Optimal Cefazolin Dosing Recommendations in Patients Receiving Home Hemodialysis
Differ from Those for Conventional Hemodialysis

Cefazolin Dosing Recommendations in Patients Receiving Home Hemodialysis with Monte Carlo Simulation

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Background
• Home hemodialysis (HHD) uses different dialysis regimens including frequency, duration, and dialysate volume from those in conventional thrice-weekly intermittent hemodialysis.
• HHD is increasingly used because its increased frequency and longer duration has shown to benefit patient outcome.
• Cefazolin is commonly prescribed in end stage kidney disease (ESKD) patients receiving dialysis.
• Recommended cefazolin doses for intermittent hemodialysis will not likely be optimal for patients receiving home hemodialysis.

Objective
• This study was to predict optimal cefazolin dosing regimens in patients receiving common HHD regimens, using the Monte Carlo simulation techniques.

Methods
I. Pharmacokinetic Modeling
• A one-compartment, first order pharmacokinetic (PK) model was built using body weight data from patients receiving HHD in Fresenius outpatient dialysis centers and published pharmacokinetic (PK) data in ESKD patients receiving high-flux dialysis to predict one-week of cefazolin exposure in 5,000 virtual patients 1,4 (Table 1).
• All patients were assumed to be anuric.

II. HHD Settings
• Ten HHD settings commonly used in outpatient dialysis center were modeled and differed in duration, dialysis frequency/schedule, and dialysate volume:
  1. 3-hour diurnal HHD occurring 4x/week (M-T-Th-F) with total dialysate volume 30L, 40L or 50L
  2. 3-hour diurnal HHD occurring 5x/week (M-T-W-Th-F) with total dialysate volume 20L or 30L
  3. 7-hour nocturnal HHD occurring every other day with total dialysate volume 30L, 50L or 60L
  4. 7-hour nocturnal HHD occurring 5x/week (M-T-W-Th-F) with total dialysate volume 30L or 60L

III. Pharmacodynamic Targets 5-6
• Pharmacodynamic target was ≥60% free serum concentrations above 4 times the minimum inhibitory concentration (RT=4xMIC; MIC=8 mg/L for Staphylococcus aureus).
• The smallest doses attaining probability of target attainment ≥90% during 1-week of therapy were considered optimal.

Results
• Optimal cefazolin doses in ten HHD regimens were different on interdialytic-period (e.g. 1-3 days) and the prescribed dialysate volume (Table 2).

Discussion & Conclusion
• This is the first PK modeling simulation to determine the optimal cefazolin dosing regimen in realistically estimated ESKD patients receiving HHD.
• MCS predicted that optimal cefazolin dosing recommendations for HHD patients are 1g LD, followed by 500-700 mg post HHD and differ from those for conventional thrice-weekly hemodialysis.
• These dosing recommendations should be clinically validated.

References
1. Internal data from the NxStage

Acknowledgments
This research project was funded by NxStage Medical Inc.
• Authors declare no conflict of interest.

Table 1. Demographic & PK data
<table>
<thead>
<tr>
<th>Body weight (kg)</th>
<th>Vd (L/kg)</th>
<th>Non-renal CL (L/hr)</th>
<th>Protein binding (%)</th>
<th>Saturation coefficient (SA)</th>
</tr>
</thead>
<tbody>
<tr>
<td>93.5 ± 30</td>
<td>0.10839 ± 0.01574</td>
<td>0.1716 ± 0.039</td>
<td>80</td>
<td>0.1-0.2</td>
</tr>
</tbody>
</table>

Table 2. Optimal Cefazolin Doses in 10 HHD Settings

<table>
<thead>
<tr>
<th>HHD Type</th>
<th>HHD Frequency (Days/week)</th>
<th>Dialysate Volume (L/HHD)</th>
<th>Optimal Initial Cefazolin Dose for a Week</th>
</tr>
</thead>
<tbody>
<tr>
<td>3-Hour Diurnal</td>
<td>4 (M-T-Th-F)</td>
<td>30</td>
<td>1g LD-750mg-500mg-750mg post-dialysis</td>
</tr>
<tr>
<td></td>
<td>5 (M-T-W-Th-F)</td>
<td>50</td>
<td>1g LD-500mg-500mg-500mg post-dialysis</td>
</tr>
<tr>
<td>7-Hour Nocturnal</td>
<td>3.5 (M-W-F-Sun)</td>
<td>30</td>
<td>1g LD-750mg post-dialysis</td>
</tr>
<tr>
<td></td>
<td>5 (M-T-W-Th-F)</td>
<td>60</td>
<td>1g LD-500mg-500mg-500mg post-dialysis</td>
</tr>
</tbody>
</table>

LD: loading dose