ORIGINAL ARTICLE

Povidone Iodine Swabbing as A New Treatment Approach in Recurrent Vulvovaginal Candidiasis

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Abstract

Objectives: ***This study aims to evaluate the effectiveness of povidone-iodine as a therapeutic intervention for recurrent vulvovaginal candidiasis (RVVC).***

Methods: ***This prospective comparative study was conducted at the gynaecological outpatient clinic of Al-Azhar University Hospital in Damietta. The research involved adult females of reproductive age who presented symptoms consistent with acute episodes of RVVC, which were confirmed through culture analysis of vaginal discharge. A total of 162 women participated, divided into two groups of 81 patients each. Group one received antifungal medications, while group two was treated with a combination of vaginal swabbing using povidone-iodine and antifungal medications. A follow-up assessment was performed after three months to determine the efficacy of the treatments, focusing on rates of remission and recurrence.***

Results: ***In the antifungal treatment group, 17.2% of patients did not achieve remission, whereas only 6.1% of those receiving the combined antifungal and vaginal betadine treatment failed to reach remission. In terms of complete remission, 44.4% of patients in the antifungal group achieved this outcome, which is considerably lower than the 70.3% observed in the combined antifungal and vaginal betadine group. Recurrence rate was higher among patients in the antifungal group, with rates of 20.9% compared to 8.6% in the other group.***

Conclusion: ***Povidone-iodine represents an effective and efficient strategy in managing RVVC, demonstrating a lower recurrence rate and a higher rate of complete symptom resolution compared to conventional antifungal therapies, while also addressing the issue of resistance to antifungal agents.***

Keywords: Recurrent vulvovaginal candidiasis; Fluconazole; Povidone-Iodine

1. Introduction

Vulvovaginal candidiasis (VVC) ranks as the second most prevalent vaginal infection, marked by inflammation of the vulvar and vaginal epithelium. It impacts 75–80% of women at least once during their lifetime, predominantly occurring during their reproductive years. Recurrent vulvovaginal candidiasis (RVVC) is characterized by three or more symptomatic acute episodes of VVC occurring within 12 months.[1]

Candida albicans has been identified as the causative agent in 85% to 95% of cases of VVC. While it is estimated that only 9% of women with VVC experience RVVC, a comprehensive systematic review conducted in 2018 projected the global annual prevalence of RVVC to be approximately 138 million women. This figure is anticipated to rise to nearly 158 million women by the year 2030.[2]

The clinical presentation of vaginal candidiasis is characterized by irritation, itching, and burning sensations in the vaginal and vulvar areas. These symptoms frequently intensify in the days leading up to menstruation. During a pelvic examination, typical observations may include erythema of the vulva and vagina, excoriations, a thick white discharge that adheres to the vaginal walls, and swelling. It is important to note that some individuals may exhibit minimal to no discharge. In cases of candidal vulvovaginitis, signs of inflammation are usually apparent upon examination; however, the cervix generally appears normal and is not inflamed.[3]

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Vulvovaginal candidiasis is recognized as a multifactorial condition, influenced by an imbalance in the vaginal microbiota, various host predisposing factors, genetic predispositions, and the presence of specific Candida strains, all of which may contribute to the development of the disease. In many women, Candida exists as a commensal organism within the vaginal environment, having migrated from the lower gastrointestinal tract. This colonization can persist in a balanced and asymptomatic state for extended periods. However, an overgrowth of Candida can lead to the onset of symptomatic infection.[2]

The proliferation of Candida within the vaginal epithelium may be affected by various behavioural factors, including sexual intercourse, the utilization of sponges or intrauterine devices, and the administration of oral contraceptives or hormone replacement therapies. Additionally, changes in health conditions and immune defences, such as those seen in type 1 diabetes and HIV, have been identified as possible contributing elements. Notably, in around 20% to 30% of women, no identifiable predisposing factors are present.[4]

Fluconazole is a widely utilized medication for the treatment of VVC. It is characterized by its affordability, favourable tolerability, and ease of oral administration, making it the most frequently prescribed antifungal agent. However, over the past ten years, instances of fluconazole resistance have been documented in women suffering from RVVC. Earlier epidemiological investigations indicated that nearly all women identified with fluconazole-resistant Candida albicans had a history of prior fluconazole exposure. Recent research has suggested that the resistance observed in these isolates may be associated with the overexpression of the CDR1 gene, which could be further influenced by the prescribing practices of healthcare providers regarding both treatment and prophylactic measures.[5]

Recurrence may also occur as a consequence of the development of resistance to antifungal therapies, which is often linked to the extended or repeated administration of a single antifungal agent. With the growing availability of over-the-counter (OTC) antifungal medications, certain strains of Candida that were once susceptible have developed resistance. Consequently, women infected with these resistant strains may struggle to attain symptom relief due to the restricted range of effective treatment options available for azole-resistant Candida species.[6]

Iodine povacrylex (PVP-I) has increasingly been utilized, particularly in patients suffering from RVVC. This chemical complex comprises 9–12% active iodine and exhibits a wide-ranging germicidal efficacy against both Gram-positive and Gram-negative bacteria, as well as viruses and fungi. Its availability and extensive application in clinical settings for skin disinfection, antisepsis, and the management of superficial infections are notable, especially given the absence of documented resistance. PVP-I is available in various forms, including topical antiseptic solutions, ointments, and vaginal suppositories.[7]

The mechanism by which it operates relies on the oxidation of amino acids. Research indicates that PVP-I facilitates the recovery of the natural microbiota following bacterial infections, particularly in instances of bacterial vaginosis, leading to a swift recolonization by native lactobacilli.[8]

The use of PVP-I appears to provide rapid relief from symptoms. In vitro studies have shown its fungicidal effects on Candida species, along with its efficacy against Trichomonas vaginalis and a range of other microorganisms. Furthermore, PVP-I has been recognized for its capacity to inhibit biofilm development. Although adverse reactions like allergic dermatitis are rare, pre-existing lesions or tissue damage may enhance the absorption of iodine into the bloodstream.[9]

This study determines the most rational application of antifungal medications for treating RVVC and identifies the optimal route of administration. A comparative evaluation of various treatment regimens facilitates the selection of the most effective option based on established safety and efficacy standards. This research further aids in evaluating a more economically viable and effective therapeutic strategy for both patients and the healthcare system. In cases where vaginal treatments demonstrate equal or greater efficacy than oral alternatives, they serve as the preferred choice, particularly for patients experiencing adverse effects from oral medications. Understanding the efficacy profiles of different drugs in managing RVVC supports the development of a treatment protocol that reduces the likelihood of heightened antifungal resistance. Hence, the objective is to explore the effectiveness of povidone-iodine as a therapeutic intervention for recurrent vulvovaginal candidiasis, as well as to monitor any instances of recurrence during the follow-up period.

2. Patients and methods

Study design, setting and duration: This prospective comparative study was carried out at the gynecological outpatient clinic of Al-Azhar University Hospital in Damietta, spanning the period from December 2024 to March 2025.

Study population: The study included adult

females of reproductive age, specifically those between 18 and 40 years old, who exhibited symptoms indicative of acute episodes of recurrent vulvovaginal candidiasis, as confirmed by culture analysis of vaginal discharge. Exclusion criteria encompassed pregnant and lactating women, virgins, and individuals with immunodeficiency disorders, such as diabetes mellitus.

Sample size: The sample size was determined utilizing Epi Info STATCAL, taking into account a 95% confidence level, an 80% power, and a 1:1 ratio of exposed to non-exposed individuals. This calculation was informed by the cure rate of vulvovaginitis as reported by Ebrahimy et al.[10] Consequently, the minimum required sample size was established at 81 participants for each group.

Data collection procedure and treatment protocol: A total of 162 women participated in the study, divided into two groups of 81 patients each, based on the sample size rationale.

Group 1: Treated with antifungal medications.

Group 2: Treated with a combination of vaginal swabbing with povidone-iodine and antifungal medications.

Following the acquisition of informed consent, a detailed medical history was obtained from each participant, accompanied by a comprehensive physical examination and a focused vaginal assessment. The local clinical evaluation was conducted with the patient in the lithotomy position to identify erythema, edema, or other clinical signs. A speculum examination was performed for enhanced visualization of the vulva and vagina. All vaginal secretions were systematically assessed based on color, odor, and consistency. The speculum was inserted laterally with the blades closed, angled downward and backward, while the labia were separated using the left hand. The blades were then gently opened to achieve a clear view of the cervix. Secretions were meticulously removed using sterile gauze, and the vaginal area, along with the fornices, was swabbed multiple times with cotton swabs soaked in 10% povidone-iodine until all discharge was eliminated. The procedure concluded with the removal of the speculum.

Treatment Regimens

Group 1: Fluconazole Treatment

Initial treatment: Fluconazole was administered topically for 7 to 14 days, along with an oral dose of 150 mg on days 1, 4, and 7 (three doses in total).

Maintenance therapy: A weekly oral dose of 150 mg fluconazole was administered for three months.

Group 2: Combination of Povidone-Iodine and Fluconazole

Initial treatment: Vaginal swabbing with povidone-iodine was performed twice a week for one month, in conjunction with an oral dose of 150 mg fluconazole on days 1, 4, and 7 (three doses in total).

Maintenance therapy: A weekly oral dose of 150 mg fluconazole was administered for three months.

Follow-Up and Outcome Assessment

A follow-up evaluation was conducted after three months to assess treatment efficacy. The remission rate was determined by calculating the proportion of clinically improved women relative to the total number of patients in each treatment group. Additionally, the recurrence rate was evaluated by identifying patients who exhibited recurrent symptoms and had a positive culture of vaginal discharge during the follow-up period.

Statistical Analysis: Descriptive statistics, including means and standard deviations (SD) for continuous variables and frequencies (n) and percentages (%) for categorical variables, were calculated to summarize the data. Independent t-tests were used for continuous variables to compare means between treatment groups, while one-way ANOVA assessed differences across remission categories. For categorical variables, chi-square (x^2) tests were performed to determine associations between treatment groups, various demographic and clinical characteristics, and remission outcomes. In cases where expected frequencies were low, Fisher's Exact Test or the Monte Carlo test was used as an alternative to the chi-square test. The significance of differences was evaluated using p-values, with a threshold of $p<0.05$ considered statistically significant. All statistical analyses were conducted using SPSS version 27 software.

Ethical considerations: The research protocol received approval from the Institutional Review Board (IRB) of Damietta Faculty of Medicine, Al-Azhar University (IRB NUMBER: 0012367-24-12-009). Informed consent was obtained from each participant, and the study was conducted in accordance with the ethical guidelines outlined in the Declaration of Helsinki for research conduct and reporting.

3. Results

General characteristics and medical history of female patients:

In this study , we categorized female patients diagnosed with vulvovaginitis into two distinct groups: one group received antifungal therapy (N=81), while the other group was administered a combination of antifungal and vaginal betadine treatment (N=81). The demographic evaluation indicated that there were no statistically significant differences between the two groups in terms of age, place of residence, or marital status, (p-values > 0.05), (Table 1).

The analysis of the participants' medical history revealed that the parity status did not show a statistically significant difference between the two groups (p-values > 0.05). In contrast, a significant difference was noted in contraceptive use (p<0.05), suggesting that a greater percentage of patients in the combined treatment group either did not use contraceptives or were currently lactating, compared to those in the antifungal group, (Table 2).

Remission of vulvovaginitis among the studied female patients:

The findings related to the remission of vulvovaginitis in the female patients examined reveal notable differences between the two treatment groups (p<0.05). In the antifungal treatment group, 17.2 % of patients did not achieve remission, whereas only 6.1 % of those receiving the combined antifungal and vaginal betadine treatment failed to reach remission. Furthermore, 38.2% of patients in the antifungal group experienced partial remission, a figure significantly higher than the 23.4% seen in the combined treatment group. In terms of complete remission, 44.4% of patients in the antifungal group achieved this outcome, which is considerably lower than the 70.3% observed in the combined antifungal and vaginal betadine group. Additionally, when examining the culture of vaginal discharge, 24.7% of patients in the antifungal group tested positive, compared to just 11.1% in the combined treatment group. It is also noteworthy that the recurrence rate was higher among patients in the antifungal group, with rates of 20.9% compared to 8.6% in the other group (Table 3).

The relationship between the remission status of vulvovaginitis and medical histories of the studied female patients:

Regarding the evaluation of the relation between medical history, which encompasses parity and contraceptive methods and remission status, there were no statistically significant differences (p-values >0.05), (Table 4).

Table 1. General characteristics of the studied female patients

VARIABLE	LABEL	ANTIFUNGAL GROUP (N=81)	COMBINED ANTIFUNGAL AND VAGINAL BETADINE GROUP (N=81)	SIGNIFICANCE TESTS AND P-VALUES
AGE	Mean±SD	31.12±5.76	31.40±6.59	t=0.27 p=0.781
RESIDENCE	Urban n(%)	22 (27.2)	18 (22.2)	x^2=0.53 p=0.585
	Rural n(%)	59 (72.8)	63 (77.8)	
MARITAL STATUS				
	Married	75 (93.8)	76 (92.5)	Fisher Exact=0.30 p=1.00
	Widow	4 (5.0)	4 (5.0)	
DIVORCED				
1 (1.3)	2 (2.6)			
BMI KG/M^2				
MEAN±SD	25.81±3.50	26.01±3.26	t=0.37 p=0.711	

BMI: Body mass index. SD: Standard deviation

Table 2. Medical history of the studied female patients

VARIABLE	LABEL	ANTIFUNGAL GROUP (N=81)	COMBINED ANTIFUNGAL AND VAGINAL BETADINE GROUP (N=81)	SIGNIFICANCE TESTS AND P-VALUES
PARITY	Nulli-para	2 (2.5)	2 (2.5)	Fisher Exact=0.28
	Uni-para	16 (19.8)	18 (22.2)	p=0.942
	Multi-para	63 (77.8)	61 (75.3)	
PARITY NUMBER	Mean±SD	2.11±0.86	2.12±3.26	t=0.09 p=0.929
CONTRACEPTIVE USE	No/Lactating	25 (30.9)	42 (51.9)	x^2=8.24
	IUD	26 (32.1)	22 (27.2)	p=0.016*
	Hormonal	30 (37.0)	17 21.0)	

*Statistically significant (p<0.05). SD: Standard deviation. IUD: Intrauterine device.

Table 3. Clinical improvement of vulvovaginitis, recurrence rate and the result of culture for vaginal discharge among the studied female patients

VARIABLE	LABEL	ANTIFUNGAL GROUP (N=81) N (%)	COMBINED ANTIFUNGAL AND VAGINAL BETADINE GROUP (N=81) N (%)	SIGNIFICANCE TESTS AND P-VALUES
REMISSION	Not improved	14 (17.2%)	5 (6.1%)	
	Partially improved	31 (38.2 %)	19 (23.4 %)	x^2=27.29 p<0.001*
	Completely improved	36 (44.4%)	57 (70.3 %)	
CULTURE	Positive	20 (24.7%)	9 (11.1%)	x^2=8.57

	Negative	61 (75.3%)	72 (88.9%)	p<0.014*
RECURRENCE RATE	Recurrent	17 (20.9 %)	7 (8.6%)	x^2=20.8 p<0.001*
	Not recurrent	64 (79.1)	74 (91.4%)	

*Statistically significant (p<0.05).

Table 4. Comparison of remission of vulvovaginitis regarding medical history of the studied patients

VARIABLE	LABEL	NO REMISSION (N=19)	PARTIAL REMISSION (N=50)	COMPLETE REMISSION (N=93)	SIGNIFICANCE TESTS AND P-VALUES
PARITY NUMBER	Mean±SD	2.00±0.66	2.08±0.80	2.16±0.94	F=0.12 p=0.886
PARITY	Nulli-para	0 (0.0)	0 (0.0)	4 (4.3)	Monte Carlo
	Uni-para	4 (21.1)	14 (28.0)	16 (17.2)	p=0.281
	Multi-para				
15 (78.9)	36 (72.0)	73 (78.5)			
CONTRACEPTIVE USE	No/Lactating	7 (36.8)	20 (40.0)	34 (36.5)	x^2=0.59
	IUD	6 (31.6)	14 (28.0)	30 (32.2)	p=0.963
	HORMONAL#				
6 (31.6)	16 (32.0)	29 (31.1)			

SD: Standard deviation. IUD: Intrauterine device. #Hormonal includes Combined Oral Contraceptives (COC), Progestin-Only Pill (POP) and Depot Medroxyprogesterone Acetate (DMPA)

4. Discussion

Effective treatment of RVVC, with adequate control of symptoms and eradication of the fungus, represents a challenge in daily clinical practice. Many antifungal regimens are available for treatment, some of them with adverse effects that end up reducing women's adherence to treatment. The lack of clear criteria for the indication of available drugs and their free use due to self-medication by women has contributed to the increasing antifungal resistance found in some clinical trials. This study was performed to assess the efficacy of povidone iodine in the treatment of recurrent vulvovaginal candidiasis.[11]

We selected povidone iodine as it was easily available, chemically stable, and inexpensive, and its resistance to bacteria and fungi has yet to be reported. Excessive and indiscriminate use of any topical antibiotic and antimicrobials may lead to the emergence of resistant organisms. Povidone iodine overcomes this problem, as there are no studies to date showing the development of resistance, which is an increasing cause of concern in this era.[12]

In the present study, there was no statistically significant difference between the two studied groups in terms of sociodemographic and clinical characteristics (p > 0.05) and this was the same finding in the study of Zahra Mollazadeh, et al and Fardyazar, et al, where the demographic characteristics of Patients were of no significant difference between the studied groups.[13,14]

However, regarding the type of contraception used, the results in the current study were the same as those of Shaheen, Abd Elhamid, et al where there was a non-significant correlation between the method of contraception and prevalence of candida infection and we found that the prevalence of candidal infection between the studied groups was more in patients who didn't take any contraception either before treatment or after follow up period followed by IUCD user than those with hormonal contraception.[15]

But these results were in disagreement with Yusuf et al, who found that, among the types of contraception used, the highest prevalence of vaginal infections by Candida species was found in oral contraceptive pill users, followed by injectable and IUCD users. They explained such results, claiming that contraception containing estrogen and progesterone increases glycogen that is converted to lactic acid, so overgrowth of Candida occurs owing to decreased PH .[16]

In the study of Zahra Mollazadeh et al, probiotics were less effective than fluconazole in improving and preventing the recurrence of discharge and vulvovaginal erythema. This was such that in the probiotic group, only six persons (16.7%) and in the fluconazole group, only one person (2.8%) complained of severe discharge (p = 0.035). In the current study, the recurrence rate in the antifungal group was higher (20.9%) in comparison to (8.4%) in the group of combined treatment, and this indicated the effectiveness of adding povidone iodine to the treatment.[13]

Due to the differing follow-up period in the study by Li et al., the clinical cure rate for the

two-dose regimen of 150 mg fluconazole was 56.1% during the follow-up on days 30–35. This finding contrasts with the results of the current study, which showed a fluconazole cure rate of 44.4% after a follow-up of three months.[17]

In addition, Carriero et al came up with a result similar to the current study, showing that the proportion of symptoms improvement in the group receiving Lactiplantibacillus plantarum after fluconazole treatment was higher than that in the group getting fluconazole alone (90% versus 67.5%, p<0.03) and in the present study the clinical improvement in the antifungal group in comparison to the combined group was 44.4 % versus 70.3%.[18]

In the research conducted by Hacioglu et al, a swift reduction in viable fungal counts was observed following treatment with PVP-I, with no significant difference noted between Candida albicans and non-albicans species. In contrast, the efficacy of boric acid and NCT was markedly slower ($p < 0.01$). These findings align with the current study, which reported a positive culture rate of 27.4% for vaginal discharge in the antifungal group after a three-month follow-up, compared to only 11% in the group receiving a combination of povidone iodine and antifungal treatment.[19])

4. Conclusion

The introduction of povidone-iodine as a novel therapeutic approach to RVVC has demonstrated promising efficacy, with a lower recurrence rate and a higher rate of complete symptom resolution compared to conventional antifungal treatments. Additionally, this strategy has the potential to reduce the financial burden on patients while addressing the growing concern of antifungal resistance. Further research is warranted to explore optimal dosing regimens, treatment duration, and long-term follow-up to accurately assess recurrence rates and ensure sustained therapeutic efficacy.

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