Comparison of susceptibility of vaginal isolates of *Candida* to Lamisil and clotrimazole

Majid Zarrin¹, Ali Zarei Mahmoudabadi¹,², Zeinab Shangal¹, Babak Vazirianzadeh²

¹Department of Medical Mycology, School of Medicine, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran
²Infectious and Tropical Diseases Research Centre, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran

Email for Correspondence: zarei40@hotmail.com, Fax: +98611 3332036

Abstract: Vulvovaginal candidiasis (VVC) is a frequent fungal disease that influences 70% of women at least once in their reproductive periods. *Candida albicans* is the main agent of VVC infections with 85%-90%. Approximately 5% of women suffer from a recurrent VVC. A variety of antifungal agents, including oral or topical drugs are available for treatment of VVC. The aim of this study was to compare the efficacy of treatment with Lamisil and clotrimazole in isolated *Candida* from VVC. One hundred isolates including 97 isolates *C. albicans* and 3 *C. glabrata* were studied. An overnight culture was grown and then a suspension with density 5×10⁷ prepared. Lamisil and clotrimazole were used in this study. The minimum inhibitory concentration (MIC) was regarded based on the lowest concentration of drugs that inhibits the growth of the *Candida* isolates. Our results demonstrated that the antifungal drugs Lamisil and clotrimazole was found to be active against all *Candida* isolates. All 100 *Candida* isolates were found to be susceptible to clotrimazole with the MIC <0.125 - 1μg/ml for *C. albicans* isolates and 0.125μg/ml for *C. glabrata*. Lamisil has been also effective against all tested isolates with the MIC 0.125 - >2μg/ml for *C. albicans* and MIC 1 - >2μg/ml for *C. glabrata*. In this study clotrimazole presented amazingly brilliant antifungal activity against *C. albicans* and *C. glabrata* isolates. In our study the antifungal activities of Lamisil against both *C. albicans* and *C. glabrata* were not promising.

Keywords: *Candida*, Lamisil, Clotrimazole, Vulvovaginal candidiasis

INTRODUCTION

The species of *Candida* are human opportunist pathogens, causing superficial, invasive or systemic infections in immunocompromised or normal persons. These infections are promoted with the use of extensive range of antibiotics and follow the diseases such as AIDS, diabetes and cancer. Vulvovaginal candidiasis (VVC) is a frequent fungal disease that influences 70% of women at least once in their reproductive periods (Ehrstrom et al., 2005 and Mohanty et al., 2007). *Candida albicans* is the main agent of vulvovaginal infections with 85%-90%. Approximately 5% of women suffer from a recurrent VVC (Chen et al., 2007 and Nozari et al., 2012).

The occurrence of *Candida* spp. in vagina, in the persons without immunosuppression or damaged mucosa, is typically not connected with any symptoms of infection and consequently associated to colonization. Contrary to asymptomatic colonization, VVC is described as symptoms of inflammation when *Candida* is presented and in absence of other etiology of infection. The classification of VVC into complicated and uncomplicated is internationally accepted (Pappas et al., 2009 and Workowski and Berman, 2006). *C. albicans* is the frequent species which associated with VVC, nevertheless, other yeasts are able to cause this disease. Direct examination of vaginal fluid samples and culture are two approaches for diagnosis of infections. A variety of antifungal agents, including oral or topical drugs, are available for treatment of VVC (Sobel et al., 2003).

Lamisil is most effective allylamine antifungals which is used against a range of fungi. This drug is very effective against dermatophytes. Earlier researches on susceptibility of Lamisil against yeasts demonstrated weak activity, (Hiratani et al., 1991 and Ryder, 1985) whereas more recent investigations are shown that Lamisil is obviously useful at inhibition of yeasts (Favre, 1997 and Mahmoudabadi et al., 2013). Clotrimazole is an antifungal drug that is frequently used against different types of mucocutaneous *Candida* infections. Clotrimazole vaginal is used in the treatment of vaginal Candida infections.

*Candida* species have different degrees susceptibility towards antifungal drugs and the resistance to these agents has
increased during the last decades (Mahmoudabadi et al., 2013). The aim of this study was to compare the efficacy of treatment with Lamisil and clotrimazole in isolated Candida from vaginal candidiasis.

**MATERIAL AND METHODS**

**Organism**

One hundred isolates including 97 isolates C. albicans and 3 isolates C. glabrata were studied. The isolates were obtained from Medical Mycology Department, Ahvaz Jundishapur University of Medical Sciences. All isolates were recovered from vaginal wash of patients and kept in a suspension of distilled water. Before testing, the isolates were transferred on Sabouraud dextrose agar (SDA, Merck, Germany) tubes to ensure suitable growth. After 24h, a spore suspension with density 5x10^7 was prepared.

**Antifungal drugs**

The following two antifungal drugs were tested, Lamisil and clotrimazole. Stock solution of each antifungal drug was prepared in dimethyl sulphoxide (DMSO). Dilutions with density 0.5, 1, 2.4 and 8 percent were made from each drug.

**Inoculums preparation**

All Candida isolates were sub-cultured on SDA to ensure purity. Then a suspension of overnight cultures was prepared and adjusted to 0.5 McFarland. Agar diffusion test was taken for the evaluation of antifungal drugs. Dipping a sterile swab into the fungal suspension and rolled on the surface of the agar medium (Mahmoudabadi et al., 2010). Five wells were punched on each plate. Then wells were filled with antifungal drugs dilutions. The Petri dishes were incubated at 37°C for 24h. The minimum inhibitory concentration (MIC) was regarded based on the lowest concentration of drugs that inhibits the growth of the Candida isolates. DMSO was considered as negative control. The antifungal activities were assessed with measure of inhibition zone.

**RESULTS AND DISCUSSION**

Vaginal candidiasis is the most frequent infection of women. Among Candida species, C. albicans is the major agent of vaginal candidiasis. A number of antifungal drugs are employed for treatment of infection. The main goal of this investigation was in vitro antifungal activities of clotrimazole and Lamisil against C. albicans and C. glabrata isolates from candidal vaginitis. Over the past few years, the imidazoles such as clotrimazole have become the most extensively used medicine for the VVC treatment.

The results of this study demonstrated that the antifungal drugs Lamisil and clotrimazole was found to be active against all Candida isolates (Table 1). All 100 Candida isolates were found to be susceptible to clotrimazole with the MIC range <0.125 - 1μg/ml for C. albicans isolates and MIC 0.125μg/ml for C. glabrata. Lamisil has been shown react against all 100 isolates of Candida with the MIC range 0.125 - >2μg/ml for C. albicans and MIC rang 1 - >2μg/ml for C. glabrata.

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**Table 1. In vitro susceptibility of Candida isolates against clotrimazole and Lamisil**

<table>
<thead>
<tr>
<th>MIC (μg/ml)</th>
<th>Candida albicans</th>
<th>Candida glabrata</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clotrimazole</td>
<td>Lamisil</td>
</tr>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>2</td>
<td>0</td>
<td>0.0</td>
</tr>
<tr>
<td>1</td>
<td>28</td>
<td>28.86</td>
</tr>
<tr>
<td>0.5</td>
<td>20</td>
<td>20.61</td>
</tr>
<tr>
<td>0.25</td>
<td>16</td>
<td>16.49</td>
</tr>
<tr>
<td>≤0.125</td>
<td>33</td>
<td>34.01</td>
</tr>
<tr>
<td>Total</td>
<td>97</td>
<td>100</td>
</tr>
</tbody>
</table>
In this study, clotrimazole presented amazingly brilliant antifungal activity against C. albicans and C. glabrata isolates with 34% of C. albicans isolates in 0.125μg/ml or less (p<0.001) and 100% of C. glabrata isolates in 0.125μg/ml from vaginal wash. (Richter et al., 2005) demonstrated the clotrimazole had activity against 94.3 to 98.5% of C. albicans isolates at ≤1μg/ml. In vitro antifungal activity researches showed that clotrimazole was effective against 70% of Candida species at MIC 16 and 8μg/ml (Khan and Baqai, 2010). (Falahati et al., 2009 and Salehi et al., 2012) were tested C. albicans recovered from vulvovaginal candidiasis and showed 4.3% and 1.9% resistance to clotrimazole, respectively. Lamisil, an allylamine class, has antifungal reaction against many fungi such as dermatophytes and C. albicans. Lamisil is recognized as effective on C. albicans in VVC (Ferahbas et al., 2006). In our study the antifungal reactions of Lamisil against both C. albicans and C. glabrata were not promising. Therefore, for the prevention of recurrent vulvovaginal candidiasis and to prescribe correct antifungal, it is essential to carry out sensitivity tests in clinical laboratories.

ACKNOWLEDGMENT

This study was a MD thesis (Zeinab Shangal) supported by a grant (No: U-88015) from the Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran. We are thankful Jundishapur Infectious and Tropical Diseases Research Centre for cooperation this study.

Conflict of interest

The authors state no conflict of interest.

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