SHORT REPORTS

Intraperitoneal Voriconazole in a Patient with *Aspergillus* Peritoneal Dialysis Peritonitis

KEY WORDS: Fungal peritonitis; voriconazole.

Fungal peritoneal dialysis (PD)–associated peritonitis is associated with high rates of hospitalization and death (1,2). Standard treatment includes antifungal therapy, removal of the PD catheter, and transfer to hemodialysis (2). In the case of *Aspergillus* infections, treatment regimens based on amphotericin and flucytosine are complicated by side effects, and so alternative therapies should be explored (1).

A 49-year-old man diagnosed with a culture-negative PD-associated peritonitis was treated with intraperitoneal (IP) meropenem and vancomycin for 3 weeks. At the conclusion of treatment, the PD effluent had cleared, and the man embarked on a holiday to Australia. One week after arrival, he presented to hospital with a 2-day history of difficulty with PD exchanges and cloudy effluent, but no abdominal pain or systemic symptoms of infection. Microscopic review of the PD effluent was consistent with PD peritonitis, and empiric IP cephalothin and gentamicin were commenced. Turbidity of the PD fluid was slow to clear, and symptoms of anorexia and lethargy increased. Three days later, *Aspergillus flavus* was isolated in effluent.

Unfortunately, the patient's travel insurance did not cover treatment of his condition, and the private cost was high. After extensive discussion, he decided to return home for definitive treatment. While awaiting the next flight, treatment included CAPD (2.5-L exchanges, 4 times daily), once-daily IP voriconazole 200 mg (2.5 mg/kg), and careful monitoring. We elected to administer the parenteral formulation IP to maximize the concentration in the peritoneal space. It was highlighted to the patient that, under current standards (2), retaining the PD catheter was suboptimal treatment and that his infection could progress. Further, we were not aware of any published experience with IP administration of voriconazole, and so its use was experimental.

The patient was reviewed daily, and a blood sample was obtained before each dose of voriconazole for drug monitoring. Voriconazole administration generated no discomfort, and the PD effluent cleared; however, only a slight symptomatic improvement occurred. The man flew home 72 hours post diagnosis, the PD catheter was removed 72 hours later, and hemodialysis was subsequently commenced and progressed well.

Drug monitoring confirmed that voriconazole was absorbed from the peritoneal compartment and also that a therapeutic plasma concentration [>1 mg/L (3)] was achieved by 48 hours after therapy initiation. Before the present report, it was not known whether voriconazole would distribute from the peritoneal space, thereby treating systemic infection or predisposing the patient to adverse effects. Voriconazole has unpredictable pharmacokinetics because of saturable drug metabolism and also drug–drug interactions (although none were present in this patient), and so drug monitoring is recommended. The voriconazole concentration in the effluent was consistently lower than that in the plasma (data not shown), which might reflect protein binding (the protein concentration in the PD effluent was not determined) or slower redistribution from plasma to the peritoneal space, which may limit the efficacy of oral or intravenous therapy.

More research is required to determine whether IP voriconazole is effective in the treatment of fungal PD peritonitis. It would also be interesting to confirm our observation that voriconazole may distribute slowly into the peritoneal space from the systemic circulation, because such a finding would further support the requirement for IP administration when the PD catheter is retained.

DISCLOSURES

The authors have no financial conflicts of interest relevant to this report to declare.

Darren M. Roberts^{1*}
Geoffrey Kauter¹
John E. Ray²
Adrian G. Gillin¹

Department of Renal Medicine¹
Royal Prince Alfred Hospital, Camperdown
Department of Clinical Pharmacology²
St. Vincent's Hospital, Darlinghurst
New South Wales, Australia

*email: 1darren1@gmail.com

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