
POSACONAZOLE TREATMENT FOR REFRACTORY OROPHARYNGEAL CANDIDIASIS: A REPORT OF TWO CASES

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Purpose: More than 90% of patients with acquired immunodeficiency syndrome (AIDS) will develop oropharyngeal or esophageal candidiasis (OPC/EC) at least once during their illness. The discomfort of OPC/EC interferes with adequate food and fluid intake and oral medical therapy, resulting in a vicious cycle that compromises both quality of life and overall survival. Typical treatment options include orally administered azoles in either locally or systemically active forms. However, the long-term clinical utility of azoles is often limited by the development of clinical resistance, characterized by increased MIC values and the inability to control symptoms on the usual prescribed regimens. When oral therapy fails, parenteral therapy is an expensive option that cannot be sustained long-term.

Posaconazole is a triazole antifungal agent with potent in vitro activity against a wide array of moulds and yeasts, including azole-resistant *Candida* spp. In vitro studies with *C. albicans* have shown that multiple mutations in *ERG11* are required before resistance to posaconazole develops. In humans, posaconazole was found to be as effective and safe as fluconazole for the treatment of OPC in a randomized, evaluator-blinded study of adults infected with human immunodeficiency virus (HIV). As an oral suspension, posaconazole may offer the additional benefit of providing both systemic and topical activity in patients with OPC.

Clinical problem: Two male, HIV-infected patients were considered to have refractory OPC after conventional therapies failed to produce a sustained clinical response. Both patients had a past medical history of chronic neutropenia.

Clinical approach: Posaconazole oral suspension 800 mg/day was administered in divided doses in an open-label clinical study.

Patient Outcome: Each patient was initially treated with fluconazole but eventually developed fluconazole-resistant disease. Although subsequent treatment with itraconazole or voriconazole resulted in initial clinical improvements, the patients' OPC eventually relapsed. Shortly after posaconazole therapy was initiated, both patients experienced complete resolution of their OPC and its associated symptoms (ie, pain, dysphagia, esophagitis within 72 hours). Seventy-two hours of noncompliance with posaconazole therapy resulted in recurrence of OPC symptoms; however, resolution of all symptoms were noted when posaconazole therapy was resumed. Currently both patients are symptom free and considered clinical successes.

Conclusions: The successful outcomes of these two cases, which demonstrate that posaconazole is an effective treatment for OPC that had failed all other available azole alternatives, are in agreement with the results of earlier clinical and in vitro studies. Posaconazole caused rapid resolution of all clinical signs and symptoms of OPC, even in recurrent, relapsing disease. Recurrence of symptoms was primarily associated with noncompliance to therapy, but symptoms quickly resolved when posaconazole therapy was resumed. Posaconazole appears to be a promising potential alternative to parenteral antifungal agents for treatment of patients with OPC or EC who have failed other oral azoles.