Antifungal activity of posaconazole against *Candida* spp. and non-*Candida* clinical yeasts isolates

ABSTRACT

The *in vitro* antifungal activity of posaconazole was tested against 315 yeast clinical isolates and 11 ATCC reference strains by means an agar diffusion method (Neosensitabs, Rosco, Denmark) based in CLSI M44-A2 document. Posaconazole activity was excellent against *Cryptococcus* and *Rhodotorula* species studied and showed very good activity against most species of *Candida* tested. A total of 13 clinical isolates (4.1%) were resistant: *Candida albicans* (n=5), *Candida glabrata* (n=5), *Candida tropicalis* (n=1), *Geotrichum australiensis* (n=1) and *Geotrichum capitatum* (n=1). Our results suggest posaconazole is an effective antifungal agent against the most clinically important yeasts species (92.7% of susceptibility). Agar diffusion method provides good conditions for the posaconazole susceptibility study in the routine laboratory.

Keywords: Antifungal agent, susceptibility, posaconazole, yeasts, *Candida*, *Cryptococcus*, *Rhodotorula*

INTRODUCTION

Posaconazole is a third generation triazole antifungal agents designed to improve clinical profiles of fluconazole or itraconazole against *Candida* and *Aspergillus* spp. Posaconazole mode of action is directly based in the inhibition of lanosterol 14α-demethylase activity1, resulting in a high *in vitro* activity against a wide spectrum of pathogenic yeast-like and filamentous fungi and also protozoans2,3. Posaconazole activity was demonstrated in fungal infections of different immunocompromised animal models and also in clinical trials against usual and unusual fungal infections. Posaconazole was effective in candidiasis, disseminated aspergillosis and zygomycoses, pulmonary histoplasmosis, coccidiodomycosis and disseminated fusariosis and also is useful for the treatment of refractory mycoses, trypanosomiasis and leishmaniasis4. The purpose of this study was to determine the *in vitro* antifungal activity of posaconazole against common and uncommon yeasts and yeast-like clinical isolates by means an agar diffusion method that could be more reliable for routine laboratory work5.

MATERIAL AND METHODS

Strains. A total of 326 clinical isolates and type culture collection strains of pathogenic fungi were studied, including *Candida albicans* (*C. albicans*) (n=129), *C. colliculosa* (n=1), *C. dubliniensis* (n=25), *C. famata* (n=10), *C. glabrata* (n=59), *C. guilliermondii* (n=9), *C. intermedia* (n=2), *C. kafyr* (n=3), *C.
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**DISCUSSION**

The *in vitro* susceptibility tests give us useful information for management of invasive fungal infections. The detection of a resistant isolate can be a warning for the clinician and an important data for the therapeutic. Posaconazole has a good *in vitro* activity profile against many yeast and filamentous fungi with low resistant isolates percentages. Resistance percentages for posaconazole observed in this study was 3.9%. Using the same agar diffusion method and microdilution methods, resistance percentages for fluconazole (10%), itraconazole (18%) and amphotericin B (2-3%) reported for another authors, show the high activity of posaconazole against clinical yeasts isolates. In addition, our results agree with those obtained by microdilution methods showing posaconazole ranges of activity between 0.03-0.125 mg/L for most isolates.

As describe some authors in other countries, the *in vitro* antifungal activity of posaconazole seems to be influenced by the origin of the clinical sample and the geographical factors, even in the same geographical area. This reason can be explain the differences between our results and published data.

In the current study, an excellent activity of posaconazole against *C. tropicalis* was observed in comparison with data from Ostrosky et al. These authors reported an increased MIC values due to the trail effect and the observation of an even greater susceptibility of 366 isolates MICs under 0.5 mg/L. The agar diffusion method could solve the trail effect simplifying the reading interpretation.

A reduced susceptibility for *C. glabrata* (5 resistant and 7 intermediate isolates) was observed in this study observing a high activity of posaconazole against species less susceptible echinocandins such as *C. parapsilosis, C. krusei, and G. capitatum*. Also, *in vitro* antifungal activity of posaconazole was obtained against all *C. dubliniensis* isolates.

*In vitro* antifungal activity of posaconazole covers most aetiological agents involved in moderate and severe mycoses in the Western world. The fact that posaconazole shows a good activity against most *C. glabrata* and *C. krusei* isolates, allows considered this drug as an excellent alternative to fluconazole for disseminated candidemia and invasive candidiasis treatment caused by these species.

Furthermore, the broad spectrum antifungal *in vitro* action observed for posaconazole against usual and unusual yeasts...
like microorganisms, converts this drug in a useful alternative to amphotericin B or fluconazole for the treatment of severe fungal infections. This agar diffusion method allows the antifungal susceptibility testing determination and the detection of resistant strains in a routine laboratory, reduces the experimental procedure of microdilution methods and avoids some problems such as the trailing or Eagle effect described for dilution tests 15,27,28.

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REFERENCES