Case Report

Effectivity of Dequalinium Chloride Vaginal Tablets in Pregnant Women with Vulvovaginal Candidiasis

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Abstract

Objective: To evaluate the efficacy of Dequalinium Chloride (DQC) in treating vulvovaginal candidiasis (VVC) caused by *Candida albicans* during pregnancy.

Methods: a twenty seven year-old primigravida woman in her third trimester presented with odorless, thick, curd-like vaginal discharge accompanied by severe itching (VAS 9/10) and pain for three months. Clinical examination revealed erythema of the labia majora and abundant thick discharge on the labia minora, vagina, and cervix. Microscopic examination of vaginal discharge with 10% KOH showed pseudohyphae. Gram staining demonstrated pseudohyphae and more than 30 polymorphonuclear cells in vaginal samples, as well as pseudohyphae in cervical discharge. VITEK-2 culture confirmed fluconazole-sensitive *C. albicans.* The patient was treated with intravaginal DQC tablets for 10 days.

Results: The patient showed marked clinical improvement and complete microscopic resolution of infection following DQC treatment.

Discussion: Intravaginal DQC appears to be effective in treating VVC during pregnancy. Early and appropriate management of VVC is essential to prevent potential adverse perinatal outcomes.

Conclusion: Dequalinium Chloride vaginal tablets demonstrated effective clinical and microbiological resolution of *Candida albicans* VVC in pregnancy, supporting their role as a safe therapeutic option for pregnant patients.

Keywords: C. Albicans, dequalinium chloride, pregnancy, vulvovaginal candidiasis.

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INTRODUCTION

Vulvovaginal Candidiasis (VVC) is defined as vulva-vaginal inflammation caused by opportunistic fungi, the *Candida* species. There are various types of *Candida* such as *C. glabrata, C. tropicalis,* and *C. krusei.* Nevertheless, *Candida albicans (C. albicans)* is the most common etiology in VVC and other fungal infections.[1] *Candida* species has various virulence factors that help in fungi colonization, initiation, and spread of infection. Pathogenesis of *C. albicans* begins with asymptomatic colonization, morphogenesis, activation of the innate immune system, and migration of polymorphonuclear (PMN) into the lumen, which leads to the emergence of symptoms.[2] Symptoms include itching or pain in the vulva and vagina, abnormal vaginal discharge, dyspareunia, and distal dysuria.[3,4] These signs and symptoms need to be supported by supporting examinations to establish the diagnosis.[3]

Around 75% of women experience at least 1 episode of VVC during their life. VVC is classified into two, non-complicated and complicated VVC. Pregnancy VVC is included in the complicated category.[3] Vaginal candida colonization prevalence is 17-90% in pregnant women. Pregnancy is a risk factor for VVC since it causes physiological changes that facilitate Candida invasion, including an increase in reproductive hormones and a decrease in the immune system.[5] VVC during pregnancy interferes with the placental formation, thus affecting the condition of the fetus.[6] Pregnancy also narrows

down the VVC therapeutic options.[3] Selection of adequate therapy with the most effective route of administration needs to be considered to eliminate the causative agent of VVC and prevent perinatal adverse effects.

Dequalinium Chloride (DQC) is an ammonium compound with broad-spectrum antimicrobial activity that can fight all pathogens of vaginal infections such as gram-positive and negative bacteria, yeast, and protozoa.[7]

The following case report presents a case of *C. albicans* VVC in a primigravida that showed clinical and microscopic improvement following DQC intravaginal administration for 10 days. This report will also further discuss *C. albicans* as well as VVC in pregnancy and its therapeutic options.

CASE

A twenty seven-years-old primigravida female was presented with chief complaints of her first vaginal discharge. The vaginal discharge was white, thick with curd-like consistency, odorless, and accompanied by itchiness (VAS of 9/10) that disturbed patient sleep since the second trimester of pregnancy (3 months before admission). Itchiness was temporarily relieved by cold water genital douching. Patient had never applied feminine hygiene or any irritating substance to the genital area.

The patient was married for 2 years , worked as an employee at the tax office. Since pregnancy, specifically in the third trimester, the patient often sweats. However, the patient did not routinely change her underwear even though it was damp. The patient regularly changes underwear 2x a day.

Venereological examination on the *ostium urethrae externum* (OUE), pubis, perineum, and anus were within normal limits. Labia majora was erythematous. On the labia minora, vaginal introitus, and cervix, a large quantity of thick white discharge was found. On litmus paper examination, vaginal pH was 5. The whiff test showed negative results. Microscopic examination with wet preparation samples did not reveal the presence of *Trichomonas vaginalis.* A vaginal discharge examination using 10% potassium hydroxide (KOH) revealed the presence of hyphae. Vaginal Gram examination showed pseudohyphae, polymorphonuclear cells (PMN) >30, coccus cells, bacillus cells, and budding yeast (-). Gram examination of the cervix revealed PMN >30, pseudohyphae, and bacilli cells, budding yeast (-). Gram OUE examination showed epithelium and bacilli cells, budding yeast (-). VITEK-2 culture results in fluconazole-sensitive *C. albicans*.

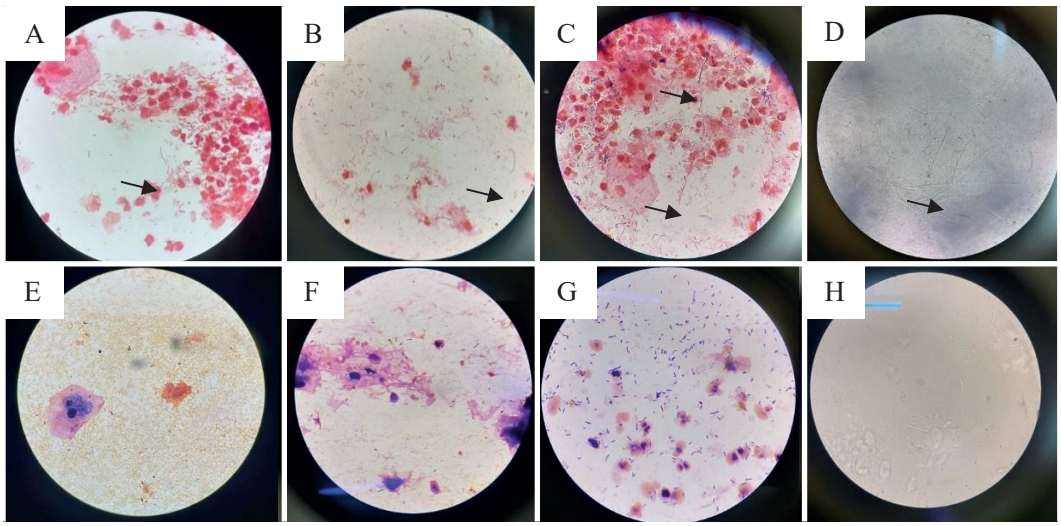
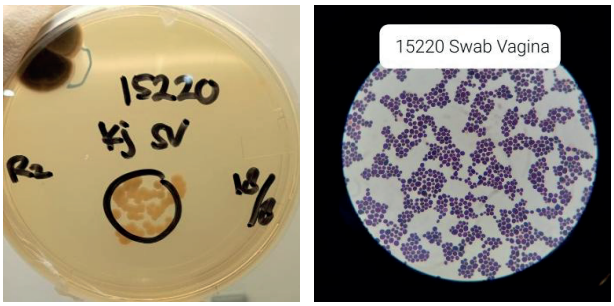


Figure 1. Comparison between admission day (A-D) and 10 days post-treatment (E-H) discharge supporting examination.

(A) Vaginal Gram examination: positive pseudohyphae (→) (x1000) (→);
(B) OUE Gram examination: positive pseudohyphae(→), epithelial cells and coccus (x1000);
(C) Cervix Gram examination: positive pseudohyphae (→) (x1000);
(D) 10% KOH examination: positive pseudohyphae (→) (x400).
(E) Vaginal Gram examination: no pseudohyphae (x1000);
(F) OUE Gram examination: epithelial cell without pseudohyphae (x1000);
(G) Cervix Gram examination: no pseudohyphae (x1000);
(H) 10% KOH examination: minimal pseudohyphae (x400).



A B

Figure 2. VITEK-2 Culture.
Candida albicans figures were visible.

The patient was diagnosed with complicated vulvovaginal *candidiasis* (VVC) and G1P0Ab0 GA 28-30 weeks and received vaginal Dequalinium Chloride (DQC) tablet therapy once daily for 10 days. Written informed consent was obtained from the patient for the publication of this case report. Dequalinium Chloride (DQC) vaginal tablets were selected as the treatment for this patient due to their broad-spectrum antimicrobial and antifungal properties, including potent activity against *Candida albicans*. DQC acts locally within the vaginal environment, disrupting the cell membranes of pathogens, leading to rapid cell death. Its high local concentration after vaginal dissolution exceeds the minimal inhibitory concentrations for common vaginal pathogens, ensuring effective eradication. Additionally, DQC has a well-established safety profile in pregnancy and low risk of microbial resistance, making it a suitable and effective option for treating vulvovaginal candidiasis in pregnant women. Ten days following treatment, vaginal discharge and itching (VAS 2/10) were lessening. Venereological status examination revealed positive white discharge on the vaginal introitus and cervix and without erythema on the labia majora. Pseudohyphae had minimal numbers in 10% KOH preparations from the cervical body fluid. Gram examination of the cervix, vaginal introitus, and OUE did not reveal any pseudohyphae. The patient was educated about vaginal hygiene to prevent recurring complaints.

DISCUSSION

The prevalence of VVC or *candida* colonization in the vagina during pregnancy has a wide range of 17-90%. Differences in prevalence might be related to geographic, ethnic, and socioeconomic factors, as well as various sampling techniques.[5] In this report, *Candida albicans* was found on VITEK-2 culture examination. *Candida* species is an opportunistic pathogen. *Candida albicans (C. albicans)* is the most common pathogen in VVC cases compared to other *Candida* species, for instance, *C. glabrata, C. tropicalis,* and *C. krusei.*[1] *C. albicans* is the main etiology of fungal infection, amounting to 70%.8 *C. albicans* also form biofilms on the surface of the host or abiotic. The polymorphology of *C. albicans* supports the complexity of biofilm structure.[8]

The immunopathogenesis of *C. albicans* begins at yeast colonization on the vaginal epithelium without causing symptoms even though there are various pattern recognition receptors (PRR) on the epithelial surface. *C. albicans* begins to transform into hyphae under conditions that induce morphogenesis such as increased estrogen, increased vaginal pH, and disruption of the microbiome. Recognition by augmented PRRs, increased hyphal biomass, expression of hyphae-associated virulence factors, activation of NLRP3 inflammasome signaling, and recruitment of inflammatory cytokines and chemokines in the vaginal epithelium led to early migration of PMNs from the lamina propria to the vaginal lumen. Subsequently, failure of adequate immunopathological trigger reduction occurs and is followed by continuous production of innate immune system effector on vaginal epithelium. Combined with secondary amplification of immune effectors by existing PMNs, this cascade will induce infections with immunopathological symptoms and characteristics.[2]

The patient had VVC risk factors, which are pregnancy and poor underwear hygiene habits. Risk factors for VVC are divided into pregnancy-related factors, clinical factors, and habits.

Pregnancy causes an increase in reproductive hormones, glycogen deposition, and pH level, as well as decreased immunity. During pregnancy, there is an increase in progesterone and estrogen. High progesterone levels facilitate *Candida* implantation in the vagina and inhibit the effects of anti-candida neutrophil activity. High estrogen levels facilitate yeast attachment, stimulate growth, multiplication, and formation of pseudohyphae, and increase colonization. These two hormones cause increased glycogen deposition which will then provide a carbon source. This helps the growth and germination of Candida on the vaginal walls. Apart from that, pregnancy also increases the vaginal pH level which usually ranges from 4.0-4.5 to 5.0-6.5. In addition, pregnancy increases emotional stress. Excessive stress causes a decrease in the immune system. CD4+, CD8+, T, and natural killer (NK) cell activity also subsided. Associated clinical factors are diabetes mellitus, HIV, and previous history of candidiasis. Meanwhile, habitual factors include the use of oral contraceptives, intrauterine devices (IUDs), antibiotics, tight clothing and synthetic materials, feminine area cleaning products, and douching habits.[5,9]

Common symptoms of VVC include pruritus, vaginal pain, dyspareunia, dysuria, and abnormal vaginal discharge. Supporting examinations may show the presence of budding, yeast, hyphae, and pseudohyphae in wet vaginal discharge preparations or positive results on culture or other tests. Candida vaginitis generally occurs at normal vaginal pH. The use of 10% KOH in wet preparations improves yeast and mycelia visualization by disrupting cell material which can disguise the appearance of yeast or pseudohyphae. KOH examination needs to be carried out on all women with VVC signs and symptoms. Women who have positive results should be treated. If a patient with clinical candidiasis has a negative result on a wet preparation, a discharge culture is necessary.[3]

Pregnancy in this patient is one of the considerations in selecting therapy. Based on the 2021 CDC guidelines, the only recommended VVC therapy in pregnancy is only azoles for 7 days.[3] The azole group consists of azole rings with 2 (imidazole) or 3 (triazole) nitrogen atoms attached to the side of the chain complex. Azoles mechanism of action is through inhibition of ergosterol synthesis in the endoplasmic reticulum. Afterward, lanosterol 14-α-demethylase enzyme disruption takes place, which is involved in the transformation of lanosterol into ergosterol. Fluconazole is the drug of choice for Candida infections.[1] However, epidemiological studies show that administration of single-dose fluconazole 150 mg is associated with spontaneous abortion and congenital anomalies. Therefore, fluconazole is not given in pregnancy cases.[3] In addition, the azole group has side effects in the form of craniosynostosis, humoral-radial fusion, bowed tibia and femur and bilateral femoral fractures, heart defects, d-transposition of great arteries, cleft lip with cleft palate, hepatotoxicity, and spontaneous abortion was reported.[10]

In this report, the patient was given DQC vaginal tablets intravaginally once a day for 10 days. DQC is a quinoline derivative with antiseptic and disinfectant properties used as a topical bacteriostatic for infection and inflammation of the oral cavity.[7,11] Apart from being antibacterial, DQC also has benefits as an antifungal, antiparasitic, antiviral, and anticancer. and neuroprotector. Initial research shows that DQC fungistatic properties reduce cell adhesion and pathogen invasion.[7] DQC primarily works by increasing microbiome cell permeability followed by loss of mitochondrial ATP synthesis through F1-ATPase inhibition and leading to cell death.[12] *C. albicans* is the most sensitive strain with a Minimum Inhibitory Concentration (MIC) of 0.5-2.9 µg/ml.7 DQC reduced the prevalence of Candida in women with normal microflora.[13] In women with VVC, DQC has a cure rate of 70-90%.[14] Previous study found that the administration of 10 mg DQC vaginal tablets is equivalent to 100 mg clotrimazole in clinical improvement for vaginal candidiasis. However, clotrimazole showed better improvement in microscopic examination and fungal culture.[15] DQC is well tolerated and has low side effects in 7.8% of patients. Side effects include vaginal candidiasis, vaginal discharge, and itching or burning of the vulva and vagina.[11] DQC can be administered as therapy for vaginal inflammation in pregnant (in all trimesters) and breastfeeding women. A previous study involving 181 pregnant women treated for bacterial vaginosis and vulvovaginal candidiasis (VVC) found no maternal, fetal, or neonatal side effects based on pH, Apgar scores, and one-year monitoring following DQC administration, which can be safely given for 8–10 days during pregnancy.[12] However, DQC should not be used within 12 hours before delivery.[11,16] DQC broad spectrum antimicrobial activity for vaginal

infections and negligible systemic absorption are the main factors that make DQC as treatment of choice in most vaginal infections.[12]

One of the VVC therapy options is a topical medication, including creams and gels which are easier to obtain. Topical preparation is non-toxic and non-irritant to the vaginal mucosa. However, this preparation tends to be difficult to use, especially in the case of excessive vaginal discharge that reaches the cervix. The topical route may be uncomfortable for some patients. Intravaginal tablets have similar components to oral tablets with ease of use vaginally.[17] The use of vaginal tablets has also been found to increase patient compliance.[17] Intravaginal tablets disintegrate and dissolve the active substance rapidly. As soon as the intravaginal tablet comes into contact with vaginal secretions, the tablet will begin to disintegrate and DQC will be released. The DQC concentration is estimated to reach 2,000-4,000 µg/ml. These concentrations are 4-8 times higher compared to the Minimum Inhibitory Concentration (MIC).[14]

Candida infection during pregnancy may affect the condition of the neonate. Another study did not find strong statistical evidence of an increased risk of spontaneous abortion, stillbirth, preterm premature rupture of membranes, premature rupture of membranes, low birth weight, small gestational age, inflammation of the placenta or uterine, and neonatal deaths in women with vulvovaginal *Candida* yeast infections.[18] However, *C. albicans* infection during pregnancy, especially in the early trimester, may inhibit placental development which leads to poor pregnancy outcomes.[6] Therefore, early diagnosis and adequate therapy are required.

CONCLUSION

Vulvovaginal *candidiasis* (VVC) is vaginal and vulva inflammation caused by *Candida* species. Pregnancy is one of the VVC risk factors due to physiological alteration by increasing reproductive hormones and decreasing the immune system that facilitates *Candida* invasion. VVC in pregnancy may disrupt the formation of the placenta followed by disrupting the fetus. Besides being a risk factor, pregnancy should be the main consideration in VVC therapy selection. The use of DQC in vaginal infections provides great therapeutic outcomes with minimal side effects. Intravaginal DQC may increase patient compliance and is expected to deliver the precise dose. VVC in pregnancy needs to be treated adequately as early as possible to prevent unwanted neonatal complications.

Institutional Support and Patient Consent

This study was conducted with the approval of the relevant institutional ethics committee. Written informed consent was obtained from the patient after full explanation of the procedure, risks, benefits, and alternatives. The patient agreed voluntarily to participate and consented to the publication of clinical details in this case report, respecting ethical standards and patient autonomy.

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