P0055
Poster Session I
How to improve fungal diagnosis

EVALUATION OF THE IN VITRO POTENCY OF ITRACONAZOLE, VORICONAZOLE, AND POSACONAZOLE AND AGAINST RARE ASPERGILLUS SPECIES

N. Wiederhold[1], A. Fothergill[1], D. McCarthy[1], C. Sanders[1], D. Sutton[1]

[1]Pathology, UTHSCSA, San Antonio TX, USA

Objective: The triazoles itraconazole, voriconazole, and posaconazole are important agents for the treatment of infections caused by *Aspergillus* species. Although species such as *A. fumigatus*, *A. flavus*, and *A. terreus* remain the primary causes of invasive infections, other rare species have been associated with disease in profoundly immunocompromised hosts. Our objective was to evaluate the *in vitro* potency of itraconazole, voriconazole, and posaconazole against rare *Aspergillus* species compared to *A. fumigatus*, and determine the rates of resistance to these agents.

Methods: The antifungal susceptibility database in the Fungus Testing Laboratory at the UT Health Science Center San Antonio was queried for itraconazole, voriconazole, and posaconazole MIC data against *A. fumigatus* (n = 886-1819), *A. calidoustus* (n = 28-64), *A. lentulus* (n = 4), *A. sydowii* (n = 9-18), and *A. versicolor* (n = 20-64) isolates from 2001 through 2013. This database is populated with antifungal MIC data against fungal isolates sent to our mycology reference laboratory. Susceptibility testing was performed according to CLSI M38-A2 guidelines. The MIC50, MIC90, and geometric mean (GM) MIC values were determined. Differences in GM MIC values were assessed for significance by ANOVA with Tukey's post-test for multiple comparisons. Isolates were also classified as resistant based on proposed clinical breakpoints (voriconazole & itraconazole >= 4 µg/ml, posaconazole >= 1 µg/ml; Verweij et al. *Drug Resist Update* 2009).

Results: Itraconazole, voriconazole, and posaconazole demonstrated potent activity against *A. fumigatus* (GM MIC range 0.191 - 0.586 mg/L). In contrast, the *in vitro* potency of each triazole was reduced against the non-*fumigatus Aspergillus* species (GM MIC range 0.457 - 4.18 mg/L). Posaconazole had the most potent activity against *A. fumigatus* and *A. sydowii*, as the GM MIC of this agent against these two species (0.191 mg/L and 0.457 mg/L) was significantly lower than those of itraconazole (0.537 mg/L and 1.26 mg/L; $p < 0.05$) and voriconazole (0.586 mg/L and 1.00 mg/L; $p < 0.05$). Against *A. calidoustus* isolates, itraconazole was the most potent agent (GM MIC 1.72 mg/L) followed by posaconazole (2.83 mg/L) and voriconazole (4.18 mg/L), while similar potency was observed for each against *A. versicolor* (GM MIC range 0.812 - 1.00 mg/L). Azole resistance was highest in *A. calidoustus* (range 25% - 88.9%) and *A. lentulus* isolates (25% - 75%), and lowest in *A. fumigatus* (2.58% to 4.06%) and *A. sydowii* (5.6% to 12.5%).

Conclusions: The *in vitro* potency of three triazoles was reduced against rare *Aspergillus* species compared to *A. fumigatus*. Resistance was also observed for each agent against each *Aspergillus* species. Although infections caused by these species are rare, further surveillance studies are needed to monitor their prevalence for antifungal resistance.