

Evaluation of Combination Therapy in the Management of Vaginitis

Vidhi Singh^{1*}, Shivani Panwar²

¹Department of Obstetrics and Gynaecology, Netaji Subhash Chandra Bose Medical College and Hospital Jabalpur, Madhya Pradesh, India

²Department of Obstetrics and Gynaecology, Netaji Subhash Chandra Bose Medical College and Hospital Jabalpur, Madhya Pradesh, India

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Corresponding author: Dr Vidhi Singh

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Abstract

Introduction: The efficacy of vaginitis treatment regimens that combine antimicrobial and antiviral agents was evaluated. Antibiotics plus probiotics or intravaginal pH modulators have shown promise in lowering BV recurrence rates. Recurrent or complex cases of VVC may benefit from a combination of topical corticosteroids and antifungal or antibacterial agents. Vaginitis treatment options include antiseptics, which have also been proposed.

Aims and Objectives: This study aims to assess the efficacy of combination therapy in the treatment of vaginitis, considering the varying causes of vaginitis.

Methods: Convenience sampling was used to enroll sixty patients with complaints of vaginal discharge from a university gynaecological clinic for this clinical trial. The patients all reported having vaginal discharge. A series of diagnostic evaluations were carried out to diagnose vaginal candidiasis, bacterial vaginosis, or non-specific vaginitis. These evaluations included symptoms, vaginal pH, fungal components, the Whiff test, gynaecological exams, the Amsel criteria, and clue cells.

Results: The study has found that the frequency of adverse effects and improvement in symptoms for vulvovaginal candidiasis, bacterial vaginosis, and non-specific vaginitis. All groups experienced considerable improvement in symptoms while on therapy. The study also showed that the typical VAS satisfaction ratings for oral metronidazole and combined treatment. Satisfaction levels were similar, comparing the two approaches to treating bacterial vaginosis and non-specific vaginitis.

Conclusion: The study has concluded that combination therapy significantly improved vaginitis than a mono-therapy of metronidazole.

Keywords: Vaginitis Treatment, Vaginitis, Metronidazole, Trichomonas.

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Introduction

Vaginitis is a common condition characterised by inflammation of the vagina, often resulting in symptoms such as itching, burning, abnormal discharge, and discomfort [1]. Various factors, including infections, hormonal changes,

and irritants, can cause it. The management of vaginitis typically involves identifying and treating the underlying cause, along with symptomatic relief [2]. Combination therapy, which involves using multiple treatment modalities simultaneously, can effectively manage

vaginitis, depending on the specific cause. Here is an evaluation of combination therapy approaches for different types of vaginitis [3-5].

In Bacterial vaginitis is the most common type of vaginitis caused by an imbalance in the vaginal microbiota. The standard management for bacterial vaginitis is antibiotics, for example metronidazole or clindamycin [6]. However, recurrence rates are high with single-agent therapy. Combination therapy, involving the use of antibiotics along with probiotics or intravaginal pH modulators, has shown promising results in reducing recurrence rates [7]. Probiotics help restore the normal vaginal flora and maintain a healthy balance, while pH modulators help maintain the optimal acidic environment in the vagina. This approach may improve treatment outcomes and reduce the risk of recurrence [8].

An overabundance of *Candida* species in VVC, a yeast infection [6–8], is the root of the problem. Antifungal agents, such as fluconazole or topical azoles, are the primary treatment options. In most cases, single-agent therapy is sufficient for uncomplicated VVC. Combination therapy is not typically recommended for uncomplicated VVC [9]. However, combining antifungal agents with topical corticosteroids or maintenance therapy with antifungal suppositories may be considered for recurrent or complicated cases. This approach addresses inflammation and prevents recurrence, but its effectiveness is still under investigation [10].

Trichomonas vaginitis, a parasite, is a component of the sexually transmitted disease trichomoniasis. It is usually treated with a single-dose oral medication, such as metronidazole or tinidazole, which is highly effective. Combination therapy is generally not required for trichomoniasis, as single-agent treatment is sufficient in most cases. However, it is essential to treat

both partners simultaneously to prevent re-infection [11].

In Atrophic vaginitis occurs due to hormonal changes, particularly decreased estrogen levels, often seen during menopause [12]. The mainstay of treatment is estrogen replacement therapy, which can be administered systemically or locally (vaginal estrogen creams, tablets, or rings). Combination therapy for atrophic vaginitis may involve vaginal moisturisers, lubricants, and estrogen therapy [13]. Vaginal moisturisers help improve lubrication and relieve symptoms, while estrogen therapy addresses the underlying hormonal imbalance. This combination can provide enhanced symptomatic relief and improve the overall vaginal health. It is significant towards noting that the choice of combination therapy must be dependent on the specific type in addition to severity of vaginitis, individual patient factors, and healthcare provider's recommendations. Additionally, patients should follow up with their healthcare provider to monitor treatment efficacy and address any concerns or side effects [14, 15].

The Center for Disease Control and Prevention (CDC) typically recommends specific treatments for different types of vaginitis. For vaginal candidiasis (VVC), a frequently utilised form of therapy is vaginal clotrimazole or oral antifungal drugs like fluconazole, recommended as a single 150 mg dose. Bacterial vaginosis (BV) is commonly cured through oral or vaginal antibiotics including metronidazole or clindamycin. According to the CDC, the recommended VVC treatment involves using vaginal clotrimazole or oral antifungal drugs like fluconazole, usually given as a single 150 mg dose. These medications are effective in combating the fungal overgrowth that causes VVC. For BV, the CDC advises using oral or vaginal antibiotics, for example metronidazole or clindamycin. These antibiotics help to eliminate the

bacteria responsible for BV and restore a healthy balance in the vaginal flora [6, 7].

Non-specific vaginitis is typically treated with oral metronidazole and vaginal clotrimazole. However, despite their effectiveness in the short term, these treatments have limited success in preventing recurrent infections, with a minimum of fifty per cent of the participants over a lengthy period experiencing recurrence [8]. In recent years, various alternative treatments, including the use of antiseptics, have been suggested for the management of vaginitis. Antiseptics have a long history of use in treating vaginal infections, dating back to the previous period. Analogous towards antibiotics, antiseptics work by eliminating vaginal anaerobic bacteria associated with these infections, facilitating the restoration of endogenous lactobacilli. Antiseptics typically exhibit a broad spectrum of activity, acting concluded the cell wall annihilation mechanism, effectively eradicating bacteria. Notably, there have been a few antiseptic obstructions, further emphasising their therapeutic potential [9].

This investigation aimed to assess the efficiency of combination treatments in managing vaginal candidiasis (VVC), bacterial vaginosis (BV), and non-specific vaginitis. The investigation aimed to evaluate the efficacy of combining different treatment modalities to improve outcomes in these conditions.

Materials and Methods

Research design

This present prospective study was conducted for a year on 60 patients. Patients with complaints of vaginal discharge were sought out from a university gynaecological clinic for this clinical investigation. Using convenience sampling, 60 patients were divided into 2 groups - Oral metronidazole group and a combination group. The oral metronidazole group received the oral metronidazole at 250 mg twice daily for

five days. At the same time, the combination group received Chlorhexidine vaginal gel, Clotrimazole vaginal gel, and Oral metronidazole. Each subset underwent a diagnostic evaluation. Vaginal candidiasis was diagnosed when symptoms, vaginal pH, fungal components, and a negative Whiff test pointed to the condition. Gynaecological exams, vaginal pH, the Amsel criteria, and clue cells were used to confirm the presence of BV. Patients with vaginitis who did not fit the diagnostic criteria for VVC or BV were classified as having non-specific vaginitis.

Inclusion and exclusion criteria

Inclusion

- Gynaecology patients who are female and seeking care at a university clinic.
- Vaginal bleeding complaints.
- Adult patients are those over the age of 18.
- Participation in the study and the ability to give informed consent.

Exclusion

- Patients that are male or younger than 18 years old.
- Individuals who have already had an adverse reaction to one or more study drugs or components.
- Chronic or severe systemic disease patients may have an impact on the results of the investigation.
- Pregnant women and nursing mothers.
- Patients who have taken an antibacterial or antifungal medicine in the preceding two weeks.
- Patients are suffering from multiple STIs or genital infections at the same time.
- Patients with recent pelvic surgery or a history of "pelvic inflammatory disease (PID)".
- Immunocompromised patients and those on immunosuppressants.

Statistical analyses

The data were analysed using SPSS 19.0. Levene's test and independent-samples t-test was used to investigate quantitative data. Ordinal data were analysed using Mann-Whitney U, Chi-square or Fisher's exact tests for qualitative data. 0.05 was chosen for significance. The vaginitis groups were analysed individually using a stratified approach.

Ethical approval

Each patient was explained the study process and the consent was obtained. The Ethical Committee of the concerned hospital has approved the study process.

Results

Table 1 presents the frequency distribution of side effects and improvement of symptoms in three groups: vulvovaginal candidiasis, bacterial vaginosis, and non-specific vaginitis. The table includes the number of participants (N) for each group and the comparison of side effects and symptom improvement between oral metronidazole and combination therapy. In the vulvovaginal candidiasis group, out of the 30 participants, none reported vaginal burning as a side effect in the oral metronidazole group. In comparison, five participants (16.67%) experienced it in the combination therapy group. The p-value for this comparison is 0.095, suggesting no statistically significant difference in vaginal burning between the two treatment options. Two participants (6.67%) in the oral metronidazole group reported nausea, while three (10%) experienced it in the combination therapy group, with a p-value of 0.085. There were no cases of vomiting reported in either group. Both groups had one participant (3.33%) with cutaneous lesions.

Regarding symptom improvement, 15 participants (50%) in the oral metronidazole group reported improvement, while a higher proportion of 29 participants (96.67%) experienced

improvement in the combination therapy group. The p-value for this comparison is 0.012, indicating a statistically significant difference in symptom improvement between the two treatment options. For the bacterial vaginosis group, no participants reported vaginal burning in the oral metronidazole group, whereas three participants (10%) experienced it in the combination therapy group. The p-value for this comparison is 0.095, suggesting no statistically significant difference. One participant (3.3%) in the oral metronidazole group and two (6.67%) in the combination therapy group reported nausea, with a p-value of 0.085.

Similarly, one participant (3.3%) in the oral metronidazole group and two participants (6.67%) in the combination therapy group reported vomiting, with a p-value of 0.099. Cutaneous lesions were not reported in the oral metronidazole group, while three participants (10%) experienced them in the combination therapy group, resulting in a p-value of 0.087. In terms of symptom improvement, 18 participants (60%) in the oral metronidazole group reported improvement, while a higher proportion of 30 participants (100%) experienced improvement in the combination therapy group. The p-value for this comparison is 0.041, indicating a statistically significant difference in symptom improvement between the two treatment options. In the non-specific vaginitis group, three participants (10%) in the oral metronidazole group and six participants (20%) in the combination therapy group reported vaginal burning, resulting in a p-value of 0.085. Two participants (6.67%) in the oral metronidazole group and one participant (3.3%) in the combination therapy group reported nausea, with a p-value of 0.074. Vomiting was reported by three participants (10%) in both the oral metronidazole and combination therapy groups, resulting in a p-value of 0.095. One participant (3.33%) in the oral

metronidazole group and three participants (10%) in the combination therapy group reported cutaneous lesions, with a p-value of 0.077. In terms of symptom improvement, 20 participants (66.67%) in the oral metronidazole group reported improvement, while a higher proportion of

30 participants (100%) experienced improvement in the combination therapy group. The p-value for this comparison is 0.026, indicating a statistically significant difference in improvement of non-specific vaginitis between the two groups.

Table 1: The frequency distribution of side effects and improvement of symptoms in the vulvovaginal candidiasis, bacterial vaginosis, and non-specific vaginitis groups

Groups	Side effects	Oral metronidazole N=30	Combination therapy N=30	P-value
Vulvovaginal candidiasis (N=30)	Vaginal burning	0(0)	5(16.67)	0.095
	Nausea	2(6.67)	3(10)	0.085
	Vomiting	0(0)	0(0)	0
	Cutaneous lesions	1(3.33)	1(3.33)	0.096
	Improvement	15(50)	29(96.67)	0.012
Bacterial vaginosis (N=30)	Vaginal burning	0.00	3(10)	0.095
	Nausea	1 (3.3)	2(6.67)	0.085
	Vomiting	1 (3.3)	2(6.67)	0.099
	Cutaneous lesions	0	3(10)	0.087
	Improvement	18 (60)	30 (100)	0.041
Non-specific vaginitis (N=30)	Vaginal burning	3(10)	6 (20)	0.085
	Nausea	2(6.67)	1 (3.3)	0.074
	Vomiting	3(10)	3(10)	0.095
	Cutaneous lesions	1(3.33)	3(10)	0.077
	Improvement	20 (66.67)	30 (100)	0.026

The table presents the mean satisfaction scores obtained using a visual analogue scale for different groups and treatment options. The groups under consideration are vulvovaginal candidiasis, bacterial vaginosis, and non-specific vaginitis. The first treatment option is oral metronidazole, while the second is a combination therapy. The table provides the mean scores and standard deviations (SD) for each group and treatment combination. For vulvovaginal candidiasis, the mean satisfaction score for the oral metronidazole group is 6.9, with a standard deviation of 1.4.

In contrast, the combination therapy group has a higher mean satisfaction score of 9.6, with a lower standard deviation of 0.6. The p-value of this comparison is 0.036, suggesting a statistically significant difference in satisfaction between the two treatment options. Moving on to bacterial vaginosis, the mean satisfaction score for the oral metronidazole group is 7.2, with a standard deviation of 1.1. The combination therapy group, on the other hand, has a higher mean satisfaction score of 9.4, with a lower standard deviation of 0.3. The p-value for this comparison is 0.041,

indicating a statistically significant difference in satisfaction between the two treatment options. Lastly, the mean satisfaction score for non-specific vaginitis for the oral metronidazole group is 7.1, with a standard deviation of 1.2. The combination therapy group has a slightly higher mean satisfaction score of 9.3, with a standard deviation 0.5. The p-value of this comparison is 0.036, suggesting a statistically significant difference in

satisfaction between the two treatment options. Table 2 shows that combination therapy consistently yields higher mean satisfaction scores than oral metronidazole in all three groups of vulvovaginal candidiasis, bacterial vaginosis, and non-specific vaginitis. The p-values associated with the comparisons indicate that these differences in satisfaction are statistically significant.

Table 2: Mean satisfaction scores based on the visual analogue scale

Groups	Oral metronidazole		Combination therapy		p-value
	Mean	SD	Mean	SD	
Vulvovaginal candidiasis	6.9	1.4	9.6	0.6	0.036
Bacterial vaginosis	7.2	1.1	9.4	0.3	0.041
Non-specific vaginitis	7.1	1.2	9.3	0.5	0.036

Discussion

Mirzaeei et al. (2021) conducted a study to examine the effectiveness of vaginal chlorhexidine gel in managing vulvovaginal candidiasis, bacterial vaginosis, and general vaginitis. The investigation involved individuals who visited the University Gynecology Clinic with complaints of vaginal discharge. The investigators used the Statistical Package for the Social Sciences (SPSS) software to analyse the results. The average patient satisfaction rating among those with vulvovaginal candidiasis was 9.06 for chlorhexidine vaginal gel and 8.29 for clotrimazole vaginal cream. The mean visual analogue scale (VAS) ratings among these two categories did not show a difference of statistical significance according to the Mann-Whitney test ($P=0.027$). The average patient satisfaction rating for those with bacterial vaginosis was 8.91 for the chlorhexidine vaginal gel category and 8.72 for the metronidazole pill group ($P=0.607$). The combined class (metronidazole + clotrimazole vaginal cream) had a mean satisfaction score of 9.17, compared to 8.83 for the chlorhexidine vaginal gel group in the non-specific vaginitis group ($P=0.401$).

Notably, the combination therapy group had the highest mean VAS score. The study's results indicate that chlorhexidine vaginal gel is an efficient treatment for vaginal infections. It shows favorable therapeutic outcomes when used alone in non-specific vaginitis, eliminating the necessity for concurrent administration of two medications [16,17].

The study revealed that patients who were treated with chlorhexidine vaginal gel exhibited the highest levels of recovery and satisfaction compared to other treatment groups, such as that receiving clotrimazole vaginal gel, oral metronidazole, in addition to combined remedies involving oral metronidazole and clotrimazole vaginal gel. Notably, chlorhexidine gel did not result in side effects apart from vaginal burning. This finding suggests that chlorhexidine vaginal gel may be a well-tolerated and effective treatment option for vaginal infections, with a favorable side effect profile compared to other treatment modalities [16].

In line with earlier research [17, 18], we found no discernible differences in average age between the three categories during our investigation, that also reported similar

findings regarding age. Additionally, there were no discernible differences within the chlorhexidine gel as well as clotrimazole cream categories when it came to cheese-like discharge, vulvar burning, negative Whiff test results, and the existence of fungal components beneath microscopy, which are diagnostic indicators for vulvovaginal candidiasis (VVC). Similarly to this, there were not any statistically significant variations in the criteria for diagnosis of bacterial vaginosis (BV) amongst the groups receiving chlorhexidine vaginal gel as well as oral metronidazole, which includes the Whiff test, Nitrazine test, and the presence of foul-smelling discharges. These findings are consistent with earlier research [19, 20] that classified the BV type. In addition, several investigations have shown a link between the clinical signs and the symptoms of vaginal discharge in patients, demonstrating that women who suffer changes in discharge can precisely characterise its features [21].

According to the study's findings, individuals who received chlorhexidine vaginal gel treatment for vulvovaginal candidiasis (VVC) had no side effects like nausea and vomiting. Three individuals experienced a burning feeling, and only one occurrence of cutaneous lesions was seen. A significant number of participants improved, and this category's level of satisfaction was higher than it was for the patients who had clotrimazole vaginal cream. Prior research noted a remarkable response rate to clotrimazole vaginal pills in 97 of 99 individuals with candidal vaginitis [22]. Other studies have recommended various antifungal agents, including triazoles (fluconazole, terconazole) and imidazoles (clotrimazole, miconazole, itraconazole, ketoconazole), as well as nystatin for treating candidal vaginitis [23]. In a study by Banaeian et al., the impact of clotrimazole and honey gel was examined in two groups of vaginally infected women [24]. According

to the authors' research, the clotrimazole group showed a considerable reduction in vaginal production and inflammation, although neither group experienced any side effects. While previous studies have reported symptom improvement with clotrimazole treatment, our study found that chlorhexidine vaginal gel had a superior effect. This finding emphasises chlorhexidine's potential significance in managing vaginal infections.

Based on the positive outcomes observed in this study, we suggest that researchers explore the inclusion of chlorhexidine vaginal gel as a potential standard healing option. Conducting more comprehensive studies would further enhance the accuracy and reliability of the findings. Comparing chlorhexidine vaginal gel to combined treatment, the clinical results of addressing vaginal infections with chlorhexidine vaginal gel, clotrimazole, oral metronidazole, as well as combined treatment show that chlorhexidine vaginal gel, used alone, is the best option for dealing with vulvovaginal candidiasis, bacterial vaginosis, and non-specific vaginitis.

Conclusion

The study has concluded that combination therapy significantly improved vaginitis than a mono-therapy of metronidazole. Chlorhexidine vaginal gel was more effective as a stand-alone treatment for vulvovaginal candidiasis, bacterial vaginosis, and non-specific vaginitis than clotrimazole, oral metronidazole, or combination therapy. Positive clinical effects were seen with vaginal chlorhexidine gel compared to combination therapy. These results support chlorhexidine vaginal gel as a viable treatment choice for these vaginal infections, suggesting that this care method may be more effective, straightforward, and convenient than others. More research and larger-scale trials may be needed to confirm these

findings and thoroughly investigate the potential of chlorhexidine vaginal gel as a solo treatment. Using a convenience sample may introduce selection bias and prevent expanding the study's results to the total population. Women who sought treatment at a single university's gynaecology clinic were included in the study, which may not be representative of the population. The results may also not be transferable to other topical or systemic therapy for vaginal infections, as the study only compared chlorhexidine vaginal gel to other treatments. Additional study is needed to confirm these results and thoroughly investigate chlorhexidine's potential in treating vaginal infections, including more significant and diverse populations.

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