Harnessing Intermittent Hemodialysis to Study Individual Pharmacokinetics

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Piperacillin Pharmacokinetics

4g/h IV

4 x minimum inhibitory concentration

(4 x MIC = 64mg/l)
Hemodialysis
Piperacillin Pharmacokinetics with Hemodialysis

4 g/h IV

4 x minimum inhibitory concentration
(4 x MIC = 64 mg/l)
Two-Compartment Model

\[ \begin{align*}
  &\quad c_1 \\
  &\quad \downarrow k_{10} + k_D \\
  \quad &\quad \downarrow d \\
  &\quad c_2 \\
  &\quad \uparrow k_{21} \\
  &\quad \uparrow k_{12}
\end{align*} \]
Two-Compartment Model

\[ \frac{dC_1}{dt} = \frac{d}{V_1} - (k_{10} + k_D)C_1 - k_{12}C_1 + k_{21}C_2 \]

\[ \frac{dC_2}{dt} = +k_{12}C_1 - k_{21}C_2 \]
Two-Compartment Model: Piperacillin with Hemodialysis
Two-Compartment Model: Piperacillin with Hemodialysis

![Graph showing the concentration of Piperacillin over time for both central and peripheral compartments. The graph includes time (in hours) on the x-axis and concentration (mg/L) on the y-axis. The graph illustrates the effect of hemodialysis on the drug levels.]
Two-Compartment Model: Piperacillin with Hemodialysis

![Diagram of Piperacillin concentration over time with hemodialysis]
Conventional PK Sampling
Intradialytic PK Sampling

![Graph showing intradialytic PK sampling with central and peripheral models.]
Intradialytic PK Sampling: Potential Advantages

- sample from machine or dialysate (no phlebotomy)
- shorter sampling period
- better PK estimates
  - smaller measurement error
  - dynamic aspect informative about $k_{12}$ and $k_{21}$
Conventional PK Sampling: Simulation Example
Intradialytic PK Sampling: Simulation Example 1

![Graph showing intradialytic PK sampling simulation example 1.](graph.png)
Intradialytic PK Sampling: Simulation Example 2
Intradialytic PK Sampling: Simulation Example 3
Simulation Results

<table>
<thead>
<tr>
<th></th>
<th>$k_{10}$</th>
<th>$V_1$</th>
<th>$k_{12}$</th>
<th>$k_{21}$</th>
<th>$T &gt; 4 \times \text{MIC}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bias: Conventional</td>
<td>0.14</td>
<td>-0.43</td>
<td>0.02</td>
<td>-0.10</td>
<td>0.81</td>
</tr>
<tr>
<td>Bias: Intradialytic</td>
<td>-0.03</td>
<td>-0.02</td>
<td>0.03</td>
<td>0.01</td>
<td>-0.01</td>
</tr>
<tr>
<td>RMSE: Conventional</td>
<td>2.52</td>
<td>0.98</td>
<td>2.97</td>
<td>0.92</td>
<td>0.18</td>
</tr>
<tr>
<td>RMSE: Intradialytic</td>
<td>0.47</td>
<td>0.24</td>
<td>0.20</td>
<td>0.25</td>
<td>0.07</td>
</tr>
</tbody>
</table>
Conclusions

intradialytic sampling may:

▶ reduce sampling time
▶ reduce phlebotomy
▶ reduce blood usage
▶ improve PK estimates!
Ongoing Considerations

- interpatient PK variability
- algorithmic optimal design