nes et al. [1] was done at a long-term care facility, where the length of stay is much longer; our patients were treated in an acute-care hospital, where the length of hospital stay is shorter (table 1). Because of the retrospective nature of our study, we do not have data on any patient who may have developed diarrhea after discharge from the hospital. An additional factor may be the more strictly followed infection-control measures in an acute-care facility, compared with a long-term care facility. The second finding of our study is that a significantly higher percentage of patients developed non-CDAD infection-control measures in an acute-care hospital, where the length of stay is much longer.

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However, most of these cases are not CDAD.

Acknowledgment

Conflict of interest. All authors: No conflict.

Aman Khurana, Namita Vinayek, Rose A. Recco, Eddie S. Go, and Muhammad M. Zaman
Department of Medicine, Division of Infectious Diseases, Coney Island Hospital, Brooklyn, New York

References


Pharmacokinetics of Voriconazole in the Cerebrospinal Fluid of an Immunocompromised Patient with a Brain Abscess Due to Aspergillus fumigatus

Sir—In a recent article, Lutsar et al. [1] reported voriconazole concentrations in the CSF. We report our experience. A 51-year-old woman with a liver graft was given voriconazole for a brain abscess due to Aspergillus fumigatus. External ventricular drainage was performed for compression of the fourth ventricle. On the basis of NCCLS breakpoints, the A. fumigatus species was susceptible to voriconazole (MIC, 0.125 mg/mL) [2]. The patient received intravenous voriconazole (200 mg b.i.d., adjusted to her weight [40 kg]) after a dosing charge. With this treatment, the volume of the abscess slowly decreased, as noted on CT scans during follow-up.

Because we had easy access to CSF specimens as a result of the external ventricular drainage, we measured the concentration of voriconazole in the CSF on day 11 after the course of voriconazole therapy was started. Voriconazole concentrations were measured 2, 4, 6, 8, 10, and 12 h after the commencement of intravenous administration. CSF samples were obtained via the external ventricular drainage and were immediately frozen at −20°C until analysis. The assays were performed using high-performance liquid chromatography coupled with a diode array detector method, as described elsewhere [1]. At the time of sampling, the patient had also been receiving prazosine, paroxetine, nicardipine, metopimazine, and tacrolimus for several weeks. The CSF concentrations of voriconazole were 0.08–0.17 mg/L (median,
0.135 mg/L), with a maximum concentration 6 h after injection.

These values are in the low range, compared with previously reported ranges [1, 3]. In those 2 reports, information concerning liver function and the concomitant drugs received are not available. These low concentrations are similar to the MICs of the Aspergillus species and can explain the slow evolution of the abscess.

Three main explanations can be invoked for these low values. Pharmacokinetic interactions do not explain the low concentrations. With regard to the drugs the patient received, the interaction between tacrolimus and voriconazole leads to a higher concentration of tacrolimus and not to a lower concentration of voriconazole [4]. We did not find obvious interactions between voriconazole and prazosine, paroxetine, nicardipine, or metopimazime.

We can assess that the liver graft was not involved in these low concentrations of voriconazole, because it exhibited normal function. The sampling procedure can perhaps explain the low results. The CSF specimen was collected during 2 h through the intraventricular catheter. Therefore, the in vitro instability of voriconazole and/or adsorption of voriconazole on the lines and collection materials of the intraventricular derivation are able to decrease measured CSF concentrations. Furthermore, we noticed in the previously reported data from Lutsar et al. [1] that, among samples that yielded the 7 lowest concentrations found (which were similar to ours), 4 samples were obtained through an intraventricular catheter. A nonhomogeneous distribution of voriconazole resulting from compression of the fourth ventricle could also explain the lower concentrations in ventricles, compared with the concentration expected from a lumbar puncture.

In conclusion, voriconazole is highly active against Aspergillus species, but additional studies are needed to confirm that our low drug concentrations result from the method of sampling and not from poor efficacy of this molecule in the CSF.

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References


Use of Clinical Criteria and Molecular Diagnosis to More Effectively Monitor Patients Recovering after Severe Acute Respiratory Syndrome Coronavirus Infection

In early 2003, a novel severe acute respiratory syndrome (SARS) coronavirus (CoV) [1] spread around the world; ultimately, more than 8000 patients in 32 countries contracted SARS, many of whom died. Although gold standard methods, such as viral culture, can help diagnose SARS, these methods are by no means as efficient and rapid as PCR-based diagnostic tests. The speed and sensitivity of molecular diagnostic tests for SARS is often considerably greater than that of serological and viral culture methods [2]. Our reported enhanced real-time PCR (ERT) method [3, 4] is 100-fold more sensitive than conventional real-time PCR. The higher sensitivity of this method may reveal potential SARS CoV carriers who have SARS CoV levels that are undetectable by other methods, and the sensitivity of the ERT method may be particularly important for ensuring that patients who have had SARS are not infectious before discharge from the hospital [5].

In collaboration with Princess Margaret Hospital (PMH; Hong Kong), samples obtained from 3 patients during recovery after SARS were analyzed (table 1). Six to nine weeks after the onset of infection, SARS CoV could still be detected by ERT in certain samples (table 1), indicating that, although clinical signs and symptoms had subsided and a host immune response had been mounted, viral clearance was not complete. Patient 1 was transferred on 17 June 2003 to the Wong Tai Sin Hospital (WTSH; Hong Kong), which was converted into a specialized center for convalescent care of patients with SARS during the epidemic, but he was returned to PMH because of recurrent pneumothorax, indicated by chest radiography on 18 June. The ERT method clearly demonstrated the presence of SARS CoV in all samples obtained from the patient on 16 June (table 1), which was 1 day before his transfer to WTSH. The possible relapse of infection in patient 1 after his transfer to another hospital indeed raises the question of how patients with SARS who have PCR results negative for SARS CoV should be handled [5]. Standardization of clinical criteria and PCR-based methods should be emphasized to ensure accurate diagnosis of SARS after hospital admission and prior to hospital discharge. More studies will be necessary to determine the infectivity status of patients who have ERT results positive.