Is Azole Prophylaxis in Liver Transplant Recipients Effective in Preventing Invasive Candidiasis in the Era of Emerging Resistance?

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BACKGROUND

- Antifungal prophylaxis (px) in liver transplant (LT) recipients reduces invasive candidiasis (IC) and its associated mortality.
- Studies from our institution (UPMC) and others have shown that targeted px was as effective as universal px. [1]
- Antifungal resistance has emerged among *Candida* spp., with ~7% of the bloodstream isolates tested at CDC resistant to fluconazole. [2]
- We sought to determine if our targeted antifungal px in LT recipients remained effective in the era of rising azole resistance.

METHODS

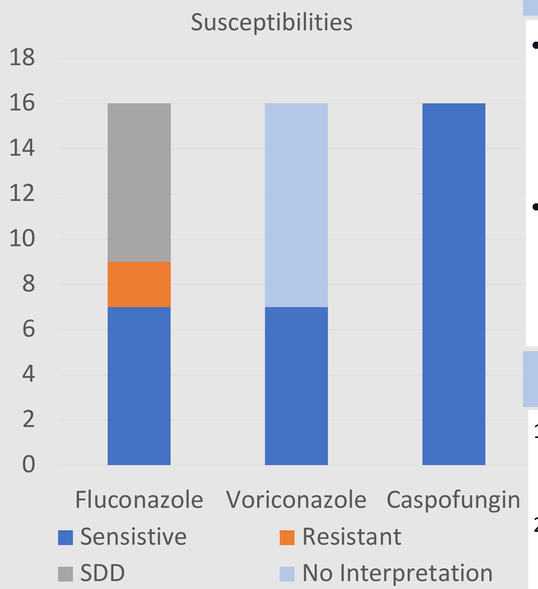
- We performed a retrospective study of patients undergoing LT at UPMC between 11/2010 and 06/2021.
- IC episodes were included if they occurred within 6 months of transplant.
- IC was defined using EORTC/MSGERC criteria, 2020. CLSI's M60 2nd edition was used for antifungal susceptibility interpretation.
- Px was with fluconazole or voriconazole, based on risk factors for yeast or mold infection, respectively.

RESULTS

- 1065 patients (pts) underwent LT over the study period. The most common indications for LT were HCC and NASH cirrhosis.
- Thirty-four pts (3%) developed IC within six months. 74% and 65% of these pts had risk factors for yeast or mold infection at some point, respectively. Twenty-five of 34 (73.5%) pts received antifungal px, with voriconazole most commonly. Sixteen pts with IC (47%) had living donor transplant, and 11 (32%) had Roux-en-Y anastomosis.
- Types of IC were intra-abdominal candidiasis in 19 (56%), fungemia in 11 (32%), and intra-abdominal IC with secondary fungemia in 4 (12%).
- Seventeen (50%) episodes were breakthrough (BT) IC (most BT occurred in the voriconazole group), eight (24%) developed after stopping px, and nine (26%) occurred in those without px.
- *C. albicans* and *C. glabrata* were the most common species. Sixteen isolates (87.5% were from the blood) underwent susceptibility testing: 12% and 44% were resistant and S-DD to fluconazole; none were resistant to voriconazole.
- Attributable mortality of IC was 8%.

Variable	N(%) = 34
Risk Factors for IC	9 (26.4)
Risk Factors for Mold Infection	6 (17.6)
Risk Factors for Both IC and Mold Infection	16 (47)
No Risk Factors for IFI	3 (9)
Antifungal Prophylaxis n(%) • Fluconazole • Voriconazole • Isavuconazole • Echinocandins	25 (73.5) 5 14 5 1

	Breakthrough IC (17 isolates)	Non-breakthrough IC (18 isolates)
C. glabrata	10	5
C. albicans	5	9
C. tropicalis	1	1
Others (*C. parapsilosis*, *C. dubliniensis*)	1	3



CONCLUSIONS

- Targeted antifungal px in LT recipients with fluconazole or voriconazole effectively prevented IC, even in the era of rising azole resistance among *Candida* spp.
- We recommend antifungal susceptibility testing for *Candida* spp. obtained from infected sites to guide antifungal therapy.

REFERENCES

1. Targeted versus Universal Antifungal Prophylaxis among Liver Transplant Recipients. Eschenauer et al. DOI: 10.1111/ajt.12993.
2. Antifungal resistance in *Candida.* Medical illustration of *Candida* spp., presented in CDC's *Antibiotic Resistance Threats in the United States, 2019*.