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RESEARCH ARTICLE

The Efficacy of Dequalinium Chloride Against Vulvovaginitis in Pregnancy

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Abstract

Introduction*: Vulvovaginitis affects pregnancy outcomes and managing it involves the use of metronidazole or nystatin, which can cause local or systemic side effects. Dequalinium chloride (DQC) is suggested as a new treatment option for vulvovaginitis during pregnancy with minimal side effects.*
Objective*: To compare the effectiveness of dequalinium chloride (DQC) versus metronidazole + nystatin (MN) in treating vulvovaginitis in pregnant women during their second and third trimesters.*
Method*: A single-blind randomized controlled trial was conducted at the Andalas Public Health Center, Padang, from January to May 2024. Pregnant women in their second and third trimesters, meeting the inclusion and exclusion criteria, were enrolled. The participants were randomly assigned to either the DQC or MN group. Vaginal swabs were taken before and after a 6-day treatment, and PCR analysis was performed.*
Results*: Eighteen patients were treated with DQC and MN. Most participants had bacterial vaginosis (DQC 78%, MN 83%), with half having candidiasis (DQC and MN 50%) and fewer cases of trichomoniasis (28% in both groups). Significant improvements were seen in the DQC group for symptoms (p=0.000), Gardnerella vaginalis (p=0.035), and Candida albicans (p=0.021). In the MN group, significant improvements were noted for symptoms (p=0.000) and Gardnerella vaginalis (p=0.002). No significant differences were observed between the groups for symptom resolution or microbial reduction.*
Conclusion*: DQC is as effective as metronidazole + nystatin in treating bacterial vaginosis and candidiasis in pregnancy.*

Keywords: *Vulvovaginitis, pregnancy, dequalinium chloride, metronidazole, nystatin*

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INTRODUCTION

Vulvovaginitis, a common gynecological condition, occurs when the stability of the vaginal flora is disrupted. Vaginitis, defined as inflammation of the vagina, is associated with various complications such as preterm labor, urinary tract infections, and pelvic inflammatory disease. It has been recognized as a highly prevalent medical issue requiring specialized care from healthcare providers.[1,2] The most frequent causes of vaginitis include bacterial vaginosis (22%–50% of symptomatic women), vulvovaginal candidiasis (17%–39%), and trichomoniasis (4%–35%).[3]

A study by Vegunopal et al. (2017), which evaluated the overall incidence of vulvovaginitis, found a prevalence of 77%, with microbiological causes attributed to bacterial vaginosis in 27%, trichomoniasis in 25%, vulvovaginal candidiasis in 22%, mixed infections (Candida and BV) in 3%, and nonspecific cases in 23%.[4] Bacterial vaginosis (BV) is a common vaginal dysbiosis among women of reproductive age, with a global prevalence ranging from 23% to 29% across regions (Europe and Central Asia, 23%; East Asia and the Pacific, 24%; Latin America and the Caribbean, 24%; the Middle East and North Africa, 25%; Sub-Saharan Africa, 25%; North America, 27%; South Asia, 29%).[5,6] Vulvovaginal candidiasis (VVC) affects nearly 75% of women, with 40%-45% experiencing two or more episodes, and approximately 10%-20% of women developing complicated VVC.[7,8] For trichomonas vaginalis, the World Health Organization (WHO) estimated 156 million cases globally in 2016, accounting for nearly half of all sexually transmitted infections that year.[9]

Research on the incidence of vulvovaginitis in West Sumatra, particularly in Padang City, is scarce, and epidemiological data on this condition is limited. A 2020 study by Febria found that 93.6% of women included in the study experienced vaginal discharge, with a high prevalence linked to a lack of knowledge.[10] Vulvovaginitis frequently affects women of childbearing age and often requires medical management. In pregnant women, the incidence is higher, affecting half of all pregnant women.[11] A study by Shawaky et al. (2022) on vulvovaginitis patients revealed that 310 (60.1%) were pregnant, while 206 (39.9%) were not, with BV diagnosed in 59.1% and VVC in 50.2% of the population. Mixed infections were present in 24% of women, with the most common combination being BV and Candida spp., detected in 21% of cases.[12] A study by Sobel et al. (2011) on coinfections in vulvovaginitis reported that 20%-30% of women with BV had coinfection with Candida species, and the coexistence of BV pathogens and T. vaginalis was even more frequent, with coinfection rates of 60%-80%. Coinfections and mixed vaginitis have significant clinical and therapeutic implications.[13]

The clinical impact of vulvovaginitis during pregnancy is serious, as bacterial vaginosis is associated with chorioamnionitis, postpartum endometritis, postoperative infections, pelvic inflammatory disease, preterm delivery (9-fold increased risk), and PPROM (7.3-fold increased risk).[11,14,15] A study by Khaskheli et al. (2021) involving 85 pregnant women with gestational ages of 28-35 weeks found that 89% of respondents experienced vaginal discharge symptoms, with 69.7% confirmed to have vaginal infections. The study reported 39.6% BV, 32.1% vaginal candidiasis, and 28.3% trichomoniasis. Furthermore, pathological vaginal discharge during pregnancy was linked to increased uterine contractions, premature rupture of membranes, miscarriage, preterm birth, and

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postpartum endometritis, with risks for the newborn, including low birth weight, low APGAR scores, neonatal respiratory distress syndrome, and neonatal death.[16] A 2022 study by Li et al. reported that 3.9% of pregnant women experienced mixed vaginitis in the third trimester, associated with an increased risk of peripartum infections.[17]

Management of vulvovaginitis is based on the causative microorganism. Bacterial vaginosis can be treated with metronidazole or clindamycin, vulvovaginal candidiasis with clotrimazole or nystatin, and trichomoniasis with metronidazole. Pregnant women with vulvovaginitis can also be treated with metronidazole and nystatin ovules, considering the high incidence of mixed infections during pregnancy.[18-21] However, research has shown that this treatment approach often results in high recurrence rates.[22]

Bradshaw et al. (2016) reported that the risk of vulvovaginitis recurrence within 6-12 months after first-line therapy is as high as 50%.[22] Verwijs et al. (2020) noted that only 16.4% of respondents experienced a reduction in anaerobic bacterial concentrations after being treated with metronidazole for vulvovaginitis. The study indicated that the high abundance of Gardnerella vaginalis is associated with increased treatment failure.[23] A 2023 study by Qulu et al. on the high recurrence rate of vulvovaginitis following metronidazole therapy suggested that continuous use of metronidazole for recurrent cases is associated with increased expression of activated T-cells and dendritic cells, which heightens susceptibility to HIV.[24] Furthermore, a 2021 study by Ajiji et al. found that metronidazole use during the first trimester increases the risk of spontaneous abortion by 1.72 times and the occurrence of severe malformations by 1.15 times, with a specific risk of congenital hydrocephalus being 4.06 times higher.[25]

Nystatin is chosen as a safe treatment for vaginal candidiasis during pregnancy, with fewer side effects. However, this therapy is less effective in treating vaginal candidiasis than azole antifungal agents, leading to a higher risk of recurrence.[26,27] Schalwyk et al. (2015) stated that current therapies for vulvovaginitis during pregnancy have only moderate success rates, with high recurrence rates.[28]

Currently, a novel treatment regimen, dequalinium chloride (DQC), has emerged for vulvovaginitis during pregnancy. This therapy has minimal side effects and considerable efficacy. Furthermore, it offers the advantage of being used during the first trimester of pregnancy. One of the benefits highlighted in several studies is that this drug can treat vulvovaginitis caused by various microorganisms, including anaerobic bacteria, aerobic Gram-positive and Gram-negative bacteria, and fungi, making it a more efficient treatment option.[29,30]

A study by Indarti et al. (2022) at Cipto Mangunkusumo Hospital compared the efficacy of DQC with metronidazole as a control. The study found that the cure rate in the DQC group was 94.12%, concluding that dequalinium chloride is a safe and effective alternative to metronidazole in treating bacterial vaginosis.[31] Additionally, a study by Mendling et al. (2016) reported very low systemic absorption of dequalinium chloride (DQC) after intravaginal administration, with clinical efficacy comparable to clindamycin in the treatment of bacterial vaginosis. Its broad-spectrum antimicrobial activity makes it suitable for treating mixed vaginal infections and cases with uncertain

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diagnoses. Moreover, pathogen resistance is unlikely due to its multiple mechanisms of action, and vaginal DQC also reduces the risk of post-treatment vaginal infections.[32] A 2019 study by Hijona et al. involving 163 women with positive Streptococcus group B cultures found that 76.12% had negative culture results after DQC administration. The study concluded that administering one 10 mg vaginal tablet of DQC the day before induction reduced the number of women colonized by Streptococcus group B without causing maternal or perinatal side effects.[33]

In 2022, Puskesmas Andalas, located in Padang City, had the highest number of pregnant women, totaling 1,419. Puskesmas Andalas is the main healthcare facility serving Padang Timur District, covering seven subdistricts, including Sawahan, Jati Baru, Jati, Sawahan Timur, Simpang Haru, Andalas, and Ganting Parak Gadang.

Given the rising recurrence of vulvovaginitis after first-line therapy, as observed in several studies, this research aims to compare the effectiveness of dequalinium chloride versus metronidazole + nystatin in treating vulvovaginitis during the second and third trimesters of pregnancy at Puskesmas Andalas.

METHODS

This clinical trial aimed to compare the effectiveness of dequalinium chloride and metronidazole + nystatin in treating vulvovaginitis during the second and third trimesters of pregnancy. The study was conducted at Puskesmas Andalas, Padang, between January and May 2024, with sample analysis performed at the Laboratory of Diagnostic and Infectious Disease Research at Universitas Andalas.

The study population consisted of pregnant women in their second and third trimesters who were diagnosed with vulvovaginitis. A total sample size of 36 was determined, with 18 participants in each treatment group (dequalinium chloride and metronidazole + nystatin). Sampling was carried out using a single-blind randomized controlled trial method, where participants were unaware of their assigned treatment.

The independent variable was the treatment type, while the dependent variable was the effectiveness of the treatment. The research tools included specula and vaginal swabs, and data collection involved univariate and bivariate analysis. The chi-square test and McNemar test were used for categorical data, and paired/unpaired t-tests were applied for continuous data, with alternative tests (Wilcoxon, Mann-Whitney U) used when normality assumptions were not met.

Ethical approval was obtained, and participants gave informed consent before enrollment. All statistical analyses were performed using SPSS, with significance set at $p < 0.05$.

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RESULT

Characteristics of the Study Sample

Table 1. Characteristics of Pregnant Women in the Second and Third Trimesters with Vulvovaginitis at Puskesmas Andalas

Characteristics	Group	
	Dequalinium chloride	**Metronidazol + Nistatin**
Maternal age (years) (Mean ± SD)	27,11 ± 5,22	28,44 ± 7,43
Gestational age (weeks) (Mean ± SD)	27,78 ± 5,72	31,44 ± 4,71
BMI (n,%)		
Underweight	0	0
Normoweight	18 (100)	18 (100)
Overweight	0	0
Obesitas	0	0
Parity (n,%)		
Primiparous	8 (44,4)	10 (55,6)
Multiparous	10 (55,6)	8 (44,4)

Table 1 shows that the average maternal age in both groups was similar, with 27.11 ± 5.22 years in the Dequalinium chloride group and 28.44 ± 7.43 years in the Metronidazole + Nystatin group. The average gestational age in both groups was also similar, with 27.78 ± 5.72 weeks in the Dequalinium chloride group and 31.44 ± 4.71 weeks in the Metronidazole + Nystatin group. All participants had a normal body mass index (BMI). Parity was also comparable between the two groups, with 8 women (44.4%) in the Dequalinium chloride group being primiparous, while 10 women (55.6%) in the Metronidazole + Nystatin group were primiparous.

Distribution of Vulvovaginitis in Pregnant Women in the Second and Third Trimesters with Vulvovaginitis

Table 2. Distribution of Vulvovaginitis in Pregnant Women in the Second and Third Trimesters with Vulvovaginitis at Puskesmas Andalas

Vulvovaginitis	Group	
	Dequalinium chloride	**Metronidazol + Nistatin**
Bacterial vaginosis (n,%)	14 (78)	15 (83)
Candidiasis (n,%)	9 (50)	11 (61)
Trichomoniasis (n,%)	5 (28)	5 (28)

Based on PCR results, 14 women (78%) in the Dequalinium chloride group were diagnosed with bacterial vaginosis, 9 women (50%) with candidiasis, and 5 women (28%) with trichomoniasis.

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Meanwhile, in the Metronidazole + Nystatin group, 15 women (83%) had bacterial vaginosis, 11 women (61%) had candidiasis, and 5 women (28%) had trichomoniasis.

Effectiveness of Dequalinium Chloride Treatment for Vulvovaginitis in the Second and Third Trimesters

Table 3. Effectiveness of Dequalinium Chloride Treatment for Vulvovaginitis in the Second and Third Trimesters at Puskesmas Andalas

Effectiveness Parameters	***Dequalinium chloride***		**p-value**
	Before therapy	**After therapy**	
Symptoms (n)			
Positif	18	0	***0,000**
Negative	0	18	
Number of *Gardnerella vaginalis* (Mean ± SD, x10^5)	41,42 ± 88,45	13,36 ± 34,37	**[a]0,035**
Number of *Candida albicans* (Mean ± SD, x10^2)	43,48 ± 67,39	12,12 ± 20,45	**[a]0,021**
Jumlah *Trichomonas vaginalis* (Mean ± SD)	34,98 ± 26,25	8,54 ± 19,10	[a]0,50

* McNemar test
[a] Wilcoxon test

Table 3 demonstrates a significant reduction in symptoms before and after Dequalinium chloride treatment. Additionally, there was a significant decrease in the average number of Gardnerella vaginalis after treatment with Dequalinium chloride (p=0.035). Table 5.3 also shows a significant reduction in the number of Candida albicans after treatment with Dequalinium chloride (p=0.021). However, there was no significant reduction in the number of Trichomonas vaginalis (p=0.50).

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Effectiveness of Metronidazole + Nystatin Treatment for Vulvovaginitis in the Second and Third Trimesters

Table 4. Effectiveness of Metronidazole + Nystatin Treatment for Vulvovaginitis in the Second and Third Trimesters at Puskesmas Andalas

Effectiveness Parameters	***Metronidazole + Nystatin***		**p-value**
	Before therapy	**After therapy**	
Symptoms (n)			
Positif	18	0	***0,000**
Negative	0	18	
Number of *Gardnerella vaginalis* (Mean ± SD, $x10^5$)	31,89 ± 64,65	1,24 ± 4,02	**[a]0,002**
Number of *Candida albicans* (Mean ± SD, $x10^2$)	5,58 ± 7,81	1,27 ± 2,91	[a]0,075
Jumlah *Trichomonas vaginalis* (Mean ± SD)	208600 ± 466397	8,95 ± 12,87	[a]0,138

* McNemar test
[a] Wilcoxon test

Table 4 shows a significant reduction in symptoms before and after Metronidazole + Nystatin treatment. Furthermore, there was a significant decrease in the average number of Gardnerella vaginalis after treatment with Metronidazole + Nystatin (p=0.002). However, no significant reduction was found in the numbers of Candida albicans and Trichomonas vaginalis, with p-values of 0.075 and 0.138, respectively.

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Comparison of the Effectiveness of Dequalinium Chloride and Metronidazole + Nystatin for Vulvovaginitis in the Second and Third Trimesters

Table 5. Comparison of the Effectiveness of Dequalinium Chloride and Metronidazole + Nystatin for Vulvovaginitis in the Second and Third Trimesters at Puskesmas Andalas

Effectiveness Parameters	***Metronidazole + Nystatin***		**p-value**
	Deualinium choride	**Metronidazo + Nistatin**	
Symptoms (n)			
Increase	0	0	[b]-
Settled	0	0	
Decrease	18	18	
Mean decrease of Gardnerella vaginalis (Mean ± SD, $x10^5$)	28,05 ± 55,91	30,64 ± 64,55	[c]0,678
Mean decrease of Candida albicans (Mean ± SD, $x10^2$)	31,31 ± 49,40	5,35 ± 7,96	[c]0,342
Mean decrease of Trichomonas (Mean ± SD)	26,44 ± 29,81	208593 ± 466401	[c]1,000

* McNemar test
[a] Wilcoxon test

Table 5 indicates that there were no significant differences in symptom improvement between the two groups. Similarly, no significant differences were observed in the reduction of Gardnerella vaginalis, Candida albicans, and Trichomonas vaginalis, demonstrating comparable effectiveness between the two therapies.

DISCUSSION

Characteristics of the Study Sample

In this study, the average maternal age was similar between groups, ranging from 27 to 28 years. A review by Disha et al. also found that the majority of vulvovaginitis cases in pregnant women occurred in the 20-29 year age group, followed by the 30-39 year age group. Another study by Yi et al. on pregnant women in Jatinangor with bacterial vaginosis found that most were under 25 years old. In a study by Ng et al. on 237 pregnant women with gestational ages between 22 and 34 weeks who experienced abnormal vaginal discharge, the average maternal age was between 29 and 30 years. The high incidence of vulvovaginitis in reproductive-age women is related to fluctuating hormone levels, which affect the composition of vaginal flora.[34-36]

The average gestational age in both groups was within the second to third trimester. A study

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by Cilik et al. on 96 pregnant women found an increase in the incidence of vulvovaginitis as gestational age increased. A similar finding was reported by Yi et al., who noted that most pregnant women with vulvovaginitis were in their second trimester.[35]

All participants had a normal BMI to avoid bias due to the influence of body weight on vaginal flora. The impact of BMI on vulvovaginitis varies across studies. Lokken et al. found that obesity was associated with a 20% lower likelihood of bacterial vaginosis compared to normoweight or underweight individuals. This protective effect was linked to higher estrogen levels in obese women, which promotes the abundance of Lactobacillus. Conversely, Qi et al. found that increased BMI was associated with higher rates of bacterial vaginosis, explaining that obesity affects personal hygiene and increases vaginal moisture, altering the vaginal environment. Obesity also impacts vaginal glycogen levels, as it decreases estrogen, leading to lower Lactobacillus and higher anaerobic bacteria levels. Additionally, poor diet can affect intestinal microbiota, which influences vaginal microecology.[38,39]

Parity was comparable between primiparous and multiparous women in both groups. Disha et al. reported a higher prevalence of vulvovaginitis among multiparous women (61.8%) compared to pauciparous (54.4%) and nulliparous (38.5%) women. Blomberg et al. found a higher tendency among multiparous women, which was associated with higher education levels and more frequent use of antibiotics during pregnancy. Sexually active women are also more prone to fungal infections.[40]

Distribution of Vulvovaginitis in Pregnant Women in the Second and Third Trimesters

PCR results revealed that most pregnant women had bacterial vaginosis, followed by candidiasis, with a smaller number having trichomoniasis in both treatment groups. This is consistent with findings by Owole et al., who examined pregnant women in their first, second, and third trimesters. Their study used vaginal swabs during antenatal care and microscopy, reporting the highest prevalence of bacterial vaginosis (38%), followed by candidiasis (36%) and trichomoniasis (2%).[41]

Conversely, Konadu et al. found higher rates of candidiasis (36.5%) compared to bacterial vaginosis (30.9%) and trichomoniasis (1.4%) in a study of 589 pregnant women using microscopy. William et al. reported similar results in a study on 200 pregnant women, finding 27% had bacterial vaginosis, 32% had candidiasis, and 2% had trichomoniasis. In these studies, poor vaginal hygiene habits, such as douching, contributed to the higher incidence of candidiasis.[42,43]

Effectiveness of Dequalinium Chloride Treatment for Vulvovaginitis in the Second and Third Trimesters of Pregnancy

This study found that Dequalinium Chloride (DQC) effectively reduces Gardnerella vaginalis in bacterial vaginosis and yeast infections in pregnant women during the second and third trimesters. However, its effectiveness against trichomoniasis was not significant. Previous studies support these findings, with Raba et al. reporting a 92.8% cure rate in bacterial vaginosis after DQC treatment. Other studies showed similar results, including a 94.12% cure rate by Indarti et al. and high

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effectiveness against Gardnerella spp. noted by Gaspar et al.

Kuraseva et al. reported improvements in vaginal microbiota without any side effects during DQC treatment. A systematic review by Eckel et al. confirmed DQC's safety and efficacy, suggesting it as a first-line treatment for vulvovaginitis.[44-46] Thamkhantho et al. found only 25.3% of participants had positive microscopic results after DQC treatment, with high satisfaction levels.[47]

Effectiveness of Metronidazole + Nystatin Treatment for Vulvovaginitis in the Second and Third Trimesters of Pregnancy

The combination of Metronidazole and Nystatin effectively reduced Gardnerella vaginalis in bacterial vaginosis among pregnant women but showed no effect on candidiasis and trichomoniasis. Indarti et al. reported a 100% cure rate for bacterial vaginosis with Metronidazole, while Raba et al. noted a 93.2% cure rate but with some patients experiencing side effects such as candidiasis and gastrointestinal discomfort.[44]

Hoz et al. found an 86.66% microbiological negativity rate and an 81.33% cure rate in pregnant women with mixed vaginitis treated with Metronidazole + Nystatin. However, they noted mild side effects like vaginal irritation.[48]

Comparison of Effectiveness Between Dequalinium Chloride and Metronidazole + Nystatin for Vulvovaginitis in the Second and Third Trimesters of Pregnancy

The study showed no significant difference in effectiveness between DQC and Metronidazole + Nystatin for treating bacterial vaginosis, candidiasis, and trichomoniasis. While Metronidazole achieved a slightly higher cure rate, it was associated with more side effects.[31]

Despite DQC's similar effectiveness and minimal side effects, Metronidazole remains the first-line treatment due to its availability and lower cost. Nystatin is still preferred for candidiasis, though studies indicate potential resistance. Overall, DQC offers an effective alternative with fewer side effects, but it is more expensive.[44]

CONCLUSION

In conclusion, the study represented that both Dequalinium Chloride (DQC) and the combination of Metronidazole and Nystatin are effective treatments for vulvovaginitis in pregnant women during the second and third trimesters, with no significant differences in their effectiveness against bacterial vaginosis, candidiasis, and trichomoniasis. DQC significantly reduced Gardnerella vaginalis and Candida albicans, while Metronidazole + Nystatin was effective in reducing Gardnerella vaginalis but showed no significant impact on candidiasis or trichomoniasis. Although Metronidazole exhibited a slightly higher cure rate, it was associated with more side effects. Overall, DQC presents a viable alternative with fewer adverse effects, though it is more costly, positioning Metronidazole as the first-line treatment due to its accessibility and lower price.

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