

## REFRACTORY FUNGAL VAGINITIS TREATED BY TOPICAL AMPHOTERICIN B. Review

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**Abstract.** Vaginitis is a common problem for women regarding a worldwide health challenge with many side effects. Vaginitis is among the most visiting to gynecology clinics. About 75% of all reproductive women had at least one fungal vaginitis infection in their life, and more than 40% will have two or more than two. *Candida* spp is the most prevalent in fungal vaginitis, while reports for unusual fungi were observed as mucor spp.

Amphotericin B (AmB) belongs to the polyene group has a wide spectrum in vitro and in vivo antifungal activity. All of the known available formulas of AmB are administrated via intravenous injection to treat severe systemic fungal infections, while the development of the topical formula of AmB is still under preliminary development including topical vaginal AmB.

Due to the revealing of antimicrobial-resistant fungi in recent years, this study explains the role of topical AmB in treating refractory fungi vaginitis that may not a response to other drugs reported in many cases that may help researchers to develop new effective formula of AmB regarding fungal vaginitis.

**Keywords:** fungal vaginitis, antifungal drugs, topical Amphotericin B, Amphotericin B formula.

**Introduction.** Most common women had vaginitis at a certain period in their lives that associated with different ages [1]. Vaginitis is the most predominant infection in the female genital tract and is recognized among women in the primary health centers and gynecology departments. vaginal infections alone account for more than 10% of patients visit women's health units [2]. Vaginitis is a common term that refers to inflammation of the vaginal wall that caused by one of three causes: fungal yeast infections, trichomoniasis, and bacterial vaginosis [3].

**Amphotericin B (AmB)** is an ancient agent used over many decades in treating various fungal infections clinically in the human [4]. Low fungal resistance and broad-spectrum antifungal activities are the most valuable pharmaceutical characters encourage continuous usage of AmB [5].

This study highlights the topical efficacy of AmB to treat fungal vaginitis depending on searches and case report studies for rare cases regarding vaginitis.

**Advantages of topical AmB.** There are many advantages to using AmB as a topical treatment of dermatophytosis. Firstly, discover new drugs or

modification old one will participate to increase the available limited number of antifungal drugs [6]. Secondly, topical preparations are much less costly than orally administered antifungal drugs and cause minimal adverse side effects [7-8].

Third, the application of the topical formula of AmB considers more safety to use and will not produce clinically relevant serum levels of AmB [8-9]. Fourth, the quality of patient life will increase if new drugs improved to cure infectious lesions in a short time [6].

**Topical usage of AmB for refractory fungal vaginitis.** Topical modern applications of AmB provide a promising way of fungal treatment to reduce the adverse effects of intravenous usage of AmB [4]. Five interesting articles have been revealed the role of topical AmB to treat refractory fungal vaginitis (table 1).

Phillips was prepared topical vaginal suppositories of 50 mg AmB showed successful management of 70% of ten women with non-albicans *Candida* vaginitis after given nightly for 14 days. Suppositories medicine is also revealed less local side effects and well-tolerated [10].

Table 1

Topical AmB used in vagina							
Ref	Fungi type	NO. patients	AmB Dose	AmB formula	Treatment duration	Result	Year
10	non-albicans <i>Candida</i>	32	50 mg nightly	AmB vaginal suppositories	14 days	70% of women treated	2005
11	<i>Candida krusei</i>	1	3% daily	AmB vaginal gell	14 days	symptoms is resolved	2016
12	<i>Mucor species</i>	1	3% 5 g daily	AmB	7 weeks	disappearing of symptoms, culture-ve	2001
13	<i>Candida glabrata</i>	3	100 mg once daily	AmB lubricating jell	2 weeks	significant improvement	2001
14	<i>Candida glabrata</i>	1	100 mg once Nightly	AmB vaginal applicator	14 days	negative culture after 2 weeks	2003

Chamorro and his colleagues studied the topical formulation of amphotericin 3 % to treat *Candida krusei* vaginitis was developed by combining amphotericin B deoxycholate with lubricating jelly Aquagel®. Propyleneglycol was used for lubricant incorporation the intravaginal formulation was given daily for 14 days; the patient had resolved her symptoms [11].

Sobel mentioned that 3 % topical amphotericin B 5 g daily has been used to treat a rare case of vaginitis caused by *Mucor* species in healthy woman, *Mucor* vaginitis appeared refractory resistant to flucytosine as well as an azole. The treatment outcome, disappearing of symptoms and she has culture-negative [12].

White et al. found that Flucytosine (one gram) and AmB (100 mg) prepared in lubricating jell were used per vagina once daily to treat vaginal *Candida glabrata* had failed to respond to antifungals therapy, significant improvement, clinical resolving and negative microbiological culture observed after 2 weeks treatment [13].

Shann and Wilson: the treatment of *Candida glabrata* resistant to antifungal drugs isolated from vaginal swabs by using vaginal applicator nightly, for 14 days of amphotericin 100 mg plus flucytosine 1 g in Aquagel. Her symptoms had resolved and culture results for *Candida glabrata* were negative [14].

**Vaginitis prevalence and management.** Vaginitis is a widely distributed problem among women mainly associated with discomfort. Symptomatic vaginitis accorded for millions of clinical visits yearly [15]. Vaginitis is a global problem that not just women, but also families and communities.

It may have dangerous complications such as ectopic pregnancy, chronic pelvic pain, abortion, infertility, increasing of HIV transmission, low-birth weight infant. For these reasons, true prevention and management of vaginitis is great important [16].

*Candida albicans* is responsible for 65-90 % of vaginal *Candida* species infections, and non-*albicans* *Candida* species are responsible for up to 30 % [17]. From 1,740 symptomatic patients, vaginal candidiasis observed in 32,8 % [18].

*Candid* spp is the leading cause beyond infectious vaginitis; it colonizes about twenty percent of vagina that considered important opportunistic fungal microbe [19]. Vulvovaginal candidiasis (VVC) is the second most commonly reported form of infectious vaginitis. However, the totality of fungal microbes found within the vagina has been grossly underestimation. On the other hand, we have large information about bacteria that harboring vaginal milieu [19].

**General features of AmB.** Amphotericin B (AmB) is an ancient agent used over many decades in treating various fungal infections clinically in the human. Opportunistic systemic fungal infection considered the most common type of fungal infection mainly treated by AmB [4].

At present, many studies focused on the topical preparation of AmB as eye drop [20] or gel [20] or

solution [21] or as nanoparticles drug [22]. However, treatment with topical AmB may not always give satisfying results as with ordinary forms of this drug in the treatment of fungal infection, while some topical applications of AmB gave performing outcomes with complete healing especially in certain cases not responded to conventional therapy.

The topical formula of AmB to treat fungal vaginitis give good results as mentioned in the previous studies, so developing this formula is necessary due to the appearance of drug-resistant fungi implicated in vaginitis.

## CONCLUSION

Vaginitis is one of the most common problems associated with discomfort and low quality of life in women that may make women under serious complications like ectopic pregnancy and abortion. Topical AmB formulas are a promising way to develop effective management of the refractory fungal vaginitis.

Using AmB in modern branches and new applications is demanded because AmB is a potential antifungal agent with rare resistance, as well as its broad-spectrum activity toward many fungal infections, more studies about topical AmB vaginal formulas are recommended.

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## МІСЦЕВЕ ЛІКУВАННЯ РЕФРАКТЕРНОГО ГРИБКОВОГО ВАГІНІТУ АМФОТЕРИЦИНОМ В.

### Огляд

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**Резюме.** Вагініт є загальною проблемою для жінок у всьому світі, з багатьма побічними ефектами. Вагініт – одна з найбільш розповсюджених причин відвідування гінекологічних клінік. Близько 75% всіх репродуктивних жінок мали принаймні одну грибову вагінітну інфекцію у своєму житті, а понад 40 % – дві або більше двох. Candida spp є найбільш поширеним при грибовому вагініті, тоді як повідомлення про незвичні гриби спостерігалися як тусог spp.

Амфотерицин В (AmB) відноситься до полієнової групи, має широкий спектр *in vitro* протигрибової активності. Всі відомі доступні формули AmB вводяться за допомогою внутрішньовенної ін'єкції для лікування важких системних грибових інфекцій, тоді як розробка актуальної формули AmB ще знаходиться на стадії попередньої розробки, включаючи місцевий вагінальний AmB.

Завдяки виявленню антимікробних стійких грибів в останні роки, це дослідження пояснює роль актуального AmB у лікуванні рефрактерного грибового вагініту, що може не відповідати на інші препарати, про які повідомляється у багатьох випадках, які можуть допомогти дослідникам розробити нову ефективну формулу AmB щодо грибового вагініту.

**Ключові слова:** грибовий вагініт, протигрибові препарати, амфотерицин В місцево, формула амфотерицину В.

## МЕСТНОЕ ЛЕЧЕНИЕ РЕФРАКТЕРНОГО ГРИБКОВОГО ВАГИНИТА АМФОТЕРИЦИНОМ В. Обзор

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**Резюме.** Вагинит является распространенной проблемой для женщин во всем мире, со многими побочными эффектами. Вагинит является одним из самых распространенных причин посещения гинекологических клиник. Около 75% всех репродуктивных женщин имели, по крайней мере, одну грибковую инфекцию вагинита в своей жизни, и более 40 % – две или более двух. *Candida spp* является наиболее распространенным при грибковом вагините, в то время как сообщения о необычных грибах наблюдались как *miscog spp*.

Амфотерицин В (AmB) относится к полиеновой группе, обладает широким спектром противогрибковой активности *in vitro* и *in vivo*. Все известные доступные формулы AmB вводятся посредством внутривенной инъекции для лечения тяжелых системных грибковых инфекций, в то время как разработка местной формулы AmB все еще находится в стадии предварительной разработки, включая актуальный вагинальный AmB.

В связи с выявлением устойчивых к противомикробным препаратам грибов в последние годы, это исследование объясняет роль местного AmB в лечении рефрактерного грибкового вагинита, который во многих случаях может не реагировать на другие препараты, о которых сообщалось, что может помочь исследователям разработать новую эффективную формулу AmB в отношении грибкового вагинита.

**Ключевые слова:** грибковый вагинит, противогрибковые препараты, амфотерицин В местно, формула амфотерицина В.