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; 2 patients were switched to another azole with minimal side effects. There was one adverse drug interaction; itraconazole was discontinued for 4 years of treatment in a patient with asymptomatic bradycardia on amiodarone. All patients with adverse reactions were successfully transitioned to another azole with minimal side effects. Prolonged azole therapy can effectively treat and prevent EFI.

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 a different azole with no side effects. Efficacy and Safety of Chronic Suppressive Azole Therapy for Endemic Fungal Infections in Solid Organ Transplant Recipients

2. Safety and Efficacy of Chronic Suppressive Azole Therapy

23 identified endemic fungal infections
15 received >1 year of azole therapy
8 excluded infections
• 5 deaths at diagnosis
• 3 no follow-up after discharge
11 with no adverse events
3 adverse reactions to itraconazole
• Occurred within 3 months of initiation
• Nausea, vomiting, poor oral intake, edema
1 drug-drug interaction with itraconazole
• Allopurinol year when started amiodarone
• Asymptomatic bradycardia
9 maintained on lifelong therapy
3 switched to different azole
• No adverse reactions
1 discontinued itraconazole
2 discontinued therapy after 2 years
• Based on trend of urine antigens to 0

Among the 15 patients with >1 year of azole therapy, there were no episodes of endemic fungal infection reactivation.

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.