Pharmacokinetic Study of Cefazolin in Short Daily Hemodialysis

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BACKGROUND
• Short daily hemodialysis (SDHD) involves 2 hours of dialysis, 6 days of the week
• SDHD has been associated with decreased cardiovascular risk, improved quality of life, and a trend towards prolonged survival
• Infection is a leading cause of morbidity and mortality in dialysis patients
• Gram-positive organisms are the leading cause of infection in hemodialysis patients
• Little is known about the pharmacokinetics and optimal dosing of cefazolin in SDHD

OBJECTIVES
Primary Objective:
• Determine clearance of cefazolin by SDHD
Secondary Objectives:
• Characterize other pharmacokinetic parameters
• Determine if current dosing regimens provide serum drug concentrations above target MICs

METHODS
Sample Collection and Analysis
• Six blood samples and two diastolic samples per patient were drawn over a 24 hour period

RESULTS
RESULTS
• Five patients enrolled and completed the study. Baseline demographics are shown in Table 1

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>62</td>
<td>61</td>
<td>72</td>
<td>85</td>
<td>56</td>
</tr>
<tr>
<td>Gender</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>86.4</td>
<td>80.4</td>
<td>60.8</td>
<td>48.5</td>
<td>137.5</td>
</tr>
<tr>
<td>Cause of ESRD</td>
<td>DM2</td>
<td>DM2</td>
<td>DM2</td>
<td>DM2</td>
<td>DM2</td>
</tr>
<tr>
<td>Vintage of dialysis</td>
<td>2 months</td>
<td>16 months</td>
<td>10 years</td>
<td>5 months</td>
<td>30 years</td>
</tr>
<tr>
<td>Residual renal function* (mL/min)</td>
<td>7.11</td>
<td>7.59</td>
<td>0.55</td>
<td>5.62</td>
<td>Anuria</td>
</tr>
</tbody>
</table>

Pharmacokinetic parameters were calculated using a one-compartment model. See Table 2
• No adverse events were reported

Table 2: Pharmacokinetic Parameters
<table>
<thead>
<tr>
<th>Parameters</th>
<th>End Observed Conc. (SDHD)</th>
<th>SDHD Removal</th>
</tr>
</thead>
<tbody>
<tr>
<td>CL (L/h)</td>
<td>[1] 0.83  [2] 0.81  [3] 0.64  [4] 0.53</td>
<td></td>
</tr>
</tbody>
</table>

Pharmacokinetic Parameters
• Small number of patients and variability in the parameters limit the analysis of results
• Further study is required with a larger cohort of patients

Assess Current Dosing Regimen
• Staphylococcus aureus breakpoint MIC for cefazolin is 4 ug/mL
• Aim for four to eight times the MIC of the bacteria (i.e. 32 ug/mL)
• All observed and calculated cefazolin plasma concentrations between dialysis sessions were above 32 ug/mL

CONCLUSION
• Estimated SDHD clearance (41.9 mL/min) is higher than with intermittent hemodialysis (30.9 mL/min) using similar dialyzers
• Current dosing recommendations of cefazolin 1 gram infused over the last 20 minutes of SDHD appear to produce adequate plasma concentrations for bacterial eradication

Legend
B1-B6: Blood Samples 1-6: Dialysis Samples

Figure 1: Observed plasma cefazolin concentration versus time curves for patient 1-5.

Figure 2: Observed plasma cefazolin concentration versus time curve, with back extrapolation to initial concentration after first cefazolin infusion for Patient 2.

Modeled Cefazolin Dosing in Practice