Extended Interval Aminoglycoside Dosing

SRH P&T
September 2011
Aminoglycoside Overview

• Includes: gentamicin, tobramycin, streptomycin, and amikacin

• Coverage:
  – Aerobic Gram positive Bacilli (Bacillus spp)
  – Broad Gram negative coverage including pseudomonas

• Concentration Dependent Killing
Dosing

• Conventional dosing utilizes standardized PKPD calculations based on population PK to target a given peak and trough
• Conventional dosing often results in administration of a lower dose more frequently compared to EID
• In the late 1990, EID/ODA was studied extensively
Concentration Dependent Killing
With Conventional Dosing
Concentration Dependent Killing With Conventional Dosing
Benefits of EID - Efficiency

• Higher level above the MIC compared to conventional dosing = more efficient bacterial eradication
• Utilization of Post-Antibiotic Effect (PAE) which continues bacterial killing with low chance of resistance
• Antibiotic-free period between doses (4hr) which decrease the chances of resistance
Benefits of EID – Adverse Effects

• Lower incidence of nephrotoxicity
• Lower/equal incidence of ototoxicity
• Decreased incidence of calculation errors
• More rapid adjustment of dose compared to conventional = less ADR
# Meta-Analysis for Efficacy and ADR

<table>
<thead>
<tr>
<th>Reference</th>
<th>No. of trials</th>
<th>n</th>
<th>Efficacy clinical</th>
<th>Efficacy bacteriological</th>
<th>Efficacy total</th>
<th>Toxicity nephrotoxicity</th>
<th>Toxicity ototoxicity</th>
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<tbody>
<tr>
<td>Gallo et al.[7]</td>
<td>16</td>
<td>1200</td>
<td>OD &gt; MD (NS)</td>
<td>OD = MD</td>
<td>OD &gt; MD (NS)</td>
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<td>Barza et al.[4]</td>
<td>21</td>
<td>3091</td>
<td>OD &gt; MD (NS)</td>
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<td>OD &gt; MD</td>
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<tr>
<td>Ferriol-Lisart et al.[5]</td>
<td>18</td>
<td>2317</td>
<td>OD &gt; MD</td>
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<td>OD &gt; MD</td>
<td>OD &lt; MD</td>
<td>OD &lt; MD (NS)</td>
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<td>Hatala et al.[8]</td>
<td>13</td>
<td>1200b</td>
<td>OD &gt; MD (NS)</td>
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<td></td>
<td>OD &lt; MD (NS)</td>
<td>OD &lt; MD (NS)</td>
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<td>Munckhof et al.[10]</td>
<td>20</td>
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<td>Freeman et al.[6]</td>
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<td>OD &gt; MD (NS)</td>
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<td>Ali &amp; Goetz[2]</td>
<td>26</td>
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<td>OD = MD (&lt; OD (NS))</td>
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<td>Bailey et al.[3]</td>
<td>22</td>
<td>2500</td>
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<td>Hatala et al.[9]</td>
<td>4</td>
<td>422c</td>
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<td>OD &lt; MD (NS)</td>
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</table>

- More than one method of meta-analysis was used and significance depended on method of analysis.
- Immunocompetent adults.
- Immunocompromised adults.

MD = multiple daily doses; n = number of patients; NS = not statistically significant; OD = once daily administration; > indicates better efficacy than; < indicates less toxicity than; = indicates equivalent to.
Summary

• EID is significantly more efficacious than conventional dosing based on over 30 studies.
• EID has significantly less incidence of nephrotoxicity compared to conventional dosing.
• EID is the standard of care for AG dosing in patients based on PKPD parameters.