

Efficacy of Cranberry Extract Bacillus Coagulans & Turmeric Extract in Patients With Bacterial Vaginosis

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ABSTRACT

Objective: The objective of this study was to assess the efficacy and safety of conventional therapies alone (antibiotic, metronidazole, antibiotic metronidazole) versus conventional therapies with combination therapy cranberry extract bacillus coagulans & turmeric extract, in patients with bacterial vaginosis.

Study Design: Observational / descriptive study.

Place and Duration of Study: This study was conducted at nine study sites from three major cities (Karachi, Lahore and Islamabad) in Pakistan from January to September 2016.

Materials and Methods: After ethics committee approval at physician discretion 150 Patients meeting the eligibility criteria received standardized conventional therapies alone (Antibiotic Metronidazole/Antibiotic Metronidazole) & 150 patients received conventional therapies with Combination therapy Cranberry extract bacillus coagulans & turmeric extract. The primary outcome measures were frequency of recurrence of vaginal infections and improvement of symptoms.

Results: For this study, 300 healthy, newly diagnosed & treatment experienced, non-pregnant women were enrolled to participate with the symptoms and signs of BV from 09 different centers from Pakistan. Amsel's criteria were significantly decreased after treatment in both groups at week 2 ($p=0.003$). The microbiological cure rate of bacterial vaginosis at week two was significantly ($p<0.001$) higher in experimental group (76.9%) as compared to conventional group (58.5%). There were significant ($p<0.001$) differences between two groups in terms of recurrence rate of bacterial vaginosis at week 12.

Conclusion: This study demonstrated the safety and efficacy of cranberry extract bacillus coagulans & turmeric extract in preventing BV recurrence. Therefore this product can be used for the improvement of clinical and microbiological parameters in patients with BV.

Key Words: Bacterial vaginosis (BV), non-antibiotic treatment, antibiotics, emerging therapies, bacillus coagulans

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INTRODUCTION

Bacterial vaginosis is the most widely recognized problem of lower genital tract and the most common reason for vaginal discharge and unpleasant odour among women of reproductive age.

One of the most eminent disorders which tops the list of all the vulvovaginal infections and adds 60% of these infections is Bacterial Vaginosis (BV).¹ The prevalence varying widely depending on the patient population and can be diagnosed both clinically and microbiologically. BV prevalence is ranging from 12% in Australian women, 29% in North American women followed by more than 50% in East/Southern Africa women.²⁻⁵

BV is a poly microbial infection resulting from many anaerobic bacterial including Gardnerella vaginalis, Prevotella species, Mobiluncus species, Atopobium vaginae and Mycoplasma species. One more factor which is taken in consideration while discussing about pathogenesis of BV is the absence or decrease in the amounts of Lactobacilli which releases hydrogen peroxide, it is witnessed that their reduction also contributes as a prime cause of BV.⁶ As BV is a very complex disorder, the complications are numerous if it is left untreated. The complications mostly comprise of low birth weight of fetus, pelvic inflammatory disorder⁷, premature birth and inability to conceive amongst others.⁸

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In contemporary times probiotics have managed to gather attention of many medical personnel because of their prominent health promoting benefits. Probiotics are basically the living microorganisms which when administered in particular amounts provide lots of health stimulating benefits.⁹ Previously many studies were done on the role of probiotics and the results made it evident that beneficial health promoting results do exist. Cranberry juice was subjected as a treatment for UTI by Kontiokari T et al, who showed that prevention of recurrence of UTI is by frequent intake of cranberry juice in increasing the count of lactobacilli.¹⁰ The objective of this study was to assess the efficacy and safety of conventional therapies alone (antibiotic, metronidazole, antibiotic metronidazole) versus conventional therapies with combination therapy cranberry extract bacillus coagulans & turmeric extract in patients with bacterial vaginosis.

MATERIALS AND METHODS

Phase IV interventional, prospective study was conducted at different centers in Pakistan from January to September 2016. Nine study sites from three major cities (Karachi, Lahore and Islamabad) were selected on the basis of patient population, facilities and equipments, data storage and security, willingness to participate in study and high quality personnel who deliver high quality data. The sample size was calculated with the WHO sample size calculator¹¹ with the assumption that the product would be $\geq 50\%$ more efficient than placebo.¹² The recommended sample size was 300 participants (conventional group, n = 150; combination therapy group, n = 150).

Groups	Subgroups	Number of Patients
Conventional	Antibiotic	50
	Metronidazole	50
	Antibiotic + Metronidazole	50
Experimental	Antibiotic + Cranberry extract bacillus coagulans & turmeric extract x BD	50
	Metronidazole+ Cranberry extract bacillus coagulans & turmeric extract x BD	50
	Antibiotic + Metronidazole+ Cranberry extract bacillus coagulans & turmeric extract x BD	50

The decision to start treatment was made by the gynecologists as per study protocol. Participants were selected by using consecutive sampling method who

willing to undergo screening after signing informed consent, the inclusion criteria were newly diagnosed & treatment experienced (had 03 episodes of bacterial vaginosis per year), non-pregnant (14-26 weeks), females outpatients 15-44 years of age with diagnosis of Bacterial vaginosis. Criteria for diagnosis of BV included presence of three out of four Amsel's clinical criteria including pH > 4.5, positive Whiff test results, a gray-white homogenous discharge, and presence of clue cells.

At 02 weeks treatment with Metronidazole 400 mg B.D/other antibiotic was stopped in groups of conventional and experimental. Cranberry extract bacillus coagulans & turmeric extract was continued till week 12. At week 12 all patients on conventional therapies with Combination therapy Cranberry extract bacillus coagulans & turmeric extract was evaluated for the recurrence through clinical symptoms & HVS test. Each patient was followed up for a period of 12 weeks. 03 study visits was performed at baseline, 02 weeks and at 12 weeks for the recurrence.

All analyses were performed on SPSS version 21. For continuous variables summary statistics included n (number of observations), mean and standard deviation as well as frequencies and percentages for categorical variables were presented. A chi square test was used to find out the difference between the categorical groups. A p-value ≤ 0.05 was considered as significant.

RESULTS

Out of 300 enrolled patients a total of 267(89%) women, 131(87.3%) in conventional group and 136(90.7%) in experimental group completed the study. In this study, no participant was excluded from the study due to an adverse event or serious adverse events related to the use of the probiotic product, while 33(11%) patients were excluded for other reasons. At week 2, two patients were lost to follow while 3 patients became pregnant; six patients left the study because of side effects of antibiotic treatment and poor compliance. At week 12, twelve patients were lost to follow, of these 5 became pregnant and 7 due to poor compliance with antibiotic treatment. There was no significant difference between two groups in terms of demographic and reproductive characteristics such as age, duration of marriage, age at first pregnancy, parity, abortion, use of contraceptive method and frequency of intercourse per week ($P > 0.05$).

At week 2, the difference between two groups in terms of clinical improvement, i.e. improvement in Amsel's criteria, was significant($p=0.003$); in other words, experimental group was more effective than conventional treatment in terms of clinical improvement (Table 1). The microbiological cure rate of bacterial vaginosis at week two was significantly ($p<0.001$) higher in experimental group (76.9%) as compared to conventional group (58.5%) (Table 2).

The results of safety evaluation in experimental group at 12 weeks are shown in Table 3. Nausea was reported in 3 patients in conventional group while none of the subjects in experimental group showed this symptom. Heartburn had the highest frequency among study subjects in experimental (6) and conventional (5) groups. Skin rash, headache, metallic taste, and abdominal pain were reported in experimental group 2, 4, 1 and 1 ($p < 0.469$). The severe adverse event was not reported in any experimental treatment group at 12 weeks. There were significant ($p < 0.001$) differences between two groups in terms of recurrence rate of bacterial vaginosis at week 12, i.e. recurrence was 33.6% in conventional group as compared to 16.2% in experimental group (Table 4).

Table No.1: Resolution of symptoms of Bacterial Vaginosis at Week Two as Reported by Patients (n=289)

Treatment Arms	Resolution of Symptoms at Week 2 n(%)			p-value
	Fully Relieved	Partially Relieved	Not Relieved	
Conventional (n=142)	71(50)	36(25.4)	35(24.6)	0.003
Experimental (n=147)	101(68.7)	28(19)	18(12.3)	

Table No.2: Microbiological Cure of Bacterial Vaginosis at Week Two (n=289)

Treatment Arms	Cure Rate (HVS) at Week 2 n (%)		p-value
	Yes	No	
Conventional (n=142)	83(58.5)	59(41.5)	<0.001
Experimental (n=147)	113(76.9)	34(23.1)	

Cure (0-1 Amsel's Criteria) absence or presence of only one of Amsel's Criteria

Table No.3: Safety Evaluation in Both Groups at Week 12(n=267)

Treatment Arms	Adverse Events n (%)	p-value	Serious Adverse Events n (%)
Conventional (n=131)	6(4.6)	0.469	Nil
Experimental (n=136)	9(6.6)		Nil

Table No.4: Recurrence of Bacterial Vaginosis in Both Groups at Week 12 (n=267)

Treatment Arms	Yes n(%)	No n(%)	p-value
Conventional (n=131)	44(33.6)	87(66.4)	<0.001
Experimental(n=136)	22(16.2)	114(83.8)	

DISCUSSION

This study exhibited that when traditional antibiotics along with metronidazole and probiotics, turmeric extract and cranberry juice were added the consequences were comparatively better. Reduction of Lactobacilli as discussed previously, plays a enormous in the infection of the vagina and even constant periods of remissions and recurrences, hence in one such study by Anukam et al and Mastromarino, they administered certain strains of lactobacilli in biologically friendly quantity, demonstrated positive results in treatment of BV due the restoration of the microbiota and even prevention of recurrences.^{13, 14} One of the major problem in treating BV and other vaginal infections is their tendency to recur. Therefore to resolve this issue, probiotics were added with the traditional antibiotics and the results were pleasantly surprising, not only BV was cured faster but even recurrences were tackled to quite an extent.^{15,16} Use of Cranberry juice to treat BV was considered to play a major role is resolution of UTI, Kontiokari T et al in the study results showed that within the period of 6 months, recurrence rate were lower in group give cranberry juice as compared to those who were not given.¹⁰ Clinical improvement based on Amsel's criteria was estimated at 80% and 70% in micosin and metronidazole treatment groups, respectively.¹⁷

In order to analyze the rate of resolution of infection after the treatment, HVS test laboratory criteria was taken into consideration. The results of the both groups showed a significant variation in recurrence of symptoms. Lactobacilli as previously discussed is one of the major treatment modality in curing BV, hence it was added with traditional antibiotics like metronidazole, clindamycin and tinidazole. The results were quite satisfying as BV was completely cured in high rates plus minimum recurrence was observed and there was early reestablishment of microbial flora.¹⁸⁻²⁰

Adverse reactions in this kind of treatment modality were either negligible or were of mild severity. Probiotics are very well tolerated by majority of adult women and have played an effective role in reduction of BV symptoms. Hence they were considered safe pharmaceutically.²¹⁻²⁵

The study purpose was primarily to exhibit the difference between the experimental preparation along with the conventional standard treatment and the standard treatment alone. It was witnessed that in those patients who experimental modality was added, recurrences were less seen when it was analyzed both clinically and microbiologically. Keeping in mind that BV is highly recurrent and prevalent in our setup and with metronidazole the choice of antibiotic multiple side effects, herbal alternative integration into the standard drug therapy can lead to fewer side effects with more effective treatment.

To be precise, probiotics, cranberry and turmeric extract along with conventional therapy demonstrate a secure and efficient way to treat the vaginal infections and equalize the balance of the vaginal microbial flora. Moreover along with reduction in recurrence rates, vaginal pH also gets normalized and there is decrease in the Amsel's score as well. We suggest the use of these alternatives in such kind of infections where rebalancing of microbiota is required.

CONCLUSION

This study demonstrated the efficacy and safety of cranberry extract, bacillus coagulans & turmeric extract in preventing BV recurrence, as this product contributes to the improvement of clinical and microbiological parameters, thereby lengthening the remission period. Our findings supported the positive effects of probiotics described in previously mentioned studies. Probiotic combination treatment regimens appear promising but larger, well-designed randomized conventional trials with standardized methodologies are needed to confirm the benefits of probiotics in the treatment of BV.

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Conflict of Interest: The study has no conflict of interest to declare by any author.

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