# EFFICACY OF METRONIDAZOLE VAGINAL VERSUS ORAL METRONIDAZOLE FOR THE TREATMENT OF BACTERIAL VAGINOSIS IN PESHAWAR PAKISTAN

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## ABSTRACT

Bacterial vaginosis (BV) is the common disease of adult women that effects vagina leading to abnormal vaginal discharge due to the overgrowth of pathogenic bacteria. The most common drugs used to eradicate BV is oral metronidazole, secnidazole, tinidazole as well as vaginal metronidazole gel or clindamycin cream. This study aims to compare the efficacy of oral and vaginal metronidazole for the eradication of BV. A total 594 clinically diagnosed BV patients were enrolled in the study which were randomly divided into two groups (1&2). Group 1 received 5gms metronidazole vaginal gel daily for 5 days while group 2 were on oral metronidazole 400mg twice daily for 5 days. All the patients were followed for 14 days. The patients were considered cured if the microscopic examination didn't reveal any clue cells. The mean age of patients in group 1 and group 2 was 32.7±2.1years and 33.4±1.5 years, respectively. Majority of patients in both groups were in between the age group of 36-45 years. The results showed that the therapeutic cure rate was high in group 1 as compared to group 2 (92.59% vs 85.85%) with p-value 0.01. Furthermore, the chances of recurrence of BV was high in group 2 (OR with 95% CI = 2.05, 1.19-3.5) suggesting that metronidazole vaginal gel is more effective in the treatment of BV as compared to oral metronidazole. The adverse events related to vaginal metronidazole is less because of its local effect and is associated with good result and relief of symptoms related to BV.

**Key words:** Bacterial vaginosis, oral metronidazole, vaginal metronidazole,

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## INTRODUCTION

Bacterial Vaginosis (BV) is the most common adult women disorder that affects vagina and is associated with abnormal vaginal discharge, characterized by reduction in the normal vaginal flora that is lactobacillus and increasing number of other pathogens including gram positive and gram negative species of bacteria most commonly Escherichia coli, Gardnerellavaginalis, Mycoplasma hominis, and Mycoplasma curtisii[(1)]. BV increases the risk sexually transmitted infections, preterm delivery and spontaneous abortions[(2,3)]. Additionally, BV also causes premature rupture of membranes, infects fetal membranes and amniotic fluids during pregnancy and can cause postpartum fever. Vaginal discharge and fishy smell are the common symptoms of BV but many patients are asymptomatic[(4,5)]. About 64% of BV is observed in women with sexually transmitted infection, up-to 20% in pregnant women and up-to 15% of women who refer to gynecologist[(6)] . Amsel's criteria is usually used for the diagnosis of BV and is confirmed if a patient had homogenous vaginal discharge, vaginal pH >4.7, clue cell on gram stain and/or fishy smell[(7)]. Once diagnosed, the management of BV is another challenge for the gynecologists. Because of no specific causative agent, the gynecologists has to find effective therapy that not only treat BV but also reduces the reoccurrence. Currently the treatment approach is more likely empirical that involves the use of nitroimidazoles, clindamycin and/or broad spectrum antimicrobials to cover an-aerobics as well. The first line treatment regimen includes 500mg metronidazole oral, twice daily for 7 days, 2% clindamycin cream intravaginal once daily for 7 days or metronidazole gel intravaginal once daily for 5 days. However, short courses for these agents are less effective to eradicate BV[(8)] . Similarly, the use of antiseptic and probiotics are also effective in the treatment of BV[(9)] but reoccurrence occurs and

extended follow up studies also reported the reoccurrence rate of 50% within 6-12[12] months. Despite increasing knowledge in the field of medical sciences, appropriate treatment is still lacking to cure the disease. Though several treatment regimen have been used for treating BV both separately and in combinations[3,10-12] but in all these treatment modalities metronidazole is the drug of choice in treating BV[10]. The current project was designed to evaluate the efficacy of metronidazole vaginal gel and oral metronidazole for the treatment of BV in adult women visiting Khyber Teaching Hospital Peshawar Pakistan.

## METHODOLOGY

### Study setting and ethics statement

The current study was conducted in the department of Gyne and Obstetrics, Khyber Teaching Hospital Peshawar Pakistan. The study was approved by the ethical board, Khyber Teaching Hospital Peshawar Pakistan. Written informed consent was also obtained from all the participant of the study.

### Inclusion Exclusion criteria & data collection

Non pregnant patients with confirmed BV according to Amsel's criteria[7] and age between 18-45 were enrolled in the study. Lactating mothers, pregnant patients, patients with diabetes and/or patients not willing to participate in the study were excluded from the project.

### Study Population

The present study includes total 594 diagnosed bacterial vaginosis patients which were randomly assigned in to two groups (1&2). The calculated sample size was 297 cases in each group, 80% power of study, taking expected percentage of effectiveness of metronidazole vaginal gel and oral metronidazole in the treatment of bacterial vaginosis i.e. 85% and 77%, respectively[13]. Sample size was calculated by using computer program Power and Sample Size Calculation version 2.1.31.The duration of the study was 12 months started from Jan 2016 to December 2016. After complete physical and vaginal examination the patients were put on standard therapies. Group 1 received metronidazole vaginal gel 5gm daily for 5 days while group 2 received oral metronidazole 400mg twice daily for 5 days. All the patients were followed for 14 days. After follow-up visit the participant were considered cured if they had no clue cells on microscopy.

### Statistical analysis

Statistical Package for Social Sciences (SPSS) version 20.0 were used to analyze the means and standard deviations in each group. Chi-square was done to determine the possible statistical difference between groups 1 and group 2 patients. The graphs were constructed using Graph-Pad Prism version 6.0. All the statistical tests carried out were two tailed. P-value <0.05 was considered significant.

## RESULTS

In group 1, 118 (39.7%) of patients were in age group 36-45 years while 28 (9.5%) of patients were below 20 years of age. Similarly, 110 (37%) and 35 (11.8%) of patients in group 2 were from the age group 36-45 and below 20 years respectively. The mean age of individuals in group 1 was 32.7±2.1 while in group 2, the mean age was 33.4±1.5. The age wise distribution of BV patients are summarized in table 1.

After 14 days follow-up the presence/absence of clue cell on microscopy was evaluated between groups. There was statistically significant difference between groups with p-value 0.01. The absence of clue cell on microscopy confirmed the patient, treated. The vaginal metronidazole (92.59%) was more effective as compared with oral metronidazole (85.85%) (table 2). Furthermore, patients using metronidazole oral have 5% change of BV reoccurrence (OR = 2.05 95% CI = 1.19-3.5). Figure 1 shows the presence and absence of clue cells between group 1 and group 2.

**Table 1: Distribution of age between groups**

| Age (year) | Group-1 (Metronidazole vaginal gel) | | Group-2 (Oral Metronidazole) | |
|---|---|---|---|---|
| | No. | % | No. | % |
| < 20 | 28 | 09.5 | 35 | 11.8 |
| 20-25 | 61 | 20.5 | 63 | 21.2 |
| 26-35 | 90 | 30.3 | 89 | 30.0 |
| 36-45 | 118 | 39.7 | 110 | 37.0 |
| Total | 297 | 100.00 | 297 | 100.0 |
| Mean±SD | 32.7±2.1 | | 33.4±1.5 | |

**Table 1: Distribution of age between groups**

| Clue cells | Group-1 | Cure rate % | Group-2 | Cure rate % | $x^2$ value | p-value | OR (95% CI) |
|---|---|---|---|---|---|---|---|
| No | 275 | 92.59 | 255 | 85.85 | 6.32 | 0.01 | 2.05 (1.19-3.5) |
| Yes | 22 | | 42 | | | | |
| Total | 297 | | 297 | | | | |

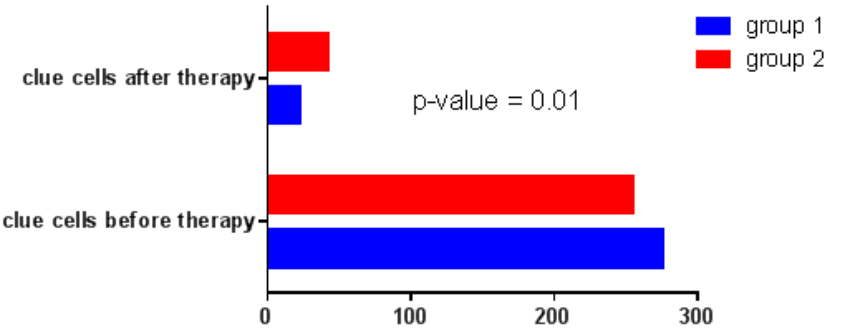


**Figure 1: Clue cells between group 1 & group 2 before and after metronidazole therapy**

## DISCUSSION

Bacterial vaginosis (BV) is currently regarded as the most prevalent cause of vaginal infection in women of reproductive age[14]. Bacterial vaginosis can also have a significant impact on a women's quality of life. The significance of BV lies not only in causing lower genital tract symptoms but more importantly in causing obstetrical and gynecological complication. BV is strongly associated with preterm delivery and is now regarded as common cause of upper genital tract infection that occur during pregnancy and those following surgical procedure[15]. To treat BV, oral metronidazole is the drug of choice . Other treatment regimens have also been used including secnidazole, tinidazole and clindamycin but their effect was similar to metronidazole, in fact metronidazole was found to be superior in treating certain species of bacteria's[16]. The present study was designed to find the efficacy of metronidazole oral vs metronidazole vaginal gel for the treatment of BV. 594 non pregnant BV patients participated in the study which were randomly divided into two groups (1&2) with 297 patients in each group. Group 1 received metronidazole vaginal gel 5gm daily for 5 days while group 2 patients were given 400mg twice a day oral metronidazole for 5 days and all the patients were followed for 14 days. The patients were considered cured if she had no clue cells upon microscopy. The analysis of the study shows that metronidazole vaginal gel was more effective in treating BV as compared to oral metronidazole (p value = 0.01). The cure rate for metronidazole vaginal is 92.59% which is higher than oral metronidazole 85.85%. Different literatures have been published which also prefers the use of vaginal metronidazole when compared oral and vaginal metronidazole though we have achieved high cure rates compared to other studies[17-20]. Similarly, the risk of reoccurrence with oral metronidazole is increased as compared to vaginal metronidazole (OR= 2.05, 95%CI = 1.19-3.5), consistent with published literatures in 2006, in which the rate of reoccurrence with oral metronidazole is high[2-21] rather than vaginal metronidazole[22].

The vaginal metronidazole is safe even if the dose of metronidazole is increased according to the published literature which uses 1.3% rather than 0.75% because the effect is local not systemic, according to the published data peak plasma concentration after oral and vaginal metronidazole in 15.56µg/ml and 1.86 µg/ml respectively[23], which also leads to lesser adverse events and increases tolerability[24]. Similarly, metronidazole is CYP450 inhibitor so co-administration of drugs that are CYP450 inducers carbamazepine, phenobarbital, phenytoin etc. may interact with metronidazole leading to drug-drug interaction. Thus the vaginal administration may be helpful not only in the reduction of adverse drug events but also avoid drug-drug interactions[25].

## CONCLUSION

The current project conclude that metronidazole vaginal gel has superior action in treating bacterial vaginosis as compared to oral metronidazole. If both vaginal and oral metronidazole have similar efficacy, even then the vaginal metronidazole might be recommended for the treatment of BV because it reduces adverse events and minimize drug interaction due to its local effect.

**Conflict of interest**
The authors declare no conflict of interest.

**Limitation of the study**
Multicenter studies as well as extended follow-up studies with large sample was the limitation of our study.

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