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Transparency declarations

None to declare.

References


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Ceftaroline CSF concentrations in a patient with ventriculoperitoneal shunt-related meningitis

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Sir,

Ceftaroline is a cephalosporin antibiotic indicated for the treatment of acute bacterial skin and skin structure infections and community-acquired bacterial pneumonia.1 Ceftaroline has been used for non-FDA-approved indications, including osteomyelitis, endocarditis, bacteraemia and epidural abscesses.2 – 5 Data on use for meningitis are limited to two rabbit models, showing penetration into CSF of 14% – 15% in inflamed meninges and 3% in uninfammed meninges.6,7 The distribution of drugs into the CSF is dependent upon multiple factors, including their lipophilicity, plasma protein binding and molecular size, and the affinity of active transport mechanisms to remove them from the CNS.8

Ceftaroline has low protein binding, is hydrophilic and has a similar volume of distribution to other cephalosporins.1 Cephalosporins distribute into the CSF relatively poorly, averaging AUCCSF/AUCserum ratios of 0.007 – 0.1 for uninfammed or mildly inflammed meninges and 0.15 for strongly inflammed meninges. However, due to their potency, many cephalosporins achieve therapeutic CSF concentrations.8 We report a case of ceftaroline for the treatment of MRSA meningitis related to an infected ventriculoperitoneal (VP) shunt. This case report was reviewed and approved by our Institutional Review Board.

A patient presented with altered mental status and lethargy for 24 h. The patient had a history of hydrocephalus with chronic VP shunt placement and 1 month prior had undergone shunt replacement due to infection with methicillin-resistant Staphylococcus epidermidis, which was treated with vancomycin.

On presentation, vitals were stable. However, the patient suddenly desaturated to 40% oxygen on room air and was intubated. The white blood cell count was 23.6/mm3 with 93% segmented neutrophils and 4% bands. Arterial blood gas results were pH 7.55, pCO2 29 mmHg, pO2 216 mmHg and HCO3 25.4 mmol/L. Serum creatinine was 0.5 mg/dL, which remained stable with an estimated creatinine clearance of >100 mL/min throughout admission. A CT scan showed new prominent dilatation of the lateral ventricles. The patient was diagnosed with obstructive hydrocephalus and taken to the operating room. Cefazolin was administered for surgical prophylaxis and a proximal shunt malfunction was addressed with insertion of a new proximal catheter. CSF was drawn from the shunt and sent for culture. The patient was transferred to the ICU.

On day 1 of admission, the CSF Gram stain report showed Gram-positive cocci in pairs and clusters. Fluid count was not completed. Infectious diseases consultation was requested for meningitis. On day 2, the patient became febrile at 39.1°C and was taken to the operating room for removal of the shunt and placement of an external ventricular drain. A repeat CSF culture and the VP shunt tip were sent for analysis. The patient was started on linezolid, ceftriaxone and nafcillin and then switched to 600 mg of ceftaroline intravenously every 8 h on day 3. Vancomycin was avoided given recent use and concern for treatment failure. The CSF culture from day 1 was finalized as MRSA with a ceftaroline MIC = 1.0 mg/L by Etest8. The CSF culture from day 2 was finalized as negative, while the shunt tip grew MRSA. By the time of finalization, the patient had been started on ceftaroline and had additional repeat CSF cultures that were negative so ceftaroline was continued. Due to the lack of data on the use of ceftaroline for meningitis, samples of
CSF from the external ventricular drain and blood were sent for analysis. CSF samples were cultured an additional seven times during the admission and were negative. On day 14, the patient developed *Serratia marcescens* line-related bacteraemia with a ceftaroline MIC=1.5 mg/L by Etest®. Gentamicin and meropenem were started empirically and streamlined to ciprofloxacin after final susceptibilities were reported. Repeat blood cultures were negative. On day 23 a new VP shunt was placed. The patient received ceftaroline and ciprofloxacin until discharge on day 27, at which point oral linezolid and ciprofloxacin were prescribed for an additional 7 days.

Simultaneous ceftaroline blood and CSF samples were collected 6 and 7 days into therapy. The blood samples were centrifuged and CSF and blood samples were frozen at −70°C. The samples were mailed on dry ice to Keystone BacteriaLabs, which analysed them by liquid chromatography–MS. All storage and handling instructions were strictly followed. Results are shown in Table 1.

By the time of CSF analysis, the patient’s symptoms of infection had abated and it is likely that little-to-no meningeal inflammation remained. Thus, the CSF:plasma ratios of 0.035 and 0.041 are consistent with those of other β-lactams in this clinical situation. Although the patient’s clinical picture resolved while receiving ceftaroline, we cannot be sure that ceftaroline was the reason since the patient’s CSF cultures cleared before it was initiated. While the drug levels from this patient help assess ceftaroline CSF penetration, we believe that ceftaroline levels collected during acute meningitis should be measured to determine the likely role of ceftaroline in the treatment of CNS infections.

### Table 1. Ceftaroline concentrations in the plasma and CSF

<table>
<thead>
<tr>
<th>Ceftaroline doses prior to sample collection (no.)</th>
<th>Timing of sample collection</th>
<th>CSF (mg/L)</th>
<th>Plasma (mg/L)</th>
<th>CSF:plasma ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>1.5 h after end of infusion of previous dose</td>
<td>0.461</td>
<td>11.323</td>
<td>0.041</td>
</tr>
<tr>
<td>17</td>
<td>0.5 h before next scheduled dose</td>
<td>0.190</td>
<td>5.428</td>
<td>0.035</td>
</tr>
</tbody>
</table>

**References**


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This study was carried out as part of our routine work.

**Transparency declarations**

J. C. G. is a speaker for Forest, Cubist and Astellas, he is a consultant for Merck. S. S. K. and M. R.: none to declare.

**References**


**Keywords**: elite controllers, PBMCs, interferon, IFN.

Sir, 
Rivera-Muñoz et al. recently reported that HIV-1 elite suppressors (ES), who maintain low viral loads without pharmacological intervention, also maintain higher levels of restriction factor SAMHD1 transcript than either healthy donors (HD) or viraemic progressors (VP) in PBMCs. This compelling finding applied to individuals with and without protective HLA-B alleles. As the authors astutely stated, however, increased SAMHD1 ‘may not be a cause but the consequence’ of suppression. Beyond this caveat, it is