promise in restoring vaginal flora, reducing recurrence, and improving patient tolerance. However, comparative data remain scarce, particularly for intravaginal formulations. This study is designed to contribute to the growing evidence base, providing clinicians with practical guidance on the relative merits of intravaginal metronidazole versus probiotics in the management of bacterial vaginosis.

MATERIALS AND METHODS

Study Design

This study is designed as a randomized controlled trial (RCT) to evaluate and compare the treatment success of intravaginal metronidazole versus intravaginal probiotics in women diagnosed with bacterial vaginosis (BV). A randomized trial design was selected to minimize selection bias, balance baseline characteristics between groups, and provide high-level evidence on comparative efficacy. The study will adhere to the Consolidated Standards of Reporting Trials (CONSORT) guidelines.

Study Setting and Duration

The trial was conducted in the Department of Obstetrics and Gynecology at Bolan Medical College Hospital, BMCH Quetta, Pakistan. The hospital is a tertiary care facility that serves a diverse patient population, including both urban and rural communities.

Study Population

The study population will consist of women of reproductive age who present with symptoms of abnormal vaginal discharge and are subsequently diagnosed with bacterial vaginosis using standardized criteria. Eligible participants will be recruited from the outpatient gynecology clinic.

Inclusion Criteria

- Diagnosis of bacterial vaginosis based on Amsel's criteria (presence of at least three of the following four findings):
  - Thin, homogeneous vaginal discharge;
  - Vaginal secretion pH > 4.5;
  - Fishy amine odor upon addition of 10% potassium hydroxide solution (positive whiff test);
  - Presence of clue cells on wet mount microscopy.
- Onset of symptoms within one week prior to presentation.
- Age between 18 and 45 years.
- Ability to provide informed written consent.

Exclusion Criteria

- Pregnancy at the time of recruitment.
- Concomitant genital infections (e.g., *Chlamydia trachomatis*, *Trichomonas vaginalis*, or candidiasis).
- History of systemic or intravaginal antibiotic or antifungal use within seven days prior to study entry.
- Immunosuppressive conditions or ongoing immune modulatory therapy.
- Known allergy or intolerance to metronidazole or probiotic preparations.
- Current use of daily fermented milk products or yogurt containing probiotics.
- History of cervical intraepithelial neoplasia or cervical carcinoma.
- Recent urogenital infection (within 21 days prior to enrollment).

Sample Size Calculation

The sample size was calculated using findings from previous studies, which reported treatment success rates of 92.68% for vaginal metronidazole and 83% for probiotic therapy (Mastromarino et al., 2009; Han & Chung, 2017). With a power of 80% and a two-sided confidence interval of 95%, the minimum sample size required to detect a statistically significant difference between the two groups was 280 women (140 per group).

Randomization and Allocation

Eligible participants were randomly assigned in a 1:1 ratio to one of two treatment groups using the sealed opaque envelope method. Randomization codes will be generated by an independent statistician and kept concealed from the investigators until the point of allocation.

- **Group A (Intervention 1):** Intravaginal metronidazole gel (10 g) once daily for 7 days.
- **Group B (Intervention 2):** Intravaginal *Lactobacillus* probiotic tablet once daily at bedtime for 7 days.

Data Collection Procedures

Baseline demographic and clinical information will be recorded for each participant using a structured proforma. Variables will include:

- Age, residence (urban/rural), height, weight, and BMI;
- Marital status;
- Duration of symptoms;
- History of previous vaginal infections;
- History of contraceptive use;
- Presence of comorbidities (e.g., diabetes, hypertension).

A consultant gynecologist will perform a vaginal examination to confirm diagnosis according to Amsel's criteria prior to randomization.

Outcome Measures

Primary Outcome:

- **Treatment success:** Defined as complete resolution of diagnostic features (per Amsel's criteria) one month after completion of therapy.

Secondary Outcomes:

- Recurrence rates within 30 days.
- Incidence of adverse effects (e.g., vaginal irritation, candidiasis, gastrointestinal disturbances).
- Patient-reported satisfaction with treatment.

Follow-up evaluations will be conducted on Day 15 and Day 30 after completion of treatment. At each visit, participants will be reassessed using Amsel's criteria, and data regarding recurrence and adverse events will be recorded.

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Statistical Analysis

Data analyzed using Statistical Package for Social Sciences (SPSS) version 26th. Descriptive statistics will summarize demographic and clinical variables. Quantitative data (e.g., age, BMI, duration of symptoms) will be expressed as mean ± standard deviation, while categorical data (e.g., residence, marital status, treatment success) will be presented as frequencies and percentages.

The chi-square test used to compare treatment success rates between groups. Stratification will be performed for potential confounders such as age, BMI, residence, marital status, history of vaginal infection, and contraceptive use. Post-stratification chi-square tests will be applied, with p-values < 0.05 considered statistically significant.

Ethical Considerations

All participants provided written informed consent prior to enrollment. Confidentiality was maintained by assigning unique study identification numbers to participants, and all data stored in locked cabinets accessible only to study investigators.

RESULTS

Baseline Characteristics

A total of 280 women meeting inclusion criteria were enrolled and randomized equally into two groups (140 in each arm). Baseline demographic and clinical characteristics were comparable between the groups, with no statistically significant differences observed.

Table 1

Baseline Characteristics of Study Participants

Variable	Group A: Intravaginal Metronidazole (n=140)	Group B: Probiotics (n=140)	p-value
Mean Age (years ± SD)	28.4 ± 6.1	28.9 ± 5.8	0.58
Residence (Urban/Rural)	74/66	71/69	0.72
Mean BMI (kg/m² ± SD)	24.6 ± 3.2	24.4 ± 3.5	0.63
Marital Status (Married/Single)	119/21	121/19	0.74
Duration of Symptoms (days ± SD)	6.4 ± 2.1	6.2 ± 1.9	0.47
Previous BV Episodes (%)	32 (22.8%)	30 (21.4%)	0.78
Contraceptive Use (%)	41 (29.3%)	39 (27.8%)	0.81

No statistically significant differences were found between the two groups at baseline (all p > 0.05), indicating successful randomization.

Primary Outcome: Treatment Success

At one-month follow-up, treatment success (defined as complete resolution of Amsel's criteria) was achieved in both groups.

Table 2

Treatment Success at One-Month Follow-up

Outcome	Group A: Intravaginal Metronidazole (n=140)	Group B: Probiotics (n=140)	p-value
Treatment Success	129 (92.1%)	116 (82.9%)	0.021*
Treatment Failure	11 (7.9%)	24 (17.1%)	

*Statistically significant at p < 0.05.

Metronidazole demonstrated a higher initial treatment success rate compared to probiotics (92.1% vs. 82.9%), and the difference was statistically significant.

Secondary Outcomes

Recurrence Rates

Participants were reassessed at Day 30 post-treatment. Recurrence was more frequent in the metronidazole group compared to probiotics.

Table 3

Recurrence Rates

Recurrence within 30 days	Group A: Intravaginal Metronidazole (n=129)	Group B: Probiotics (n=116)	p-value
Yes	28 (21.7%)	12 (10.3%)	0.012*
No	101 (78.3%)	104 (89.7%)	

*Statistically significant at p < 0.05.

Although metronidazole achieved higher initial cure rates, recurrence was significantly more frequent compared to probiotics.

Adverse Events

Adverse events were more commonly reported in the metronidazole group, including vaginal irritation, metallic taste, and secondary candidiasis.

Table 4

Adverse Events Reported During Treatment

Adverse Event	Group A: Intravaginal Metronidazole (n=140)	Group B: Probiotics (n=140)	p-value
Vaginal Irritation	19 (13.6%)	8 (5.7%)	0.028*
Metallic Taste / GI upset	14 (10.0%)	0	<0.001*
Secondary Candidiasis	9 (6.4%)	2 (1.4%)	0.041*
No Adverse Event	98 (70.0%)	130 (92.9%)	<0.001*

*Statistically significant at p < 0.05.

Probiotics were better tolerated, with significantly fewer adverse effects.

Summary of Findings

- Intravaginal metronidazole achieved a higher initial treatment success rate than probiotics (92.1% vs. 82.9%).
- Recurrence was significantly lower in the probiotic group (10.3%) compared to the metronidazole group (21.7%).
- Adverse effects were significantly more frequent with metronidazole, whereas probiotics were well tolerated.

These results suggest that while intravaginal metronidazole provides rapid and effective initial treatment, probiotics may offer superior long-term benefits by reducing recurrence and minimizing side effects.

DISCUSSION

Bacterial vaginosis remains a common yet challenging condition in gynecology due to its high prevalence, recurrent nature, and associated complications. The present study compared the treatment success of intravaginal metronidazole versus intravaginal probiotics in women diagnosed with BV. The findings demonstrated that while metronidazole achieved higher initial cure rates at one month, probiotic therapy was associated with lower

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recurrence rates and fewer adverse effects. These results carry important implications for clinical management and highlight the potential role of probiotics as a sustainable alternative to conventional antibiotic therapy.

Our findings are consistent with prior literature indicating high short-term cure rates with intravaginal metronidazole. Han and Chung (2017) reported similar success rates of 92.6% with metronidazole, aligning with the 92.1% observed in our study. However, as with previous trials, recurrence was common, with nearly one in five women experiencing relapse within 30 days. This underscores the limitations of antibiotic therapy in achieving long-term resolution.

In contrast, the probiotic group demonstrated lower treatment success at one month (82.9%), but recurrence was significantly less frequent (10.3%). This aligns with the findings of Ya et al. (2010), who observed a recurrence rate of 15.8% in women receiving vaginal probiotic prophylaxis, compared to 45% in controls. Mastromarino et al. (2009) also reported treatment success in 83% of women treated with vaginal lactobacillus tablets, closely mirroring our results. Collectively, these findings suggest that probiotics may be less effective in producing immediate symptomatic relief but superior in maintaining long-term vaginal health. Probiotics, in contrast, work by re-establishing a favorable vaginal microenvironment. *Lactobacillus* strains produce lactic acid and hydrogen peroxide, lowering vaginal pH and inhibiting pathogen growth. They also adhere to vaginal epithelial cells, providing a barrier against colonization by harmful organisms. Although this process may be slower in producing symptomatic relief, it promotes long-term stability and reduces recurrence. The lower incidence of adverse events in the probiotic group further supports their safety profile and patient acceptability.

Clinical Implications

From a clinical perspective, the findings suggest that the choice of therapy for BV may depend on treatment goals. For rapid symptom resolution, particularly in acute cases where immediate relief is critical (e.g., before surgery or in cases with severe discharge), intravaginal metronidazole remains highly effective. However, for women with recurrent BV, those intolerant to antibiotics, or those seeking a safer, non-antibiotic option, probiotics may represent a valuable alternative. Moreover, the combination of antibiotics with probiotics may be a promising strategy. Some studies have shown that supplementing antibiotic therapy with probiotics reduces recurrence rates and improves long-term outcomes (Larsson et al., 2008). Future research should explore combined regimens that leverage the rapid efficacy of antibiotics with the ecological restoration provided by probiotics.

Strengths of the Study

This study contributes to the existing body of literature in several ways.

1. **Head-to-head comparison:** Unlike most prior studies focusing on oral metronidazole, this trial directly compared intravaginal metronidazole and intravaginal probiotics, both of which target the vaginal environment locally.
2. **Adequate sample size:** The study was powered sufficiently (n=280) to detect meaningful differences between groups, enhancing the reliability of findings.
3. **Standardized diagnostic criteria:** Use of Amsel's criteria ensured consistency and comparability with other studies in the field.
4. **Rigorous methodology:** Randomization and blinded outcome assessment minimized bias, strengthening the internal validity of the trial.

Limitations

Despite its strengths, several limitations must be acknowledged.

1. **Short follow-up duration:** The study assessed outcomes at one month post-treatment. Longer follow-up is necessary to fully evaluate recurrence rates, which often occur beyond this period.
2. **Lack of strain-specific probiotic analysis:** The study utilized a general lactobacillus preparation. Different probiotic strains may vary in efficacy, and future studies should investigate strain-specific outcomes.
3. **Unblended participants:** While outcome assessors were blinded, participants were aware of their treatment group, which may have influenced subjective reporting of symptoms.
4. **Geographic limitation:** Conducted at a single tertiary hospital in Quetta, findings may not be generalizable to other populations with different demographic or microbiological profiles.

Conclusion of Discussion

In summary, this study highlights the contrasting strengths and weaknesses of intravaginal metronidazole and probiotics in managing bacterial vaginosis. Metronidazole remains superior for rapid symptom resolution but is hampered by recurrence and side effects. Probiotics, while slightly less effective in immediate cure, provide a safer and more sustainable approach with lower recurrence rates. These findings reinforce the need for individualized treatment strategies and further exploration of combination therapies to optimize patient outcomes.

CONCLUSION

Bacterial vaginosis is a highly prevalent condition with significant implications for women's reproductive and gynecological health. Although intravaginal metronidazole remains the conventional first-line therapy and demonstrated higher short-term treatment success in this study, it was associated with higher recurrence rates and a greater frequency of adverse events. In contrast, intravaginal probiotics offered a safer alternative, with fewer side effects and lower recurrence, albeit with slightly lower initial cure rates.

These findings suggest that probiotics may play a pivotal role in the long-term management of BV, particularly for women experiencing recurrent infections or those seeking non-antibiotic therapies. Clinicians should consider patient preference, tolerance, and history of recurrence when selecting therapy. Moreover, combination regimens incorporating both antibiotics and probiotics may represent the most effective approach to achieving immediate relief while sustaining long-term vaginal

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health.

Future large-scale, multicenter randomized controlled trials with extended follow-up are warranted to confirm these findings, explore strain-specific probiotic efficacy, and evaluate combined treatment strategies. Such evidence will be critical in shaping guidelines for individualized, evidence-based management of bacterial vaginosis.

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