**Fluconazole vs Voriconazole: Candida glabrata’s biofilms response to different azoles**

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**Abstract**

*Candida glabrata* is the second most prevalent yeast in fungal infections, especially in immunocompromised and/or hospitalized patients. Theazole resistance within this species is very well-known and results in a low therapeutic response of *C. glabrata* infections, particularly when associated with biofilms.

**Objective** - To understand the different efficacies of two azoles against *C. glabrata* biofilms:
- fluconazole (Flu), a long time used drug
- voriconazole (Vcz), a latest drug used only in hospitals.

**Methods**

Flu and Vcz susceptibilities were determined in pre-formed 24-hour-biofilms of two clinical isolates and one reference strain of *C. glabrata*.

1. **Gene expression analysis**: ERG3, ERG6 and ERG11 expression by qRT-PCR;
2. **Biofilm matrix composition**: carbohydrates, proteins, β-1,3-glucans and ergosterol quantification;
3. **Biofilm production**: dry weight;
4. **Biofilm cell and biomass analysis**: biofilm cultivable cells (CFU) and biofilm total biomass quantification (Violet Crystal 1% w/v);
5. **Retention of the two azoles within the biofilm matrix**: HPLC analysis.

**Results**

**ERG Genes Expression**

Overexpression of the three ERG genes in the presence of both azoles. ERG expression more dependent on the strain than on the agent.

**Carbohydrates and Proteins Contents**

In presence of antifungal: increase of carbohydrates and decrease of proteins.

**B-1,3 glucans and Ergosterol contents**

In the presence of antifungal: increase of β-1,3 glucans for all strains. Generally: no alteration on the amount of ergosterol present in the matrices of biofilms exposed to agents, in comparison to the controls.

**Antifungal diffusion through biofilm matrices**

Higher capacity of Vcz to penetrate the biofilm net: Vcz diffused better through the biofilm net (96%) than Flu (90%) and with a better connection to the fungi cells.

**Flu was unable to eliminate the C. glabrata’s biofilm cells. Vcz showed to be much more effective in the eradication of the three strains.**

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