Efficacy and Safety of Chronic Suppressive Azole Therapy for Endemic Fungal Infections in Solid Organ Transplant Recipients

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Abstract

Background: Solid organ transplant (SOT) recipients are at increased risk of developing severe disseminated endemic fungal infections (EFI). Guidelines recommend prolonged antifungal therapy in the setting of chronic immunosuppression, but there is no evidence to support this approach. While a limited treatment course reduces the risk of drug interactions related to CYP3A4 inhibition, prolonged azole therapy may prevent reactivation of EFI. A single-center, retrospective study assessed the efficacy and safety of chronic suppressive azole therapy for SOT recipients with EFI.
Methods: A retrospective analysis was conducted on SOT recipients diagnosed with EFI between 1 January 2005 and 31 December 2014 and treated with azole therapy for more than a year as of 1 January 2016. Safety endpoints included adverse reactions and drug interactions. Efficacy was defined as preventing EFI reactivation.
Results: Using microbiology and billing records, we identified 15 SOT recipients (7 kidney, 3 kidney-pancreas, 3 heart, 2 liver) diagnosed with EFI who were treated with chronic suppressive azole therapy (Figure 1). A total of 7 histoplasmosis, 5 blastomycosis, and 3 coccidioidomycosis infections were identified. Disseminated infection occurred in 7 (47%) patients. The median length of azole therapy was 6 years (range 2-10). Three (20%) patients experienced an adverse reaction to itraconazole (level range 0-1.6 mcg/mL). Symptoms included nausea, vomiting, and lower extremity edema. Adverse reactions occurred within 3 months of starting itraconazole and patients were transitioned to another azole with minimal side effects. There was one adverse drug interaction; itraconazole was discontinued after 4 years of treatment in a patient with asymptomatic bradycardia on amiodarone. Allograft rejection occurred in 4 patients. There were no episodes of EFI reactivation.
Conclusions: Chronic suppressive azole therapy was safe and effective among SOT recipients. Most adverse reactions occurred when azole therapy was initiated; otherwise, prolonged treatment was well tolerated. All patients with adverse reactions were successfully transitioned to an azole with minimal side effects. Prolonged azole therapy can effectively treat and prevent EFI.

Background

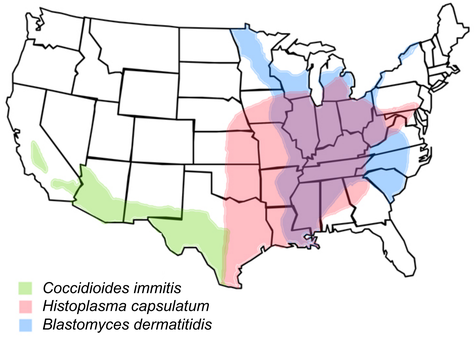


Figure 1. Geographic Regions with Endemic Fungal Infections

- Solid organ transplant (SOT) recipients are at increased risk of severe disseminated endemic fungal infections (EFI).
- There are no evidence-based guidelines on the optimal length of therapy during chronic immunosuppression.
- Limited azole course reduces the risk of drug interactions related to CYP3A4 inhibition.
- However, prolonged azole therapy may prevent reactivation of endemic fungal infections.

Photo credit: www.studyblue.com

Methods

- A single-center, retrospective study was performed to assess the safety and efficacy of chronic suppressive therapy for EFI in SOT recipients.
- The study population included SOT recipients diagnosed with EFI between 1 January 2005 and 31 December 2014
- Chronic suppressive azole therapy was defined as having treatment with azole therapy for more than a year as of 1 January 2016.
- Safety endpoints included adverse reactions and drug interactions.
- Efficacy was defined as preventing fungal reactivation.

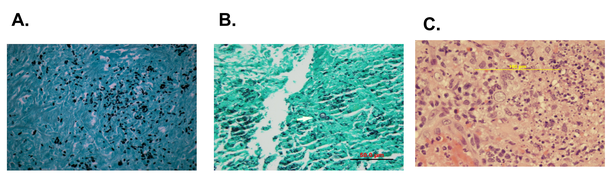


Figure 2. Histological Findings from SOT Recipients Diagnosed with EFI.

A. Histoplasma capsulatum on Grocott's Methenamine Silver Stain (GMS) of Lymph Node Biopsy.

B. Blastomyces dermatitidis on GMS Stain of Skin Biopsy.

C. Coccidioides immitis on Periodic-Acid Schiff Stain of Skin Biopsy.

Results

1. Patient Characteristics

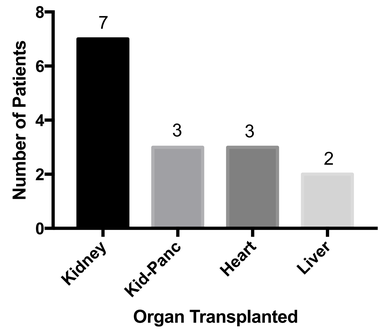


Figure 3. SOT Received among Patients with EFI (n=15).

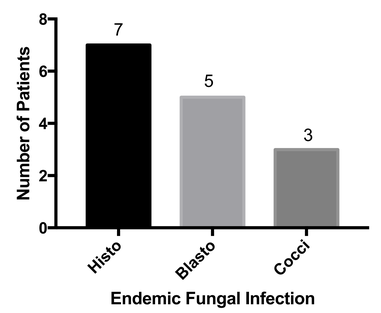


Figure 4. Endemic Fungal Infection Types among SOT Recipients (n=15).

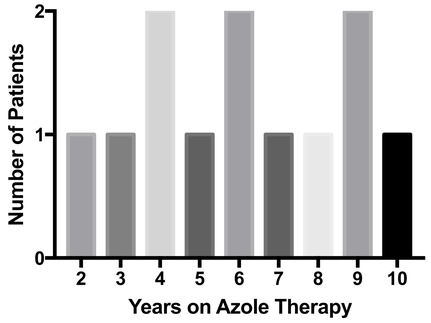
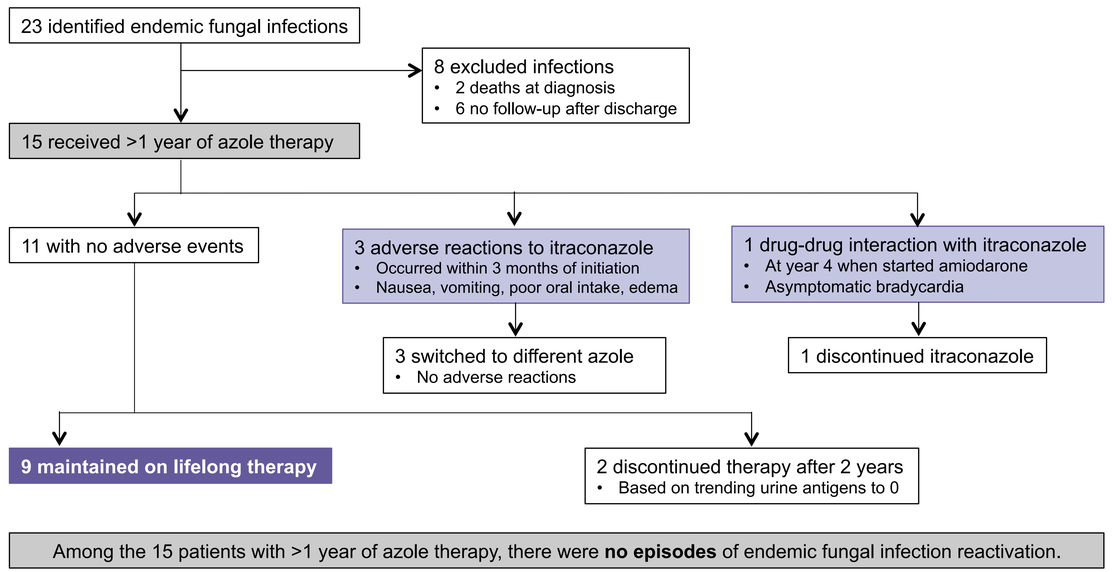


Figure 5. Length of Azole Therapy among SOT patients with EFI (n=15). The median length of therapy was 6 years.

2. Safety and Efficacy of Chronic Suppressive Azole Therapy



Conclusions

- Chronic suppressive azole therapy was safe and effective among SOT recipients.
- Most adverse reactions occurred within 3 months of azole initiation; prolonged treatment was well tolerated.
- All patients with adverse reactions were successfully transitioned to a different azole with no side effects.
- Prolonged azole therapy can effectively treat and prevent endemic fungal infections.