

Activity of clinically available antifungals against *Exserohilum rostratum*

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Objective: *Exserohilum rostratum* is a common saprobic fungus within the environment. Although rare, this organism can cause infections in humans including allergic sinusitis and keratitis. In the United States there has been a recent outbreak of central nervous system and peripheral joint infections caused by this dematiaceous fungus due the use of contaminated corticosteroids produced by a compounding pharmacy. Our objective was to measure the activity of clinically available antifungal agents against outbreak isolates of *Exserohilum* and compare these results to that previously measured against non-outbreak isolates. **Methods:** The in vitro activity of amphotericin B (AMB), posaconazole (POS), and voriconazole (VOR) were determined against 7 *Exserohilum* outbreak isolates from the sent to the Fungus Testing Laboratory at UTHSCSA. The in vitro activity of fluconazole (FLU), itraconazole (ITR), and caspofungin (CAS) were also determined against select isolates as requested. All in vitro susceptibility testing was performed according to the CLSI M38-A2 guidelines and the minimum inhibitory concentrations (MIC) were read after 48 hours of growth. We also reviewed the activity of these agents against non-outbreak *Exserohilum* isolates previously measured at UTHSCSA. For the historical data, the MIC₅₀, MIC₉₀, and geometric mean (GM) MICs were determined. **Results:** Against the 7 outbreak isolates, AMB and POS demonstrated potent activity with MIC ranges of $\leq 0.03 - 0.06$ mcg/mL and $0.125 - 0.5$ mcg/mL, respectively. VOR MICs against the outbreak isolates ranged from $0.5 - 2$ mcg/mL. The MICs for FLU, ITR, and CAS against 3 outbreak isolates are shown in Table 1. Against non-outbreak isolates, ITR and POS were the most potent antifungals as determined by their GM MIC values (0.168 and 0.127 , respectively), which were significantly lower than the other agents ($p < 0.0001$). AMB was also more potent than CAS, FLU, and VOR. FLU was the least potent antifungal against both outbreak and non-outbreak isolates. The VOR MICs against the outbreak isolates were similar to the MIC₉₀ against historical isolates (2 mcg/mL). **Conclusions:** These results demonstrate the potent activity of the extended spectrum triazoles ITR and POS and the polyene AMB against outbreak and non-outbreak isolates of *Exserohilum rostratum*. In contrast, FLU demonstrated little activity against these fungi while modest activity was observed for VOR.

Table 1. Antifungal activity against outbreak and non-outbreak *Exserohilum* isolates.

Outbreak Isolates	AMB MIC (mcg/mL)	FLU MIC (mcg/mL)	ITR MIC (mcg/mL)	POS MIC (mcg/mL)	VOR MIC (mcg/mL)	CAS MIC (mcg/mL)
1	< 0.03	---	---	0.125	0.5	---
2	0.06	32	0.25	0.125	2	1
3	0.06	32	0.5	0.25	2	1
4	0.06	32	0.125	0.25	2	0.125
5	0.06	---	---	0.5	2	---
6	0.06	---	---	0.5	2	---
7	0.06	---	---	0.5	2	---
<i>Non-Outbreak MIC Data</i>						
Parameter	AMB (N = 59)	FLU (N = 23)	ITR (N = 41)	POS (N = 43)	VOR (N = 56)	CAS (N = 26)
MIC ₅₀	0.5	32	0.25	0.125	1	1
MIC ₉₀	1	64	0.5	0.5	2	4
MIC Range	0.03 - 1	2 - 64	0.015 - 16	0.015 - 8	0.06 - 4	0.125 - 8
GM MIC	0.326	25.1	0.168	0.127	0.733	0.766