Comparison of the efficacy of metronidazole and metronidazole plus probiotics capsule in the treatment of bacterial vaginosis among non-pregnant patients seen at the outpatient department of a tertiary hospital: A single blind randomized controlled trial*

By Mary Rose Muñoz-Cruz, MD; Jennifer T. Co, MD, FPOGS and Lylah D. Reyes, MD, FPOGS

Department of Obstetrics and Gnecology, Far Eastern University - NRMF Hospital

ABSTRACT

Background: Bacterial vaginosis (BV) is the most prevalent cause of symptomatic vaginitis. In the Philippines, prevalence of BV is at 28.16%. The mainstay for the treatment of BV is Metronidazole. Although antibiotic therapy has been shown to eliminate BV associated organisms, there is extremely high recurrence rate.

Objective: To compare the efficacy of metronidazole and metronidazole plus lactobacilli tablet in the treatment of bacterial vaginosis among non-pregnant patients seen at the outpatient department of a tertiary medical center.

Methodology: The population included non-pregnant women ages 15 to 44 years old, with bacterial vaginosis diagnosed by Amsel's criteria and Nugent's scoring. The participants were randomly assigned to their treatment group, one is Metronidazole only and the other received Metronidazole plus Lactobacillus tablet. All participants followed up on day 8, 15, 22 and 56 from initiation of treatment resolution or persistence of symptoms and collection of vaginal specimen for gram stain and inquire on adverse effects.

Results: On day 8 of treatment, there were significantly more participant in the metronidazole plus probiotic arm with an estimated lactobacilli count of more than 30/hpf as compared to metronidazole alone. On day 15 post treatment, there was no statistically significant difference with the estimated Gardnerella vaginalis count, lactobacilli count, presence or absence of malodorous vaginal discharge between the metronidazole plus probiotic and the metronidazole alone arm. With metronidazole plus probiotic group, the proportion of women with less than 30 per hpf Gardnerella vaginalis count and absent foul smelling vaginal discharge were accounted among 100% of the participants from day 8 to 56 post treatment. The early reduction in the causative agent and symptoms can be attributed to an increase in the estimated lactobacilli count sustained until 56 days post treatment metronidazole plus probiotic. However, from day 15 to 22 and 56 post-treatment, the proportion of participants who had a nugent's score of less than 4 were greater for both the metronidazole plus probiotic (100%) and metronidazole alone (95%) arm, when compared to day 8 post-treatment. This finding for the metronidazole plus probiotic group is due to sustained reduction in the Gardnerella vaginalis count and increase in lactobacilli counts. Potentially, the metronidazole plus probiotic treatment was found to be more favorable in sustaining the normal flora and probiotic can be used as an adjunct may enhance the efficacy of metronidazole in the treatment of BV.

Conclusion: Metronidazole plus probiotic and metronidazole only treatment are comparable in treating bacterial vaginosis. In terms of restoring and maintaining the normal flora, metronidazole plus probiotic appears to be more significantly efficacious. Probiotic in the form of lactobacilli is a promising adjunct to enhance the efficacy of metronidazole in the treatment of bacterial vaginosis.

Keywords: bacterial vaginosis, BV, probiotic, lactobacilli, amsel's criteria, nugent score, metronidazole

INTRODUCTION

Bacterial vaginosis is the most prevalent cause of symptomatic vaginitis, with a prevalence of approximately 15% to 50%. In the Philippines, among women with symptoms of abnormal vaginal discharge or lower abdominal pain. Prevalence of BV is 28.16%. In women with BV, the most frequent symptom is an unpleasant vaginal odor, which is described as "musty" or "fishy". The vaginal discharge associated with BV is thin and gray-white. It is frothy in approximately 10% of women. Rarely will BV be associated with pruritus or vulvar irritation. It also reflects a shift in vaginal flora from lactobacilli-dominant to mixed flora, including

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genital microplasmas, *G. vaginalis*, and anaerobes, such as *peptostreptococci*, and *Prevotella* and *Mobiluncus* species.

Bacterial vaginosis is clinically diagnosed. The classic findings on wet smear are clumps of bacteria and "clue cells," which are vaginal epithelial cells with clusters of bacteria adherent to their external surfaces Leukocytes are not nearly as frequent as epithelial cells underneath the microscope. The four Amsel criteria for the diagnosis of BV are the presence of the following: (1) homogeneous vaginal discharge; (2) vaginal discharge pH equal to or greater than 4.5; (3) an amine-like odor when vaginal discharge is mixed with potassium hydroxide; and (4) clue cells greater than 20% of the vaginal epithelial cells. Three of the four criteria are sufficient to make a presumptive diagnosis. Ironically, 50% of women who have three of the four of the clinical criteria for BV are asymptomatic. If readily available, a Gram stain of vaginal secretion is an excellent diagnostic method. The Nugent Score is a Gram stain scoring system for vaginal smear to diagnose bacterial vaginosis. Gram's stain morphology score (1–10) based on lactobacilli and other morphotypes; a score of 1–3 indicates normal flora, and score of 7–10 bacterial vaginosis. Nugent score, showed a sensitivity of 97% and specificity of 98%.

The mainstay for the treatment of BV is Metronidazole. Although antibiotic therapy has been shown to eliminate BV associated organisms, there is high recurrence rate. Another problem that may occur in the management of BV is resistance to antimicrobial treatment. With the occurrence of resistance, complete cure may not be achieved. This may then increase the risk of developing the complications associated with BV. These complications include: an increased risk for susceptibility to HIV infection if exposed to the HIV virus; development of an infection following surgical procedures such as a hysterectomy as well the risk for some complications in pregnancy, such as preterm delivery and abortion.

Hence, this study would like to further investigate on the role of an adjuvant treatment that will help eradicate the organisms as well as promote restoration of the vaginal flora and prevent recurrence of BV. In a study done by Omdroff in 1998, the prophylactic use of selected Lactobacillus was found to be potentially effective in restoring the normal microbial flora in the vagina. Our study would like to address this inquiry: Are metronidazole plus probiotics and metronidazole alone be comparable in efficacy in the treatment of bacterial vaginosis among non-pregnant patients seen at the outpatient department of a tertiary hospital?

OBJECTIVES

A. General Objective:

To compare the efficacy of metronidazole and metronidazole plus lactobacilli capsule in the Treatment of Bacterial Vaginosis among Non-Pregnant Patients Seen at the Outpatient Department of a Tertiary Medical Center.

B. Specific Objectives:

To compare the following between Metronidazole and Metronidazole plus Lactobacilli capsule in the Treatment of Bacterial Vaginosis:

1. Estimated Gardenerella vaginalis count
2. Restoration of the vaginal flora
3. Presence or absence of foul smelling vaginal discharge
4. Recurrence of symptoms
5. Nugent's Score

Definition of Operational Terms

I. Bacterial vaginosis is diagnosed with the presence of foul-smelling yellowish-gray vaginal discharge plus a Nugents score reading of at least 4 or above with clue cells.

II. Independent Variable – this variable refers to the treatment that was used in the study, encoded and entered as:
   0- Metronidazole only
   1- Metronidazole with Lactobacilli capsule

III. Dependent Variables – these include the following:
   a. Estimated Gardnerella vaginalis count – this was obtained from the report of the gram-stained vaginal discharge issued by the medical technologist; this was interpreted, encoded, and entered as follows:
      1- few: < 10/hpf
      2- moderate: 10-29 per hpf
      3- plenty: ≥ 30 per hpf
   b. Restoration of vaginal flora – this variable refers to the presence of lactobacilli count and was encoded and entered as:
      0- Negative: ≤ 30 per hpf lactobacilli
      1- Postive: > 30 per hpf lactobacilli
   c. Vaginal discharge and foul odor – these variables was reported as present or absent during assessment and was encoded and entered as:
      0- Absent
      1- Present
   d. Recurrence of symptoms – refers to the reappearance of foul odored vaginal discharge noted on days 8, 15, 22, and 56 post-treatment; this was encoded and entered as:

0- Absent
1- Present

e. Nugents's Score – the score given by the medical technologist after the assessment of gram stain, this was encoded and entered as:
1- Normal: score of 1 to 3
2- Intermediate: score of 4 to 6
3- Bacterial vaginosis: score of 7 to 10 or score of 4 to 6 with clue cells

METHODOLOGY

A. Research Design: Single Blind Randomized Controlled Trial

B. Setting and Population

The population includes non pregnant women seen at the Out Patient Department of a Tertiary Medical Center ages 18 to 44 years old with bacterial vaginosis diagnosed by Amsel's criteria and Nugent's scoring. Those participants excluded are those who are diagnosed with other vaginal infections (such as vaginal candidiasis, non specific cervicovaginitis, trichomoniasis and other sexually transmitted infections) abnormal uterine bleeding, active bleeding, pregnant and lactating women, urinary tract infection, diabetes mellitus, on-going antibiotic therapy within 2 weeks, as well as those with hypersensitivity reaction to the drug (metronidazole). Those participants who were withdrawn from the study are those who had unprotected sexual intercourse during the course of treatment, participants who did not have any follow up after the baseline check up and, personally, for any reason, those participants who decided to withdraw during the study proper.

C. Methodology Proper

All women with vaginal discharge were screened for Bacterial vaginosis using the Amsel's criteria. This criteria includes presence of a homogenous vaginal discharge with fishy or odor amine odor on application of KOH (whiff test), pH greater than 4.5 detected by litmus paper test and presence of densely colonized vaginal 'clue cells'. If 3 out of 4 of the Amsel's Criteria will be fulfilled, a vaginal discharge specimen was collected for Gram stain. The gram stain specimen was submitted to the laboratory for Nugent's Scoring. If Nugent's score will be at 4 to 6 with presence of clue cells or 7 or more, a diagnosis of bacterial vaginosis will be made. Women diagnosed with bacterial vaginosis, eligible to participate in the study were asked to sign an informed consent.

The participants included in the trial were randomly assigned to their respective treatment arms using computer-generated random numbers. There were 2 treatment arms in this study. The participants assigned in Group A were given Metronidazole, 500 mg per tablet, was taken by the participants 2x a day on full stomach for 7 days. For those in Group B they were given Metronidazole plus Lactobacillus capsule 200 million unit of lactobacillus, 1 capsule once a day at bedtime was also taken for 7 days.

One resident was assigned to assess the presence or absence of discharge and its odor prior to treatment. The gram stain specimen was submitted to the clinical laboratory and is read by 1 medical technologist for Nugent's Scoring. Both the resident assessor and the medical technologist were blinded to the treatment received by the participants. Proper disposal of the specimen was observed. The liquid in the staining tray was disposed in sealed bottles as hazardous waste. The slides used were soaked in a 10% bleach solution, and then were disposed in sharps containers.

The participants in Group A and B were instructed to follow-up on day 8, 15, 22 and 56 to determine if there was resolution or persistence of symptoms such as increased volume of vaginal discharge with foul odor. Collection of vaginal specimen for gram stain was also done. Inquiry on adverse effects was also done during follow up.

The participants were advised to avoid douching and intake of alcoholic beverages as well as abstain from sexual intercourse during the whole duration of the study. If sexual intercourse cannot be avoided, the participants were instructed to use condom all throughout the duration of the study. The participants were instructed regarding the adverse effect of the medications. For metronidazole the side effects include disulfiram-like reaction (abdominal distress, nausea, vomiting, flushing, or headache) when taken concurrently with ethanol; loss of appetite; constipation; diarrhea; dizziness; headache; metallic taste; nausea and vomiting. The adverse effect of Lactobacilli it is usually mild gastrointestinal side effects and bloating. If the subjects cannot tolerate the side effects of Metronidazole or Lactobacilli, discontinuation of the treatment may be required. Clindamycin was the alternative treatment. Fortunately, the participants tolerated the treatment and were able to complete the dose required.

A standard data collection tool was used during data gathering.

D. Sample Size

The sample size calculation was based on the formula on comparison of proportions from 2 independent samples. The test of equality of proportions will be carried out at 0.05 level of significance. A sample size of 103 from each treatment arm was computed with 80% chance of rejecting the null hypothesis of equal proportions if the alternative holds.

DATA MANAGEMENT AND ANALYSIS

The data were entered and encoded using Microsoft excel and was analyzed using Strata version 9.1. Univariate analysis such as mean, median, mode and range were used to describe the age, gravidity and parity of the participants included in the study. Frequency distribution was used to determine the proportion of participants with estimated G. vaginalis count category, recurrent bacterial vaginosis, restoration of normal flora, Nugent's score category, as well as presence or absence of foul smelling vaginal discharge.

The Chi-square or Fischer exact test were used to compare the efficacy of metronidazole alone and metronidazole plus lactobacilli capsule on the reduction of estimated Gardnerella vaginalis count, restoration of normal flora, reduction of recurrence of bacterial vaginosis, as well as relief of foul smelling vaginal discharge.

RESULTS

There were 40 participants included in the trial 20 per treatment arm. The age range of our participants was 21 to 44 years old with a mean age of 31.6 years. The partcipants had a gravidity and parity of 0 to 6 with a mean of 2.

Upon inclusion in the study all participants had foul smelling vaginal discharge. Likewise they were all noted to have latobacilli count of less than 30 per high power field (hpf) and also they had an estimated Gardnerella vaginalis count of greater than 30 per hpf. There was no statistically significant difference with the baseline characteristics of the participants between the 2 treatment arms. The details can be seen in Table 1

On day 8 of treatment, a statistically significant difference was noted in the estimated lactobacilli count between metronidazole alone and metronidazole plus probiotic arm. There were significantly more participants in the metronidazole plus probiotic arm with an estimated lactobacilli count of more than 30/hpf as compared to metronidazole alone. The rest of the parameters did not show any statistically significant difference between the treatment arms. (Table 2)

On day 15 post treatment, there was no statistically significant difference with the estimated Gardnerella vaginalis count, lactobacilli count, presence or absence of malodorous vaginal discharge between the metronidazole plus probiotic and the metronidazole alone arm. However there were more participants with Nugents score of less than 4 in the metronidazole plus probiotic arm compared

Table 1. Comparison of the mean demographic and proportion according to clinical characteristics of participants between the metronidazole plus probiotic and metronidazole alone

Parameters	Metronidazole +probiotic N=20 n (%)	Metronidazole N=20 n (%)	p-value*
Age (mean in years)	37	34.5	0.78
Gravidity (mean)	1.5	4	0.40
Parity (mean)	1.5	3.5	0.29
Estimated G. Vaginalis count ≤ 30/hpf	13(65)	12(60)	0.344
Estimated lactobacilli count <30/hpf	20(100)	20(100)	1.00
Vaginal discharge and foul smelling odor	20(100)	20(100)	1.00
Nugent's score 5 to 10 with clue cells	20(100)	20(100)	0.959

Table 2. Comparison of the proportion of participants according to clinical characteristics between the metronidazole plus probiotic and metronidazole alone on day 8 of treatment

Parameters	Metronidazole +probiotic N=20 n (%)	Metronidazole N=20 n (%)	p-value*
Estimated G. Vaginalis count < 30/hpf	20(100)	20(100)	0.75
Estimated lactobacilli count > 30/hpf	18(90)	12(60)	0.028*
Absent vaginal discharge and foul smelling odor	16(80)	12(60)	0.168
Nugent's score <4	11(55)	7(35)	0.505*

- statistically significant p-value < 0.05

Table 3. Comparison of the proportion of participants according to clinical characteristics between the metronidazole plus probiotic and metronidazole alone on day 15 of treatment

Parameters	Metronidazole +probiotic N=20 n (%)	Metronidazole N=20 n (%)	p-value*
Estimated G. Vaginalis count < 30/hpf	9(45)	7(30)	0.519
Estimated lactobacilli count > 30/hpf	20(100)	20(100)	1.00
Absent vaginal discharge and foul smelling	20 (100)	20(100)	1.00
Nugent's score <4	18(90)	2(10)	< 0.001*

* statistically significant p-value < 0.05

Table 4. Comparison of the proportion of participants according to clinical characteristics between the metronidazole plus probiotic and metronidazole alone on day 22 of treatment

Parameters	Metronidazole +probiotic N=20 n (%)	Metronidazole N=20 n (%)	p-value*
Estimated G. Vaginalis count < 30/hpf	17(85)	18(90)	0.819
Estimated lactobacilli count > 30/hpf	16(80)	14(70)	0.465
Absent vaginal discharge and foul smelling	16(80)	14(70)	0.465
Nugent's score <4	10(50)	12(60)	0.525

* statistically significant p-value < 0.05

to the metronidazole alone arm. This difference was statistically significant. The details of the result are tabulated in Table 3.

On day 22 of treatment, there was no statistically significant difference with all the parameters between metronidazole and metronidazole plus probiotic arm. Although, there is slightly greater proportion of participants with G.vaginalis count of less than 30/hpf and estimated lactobacilli count of more than 30/hf in the metronidazole plus probiotic arm. While the proportion of participants in the metronidazole arm having a Nugents score of less than 4 was slightly higher. (Table 4)

On day 56 of treatment, there was a statistically significant difference between metronidazole and metronidazole plus probiotic arm with the Nugents score. Seventeen out of the twenty participants in the metronidazole plus probiotic arm had nugents score of less than 4. This was only observed in half of the participants in the metronidazole arm. Likewise the presence of foul smelling discharge vaginal discharge less commonly among participants who belong to the metronidazole plus probiotic arm but the difference was not statistically significant. The rest of the parameters did not also show statistically significant diferrence between the 2 treatment arm. (Table 5)

Table 5. Comparison of the proportion of participants according to clinical characteristics between the metronidazole plus probiotic and metronidazole alone on day 22 of treatment

Parameters	Metronidazole +probiotic N=20 n (%)	Metronidazole N=20 n (%)	p-value*
Estimated G. Vaginalis count < 30/hpf	19(95)	16(80)	0.284
Estimated lactobacilli count > 30/hpf	18(90)	14(70)	0.114
Absent vaginal discharge and foul smelling	18(90)	14(70)	0.114
Nugent's score <4	17(85)	10(50)	0.018*

* statistically significant p-value < 0.05

Comparison of gram stain result and symptoms before (at baseline) and after day 8, 15, 22 and 56 treatment was done for both the metronidazole plus probiotic and metronidazole alone arms. On day 8 post-treatment with metronidazole plus probiotic, there was a statistically significant difference in the proportion of

participants noted on all parameters when compared with the parameters observed before such treatment. The results showed that on day 8 after treatment all the participants in the metronidazole plus probiotic had less than 30/hpf Gardnerella vaginalis count. There were more participants in the metronidazole plus probiotic arm with greater than 30/hpf lactobacilli count. There were fewer participants in the same arm with a negative gram stain smear for BV based on nugents score when compared with those in the metronidzole arm. (Table 6)

When the results of day 15 post-treatment was compared with the pre-treatment data, there was a statistically significant difference in the proportion of participants noted on all parameters for both the metronidazole plus probiotics and metronidazole. Both treatment arms showed a significant reduction in the Gardnerella vaginalis count, increase in lactobacilli count, and decrease in the nugents score in almost all participants. A significantly greater reduction in the proportion of participants with foul-smelling vaginal discharge was also noted in both treatment arms. (Table 7).

Comparison of the proportions on all parameters was also done before and after day 22 of treatment for both the metronidazole plus probiotics and metronidazole arms. Similar to the other post treatment results, there was a statistically significant difference in the proportion of participants noted on all parameters for both the metronidazole plus probiotic and metronidazole arm although the lactobacilli count a markedly greater proportion of participants in the metronidazole plus probiotic group (80%) had greater 30 count than those in the metronidazole arm alone (30%).

Analysis on the comparison of the proportions of participants on all parameters done pretreatment and post treatment for both the metronidazole plus probiotics and metronidazole alone arms also showed statistically significant difference. The results showed that on day 56 after treatment, majority of the participants in the metronidazole plus probiotic arm had less than 30 per hpf of G.vaginalis count, greater than 30 per hpf lactobacilli count, absent foul smelling vaginal discharge and negative gram stain smear for BV based on nugents score while there were slightly fewer participants in the metronidazole arm had such results. (Table 9)

In this trial there were no adverse effects reported by the participants in both treatment arms. There were also no drop-outs noted in both the metronidazole plus probiotic and metronidazole alone groups.

DISCUSSION

Bacterial vaginosis (BV) reflects a shift in vaginal flora from lactobacilli-dominant to mixed flora. It is the most prevalent vaginal infection in reproductive aged women

Table 6. Comparison of the proportion of participants according to clinical characteristics before and after day 8 of treatment with metronidazole plus probiotic and metronidazole alone

Parameters	Category	Metronidazole + probiotic N=20 Before treatment n (%)	Day 8 of treatment n (%)	p-value*	Metronidazole N=20 Before treatment n (%)	Day 8 of treatment n (%)	p-value*
Estimated G. Vaginalis count < 30/hpf	≤ 30/ hpf	5(25)	20(100)	< 0.001	8(40)	20(100)	< 0.001
Estimated lactobacilli count > 30/hpf	> 30/ hpf	0(0)	18(90)	< 0.001	0(0)	12(60)	< 0.001
Vaginal discharge and foul smelling	Present	20(100)	4(20)	< 0.001	20(100)	8(40)	< 0.001
Nugent's score <4	< 4	0(0)	7(35)	< 0.001	0(0)	11(55)	< 0.001

* statistically significant p-value < 0.05

Table 7. Comparison of the proportion of participants according to clinical characteristics before and after day 15 of treatment with metronidazole plus probiotics and metronidazole alone

Parameters	Category	Metronidazole + probiotic N=20 Before treatment n (%)	Day 15 of treatment n (%)	p-value*	Metronidazole N=20 Before treatment n (%)	Day 15 of treatment n (%)	p-value*
Estimated G. Vaginalis count < 30/hpf	≤ 30/ hpf	5(25)	9(45)	0.17	8(40)	20(100)	< 0.51
Estimated lactobacilli count > 30/hpf	> 30/ hpf	0(0)	20(100)	< 0.001	0(0)	20(100)	< 0.001
Vaginal discharge and foul smelling	Present	20(100)	0(0)	< 0.001	20(100)	0	< 0.001
Nugent's score <4	< 4	0(0)	18(90)	< 0.001	0(0)	18(90)	< 0.001

* statistically significant p-value < 0.05

Table 8. Comparison of the proportion of participants according to clinical characteristics before and after day 22 of treatment with metronidazole plus probiotic and metronidazole alone

Parameters	Category	Metronidazole + probiotic N=20 Before treatment n (%)	Day 22 of treatment n (%)	p-value*	Metronidazole N=20 Before treatment n (%)	Day 22 of treatment n (%)	p-value*
Estimated G. Vaginalis count < 30/hpf	≤ 30/ hpf	5(25)	19(95)	< 0.001	0(0)	20(100)	< 0.001
Estimated lactobacilli count > 30/hpf	> 30/ hpf	0(0)	16(80)	< 0.001	20(100)	6(30)	< 0.001
Vaginal discharge and foul smelling	Present	20(100)	4(20)	< 0.001	20(100)	6(30)	< 0.001
Nugent's score < 4	< 4	0(0)	10(50)	< 0.001	0(0)	12(60)	< 0.001

* statistically significant p-value < 0.05

Table 9. Comparison of the proportion of participants according to clinical characteristics before and after day 56 of treatment with metronidazole plus probiotic and metronidazole alone

Parameters	Category	Metronidazole + probiotic N=20 Before treatment n (%)	Day 56 of treatment n (%)	p-value*	Metronidazole N=20 Before treatment n (%)	Day 56 of treatment n (%)	p-value*
Estimated G. Vaginalis count < 30/hpf	≤ 30/ hpf	0(0)	19(95)	< 0.001	8(90)	16(80)	0.001
Estimated lactobacilli count > 30/hpf	> 30/ hpf	0(0)	18(90)	< 0.001	0(0)	14(70)	< 0.001
Vaginal discharge and foul smelling	Present	20(100)	2(10)	< 0.001	20(100)	6(30)	< 0.001
Nugent's score <4	< 4	0(0)	17(85)	< 0.001	0(0)	10(50)	< 0.001

* statistically significant p-value < 0.05

reported in 8% to 29% of cases. It is the most common etiology of vaginal symptoms prompting medical care. Of 3,739 women enrolled in a nationally representative sample of the U.S. civilian non-institutionalized population from 2001 to 2004, almost one in three (29.2%; 95% C.I. 27.2 – 31.3) had bacterial vaginosis as diagnosed by Gram stain of vaginal fluid. Bacterial vaginosis has been consistently associated with adverse outcomes related to the upper genital tract, and with increased risk of HIV acquisition.

According to Gardner and Dukes, there is a strong correlation between BV and the presence of Gardnerella vaginalis. The resident Lactobacillus species in cases of BV are replaced by an overgrowth of vaginal anaerobes or gram-negative bacteria including Gardnerella vaginalis, Atopobium vaginae, bacterial vaginosis-associated bacteria, Megasphaera species, Mycoplasma hominis, Mobiluncus species, Ureaplasma urealyticum, Prevotella, and Peptostreptococcus species. Moreover, BV-associated bacteria have been shown to form a prolific polymicrobial biofilm. The main component of which was found to be G. vaginalis and A. vaginae, that adheres to the vaginal epithelium.

As stated in the review of related literature, effects of untreated symptomatic bacterial vaginosis is not life threatening, but in pregnancy it is associated with adverse pregnancy outcomes, leading to high perinatal mortality. This infection can also cause brain injuries in fetuses as well as permanent neurological brain damage. If left untreated or if treatment is inadequate due to poor compliance, recurrence may be common. This can be an added burden to those having such an infection. This will then entail greater cost of treatment due to frequent visits to the clinic for evaluation and repeated therapy with the standard antibiotic. Repeated exposure to the antibiotic may lead to emergence of resistant strains.

For Jean Pirre Menard et al the cure rate for bacterial vaginosis 7 days post treatment was at 45% compared to 14 days post treatment, which is 63%. Cure rate in our study was calculated at 67.5%. In our study the findings of less than 30 per hpf estimated Gardnerella vaginalis count with absent foul smelling vaginal discharge was noted only in all participants on day 8 post treatment in the metronidazole arm. With metronidazole plus probiotic group, the proportion of women with less than 30 per hpf Gardnerella vaginalis count and absent foul smelling vaginal discharge were accounted among 100% of the participants from day 8 to 56 post treatment. The early reduction in the causative agent and symptoms can be attributed to an increase in the estimated lactobacilli count sustained until 56 days post treatment metronidazole plus probiotic. With increased lactobacilli levels overgrowth and colonization with Gardnerella vaginalis count and other BV associated organisms will be reduced.

Furthermore, on day 8 of treatment in our trial, metronidazole plus probiotic arm had a significant decrease

in the estimated gardnerella vaginalis count. It was also observed in the same arm that participants who were observed to have significant restoration of the lactoballi, as compared to those in the metronidazole group.

In the latter arm, restoration of the lactobacilli was noted to be significant proportion of participants only on day 15 and 22 post-treatment. The faster restoration of lactobacilli in the metronidazole plus probiotic group may be attributed to the anti microbial property of metronidazole enhanced by the presence of lactobacillus specie that have host protective characteristics, including hydrogen peroxide, lactic acid and biosurfactant production, antimicrobial activity and co-aggregation with pathogens

The proportion of the participants in the metronidazole plus probiotic (16/20 = 80%) and metronidazole alone (14/20 = 70%) having such score was found to be comparable from day 8 to 22 post-treatment. However, when the before and after treatment analysis was done, there were more participants in the metronidazole plus probiotic arm who had such score as compared to those in the metronidazole arm. This effect may be explained by achieving lactobacilli count in shorter period of time in the metronidazole plus probiotic. Hence, the lactobacilli count will be greater coupled with the faster reduction in the Gardnerella vaginalis count. This then led to attainment of a lower score. However, from day 15 to 22 and 56 post-treatment, the proportion of participants who had a nugent's score of less than 4 were greater for both the metronidazole plus probiotic (100%) and metronidazole alone (95%) arm, when compared to day 8 post-treatment. This finding for the metronidazole plus probiotic group is due to sustained reduction in the Gardnerella vaginalis count and increase in lactobacilli counts. Potentially, the metronidazole plus probiotic treatment was found to be more favorable in sustaining the normal flora and probiotic can be used as an adjunct may enhance the efficacy of metronidazole in the treatment of BV.

In bacterial vaginosis, the prominent complaint is foul-smelling vaginal discharge. Hence, the evaluation of the efficacy of the agent in the management of bacterial vaginosis should not only be confined to lowering bacterial load and restoring lactobacilli but alleviating such bothersome symptoms as well. In the study conducted by Cardone et al, 40 out of 45 participants reported complete resolution of symptoms while only 3 reported a reduction in symptomatology. In our trial, starting on day 8 post treatment with metronidazole and metronidazole plus probiotic, there was resolution of the vaginal discharge and foul odor sustained up to day 56 post-treatment. The explanation for the result can be attributed to the antimicrobial property of metronidazole, which is cytotoxic to the DNA molecule of the organisms causing BV, thereby early eradication of the organisms leads to alleviation of the symptoms. Lactobacillus species maintain the vaginal ecosystem in a healthy condition by production of antimicrobial substances and this might be the reason for the sustained effect up to day 56 post treatment.

Another important factor in the management of any disease entity or infectious process is compliance. The adverse effect of metronidazole can be a limitation in terms of compliance. These adverse effects include diarrhea, dizziness or lightheadedness, headache, loss of appetite, nausea or vomiting, stomach pain or cramps. However, none of our patients reported such side effects. Even the mild gastric irritation with lactobacilli was also not noted by the patient in this trial. But still such problems in treatment should be taken into consideration. Hence, reassurance and proper education regarding the drug must be emphasized to the patient.

Our study results are promising as far as management of BV is concerned. However, we cannot make a definitive conclusion because of our limited sample size. Hence, it is sufficient to say that our preliminary findings for metronidazole plus probiotic are potentially more favorable than metronidazole alone in managing BV among patients. We cannot generalize the results since it was only done at our outpatient department among non-pregnant patients. Hence, our population may not be truly representative of the diverse characteristics of patients with such infection usually encountered in the clinics.

CONCLUSION

Our trial showed that the metronidazole plus probiotic and metronidazole only treatment are comparable in treating bacterial vagnosis. However, in terms of restoring and maintaining the normal flora, metronidazole plus probiotic appears to be more significantly efficacious. Thereby, maintaining a suppressive effect in the proliferation of Gardnerella vaginalis. Probiotic in the form of lactobacilli is a promising adjunct to enhance the efficacy of metronidazole in the treatment of bacterial vaginosis.

RECOMMENDATIONS

To be able to make a definitive conclusion further study should be done with a wider population. The follow up period should be extended up to 90 days post treatment to further evaluate the effect on long term prevention of the recurrence of bacterial vaginosis. This is important since recurrence is a vital issue in providing adequate cure for those women who had previous infection with bacterial vaginosis. Thereby, further aids in preventing the recurrence of the bothersome symptoms of the infection. ■

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