Vancomycin Clearance in an Infant Receiving Extracorporeal Liver Support and Continuous Renal Replacement Therapy

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BACKGROUND

- In the United States, the Food and Drug Administration (FDA) approved extracorporeal liver support (ELS) with albumin assisted dialysis to treat drug overdose and hepatic encephalopathy in patients with end stage liver failure.1,14 ELS uses a dialysate of human serum albumin to remove albumin-bound substances, such as bilirubin and bile acids, in addition to water-soluble products.3

- At our institution, we use albumin assisted dialysis in conjunction with continuous venous hemodiafiltration (CVVHDF) for patients with liver and kidney failure. These critically-ill patients on multiple extracorporeal therapies are vulnerable to gram-positive nosocomial infections and may require treatment with vancomycin.

- The clearance of vancomycin has been studied in patients on CVVHDF. Vancomycin was found to exhibit a sieving coefficient of 0.7, nearly equivalent to urea clearance in patients undergoing CVVHDF.7 As a significant portion of vancomycin (67%) circulates bound to protein, we expect enhanced vancomycin clearance via albumin assisted dialysis compared to CVVHDF.2 Currently, there are no published reports describing the pharmacokinetics of vancomycin in patients on albumin assisted dialysis.

CASE REPORT

- We report a case of an 8-month-old full-term male with biliary atresia and failed Kasai procedure, who was transferred to our institution for liver transplant evaluation and was treated with vancomycin. His post-operative course had been complicated by intestinal perforation, peritonitis, severe liver failure, pulmonary and gastrointestinal hemorrhage, cardiac insufficiency, and respiratory failure.

- Hospital Day 2: Started CVVHDF with pre-filter replacement (2000 ml/1.73m²/h) for 30% fluid overload and acute kidney injury

- Hospital Day 6: Increased CVVHDF diffusive clearance to 8000 ml/1.73m²/h for hyperammonemia (215 μmol/L)

- Hospital Day 7: Initiated ELS with molecular adsorbent recirculating system (MARS [Baxter, USA]) therapy for hepatic encephalopathy
  - Conducted 27 ELS treatments (2000-4000 ml/1.73m²/h), averaging 8 hours in duration, from days 7 to 62 until successful liver transplantation

- During the hospitalization, the patient had multiple episodes of sepsis. He received one 14-day course and 4 shorter courses of vancomycin. Multiple vancomycin levels were drawn to assess need for dose adjustments with his extracorporeal therapies. Vancomycin levels were found to be lower during ELS therapy than during CVVHDF alone, indicating increased clearance with albumin assisted dialysis (Table 1). The patient required 15 mg/kg/dose of vancomycin administered every 8 hours to maintain trough levels of 5-10 mg/L. This daily dose is more than two-fold higher than standard empiric dosing recommendations for adult patients on CVVHD in established drug references.6

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DISCLOSURES

The authors report no financial conflicts of interest related to the content of this presentation.

REFERENCES


TABLE 2. VANCOMYCIN MONITORING FOR PATIENTS ON ELS

<table>
<thead>
<tr>
<th>Time on ELS</th>
<th>Monitoring</th>
</tr>
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<tbody>
<tr>
<td>Days 1-3</td>
<td>1) Draw random vancomycin level immediately prior to initiation of ELS if no level obtained in the past 2 hours.</td>
</tr>
<tr>
<td></td>
<td>2) Draw a second random vancomycin level: o 4 hours after ELS initiation OR o Prior to next scheduled vancomycin dose if dose will be given before 4 hours of ELS treatment</td>
</tr>
<tr>
<td></td>
<td>3) Draw random levels every 4 hours until ELS treatment is over. **If level is below the trough goal, administer a one-time dose of vancomycin (15 mg/kg) and recheck level every 4 hours until ELS treatment is over.</td>
</tr>
<tr>
<td>Days 4+</td>
<td>1) If ELS and CRRT settings are unchanged from previous days: o Administer vancomycin doses during ELS consistent with previous days. No levels required. o If patient has not required supplemental dosing, discontinue monitoring during ELS.</td>
</tr>
<tr>
<td></td>
<td>2) If ELS and CRRT settings are changed, restart “Day 1-3” vancomycin monitoring and draw levels as specified.</td>
</tr>
</tbody>
</table>

TABLE 1. VANCOMYCIN LEVELS ON CVVHDHF and ELS

<table>
<thead>
<tr>
<th>Vancomycin Level</th>
<th>CVVHDHF only</th>
<th>ELS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of Levels</td>
<td>Median time after dose</td>
</tr>
<tr>
<td>&lt; 5 mg/L</td>
<td>0</td>
<td>--</td>
</tr>
<tr>
<td>5 - 14.9 mg/L</td>
<td>22</td>
<td>7 hours (IQR 6.1-7.5)</td>
</tr>
<tr>
<td>≥ 15 mg/L</td>
<td>6</td>
<td>4.9 hours (IQR 4.1-5.5)</td>
</tr>
</tbody>
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