Introduction

- Amikacin is increasingly being used in the management of multi-drug resistant mycobacterial infection.
- Current dosing guidelines recommend 15 mg/kg once daily (OD) or 25 mg/kg thrice weekly (TW).  
- Target concentrations for amikacin are end of infusion peaks of 35-45 mg/L (OD) or 65-80 mg/L (TW) and troughs <5 mg/L.  
- It is not clear whether the recommended amikacin dosage guidelines achieve these target concentrations.

Aim

- To determine whether amikacin dosage guidelines for multi-drug resistant mycobacterial infections achieve peaks of 35-45 mg/L (OD) or 65-80 mg/L (TW) and troughs <5 mg/L.

Methods

- Patients >18 years old with a mycobacterial infection and at least one recorded amikacin dose and peak concentration were included in the audit.
- The following data were extracted from drug monitoring forms: age; weight; height; creatinine concentration; amikacin doses, concentrations and times.
- Individual estimates of amikacin volume of distribution (V) and clearance (CL) were determined by MAP Bayesian pharmacokinetic analysis.  
- Individual CL and V estimates were used to predict the following amikacin Concentration (mg/L)  
  - 15 mg/kg daily  1 h and 24 h after the start of a 1 h infusion  
  - 25 mg/kg thrice weekly  1 h and 48 h after the start of a 1 h infusion  
- The percentages of patients who achieve amikacin concentrations below, within and above the target peak and trough ranges were determined for each regimen.

Results

- Data were collected from 83 patients (Table 1), of which 33% (OD) and 35% (TW) had predicted peaks within the relevant target amikacin range (Table 2).  
- Concentrations were more likely to be above than below the upper concentration target range (Table 2, Figure 1 and Figure 2).
- 34% of patients achieved peaks >50 mg/L with the OD regimen and 11% of patients achieved peaks of >100 mg/L on the TW regimen.
- Patients with estimated creatinine clearance <30 mL/min had troughs >5 mg/L at the end of the dosage interval.

Table 1 Patient demographic and clinical data

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Number/Median (Range)</th>
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<tbody>
<tr>
<td>Patients (Male/Female)</td>
<td>83 (49/34)</td>
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<tr>
<td>Age</td>
<td>45 (19 – 79)</td>
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<tr>
<td>Weight</td>
<td>60 (36 – 94)</td>
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<tr>
<td>Estimated Creatinine Clearance (mL/min)</td>
<td>69 (60 – 193)</td>
</tr>
<tr>
<td>Estimated Amikacin Clearance (L/h)</td>
<td>4.0 (0.49 – 10.4)</td>
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<tr>
<td>Estimated Amikacin Volume of Distribution (L)</td>
<td>17.9 (8.6 – 44.4)</td>
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Figure 1 Predicted steady state peak and trough amikacin concentrations

ONCE DAILY regimen

Figure 2 Predicted steady state peak and trough amikacin concentrations

THRICE WEEKLY regimen

Summary and Conclusions

- Amikacin guidelines for mycobacterial infections achieve peak concentrations that are typically within or above the stated target range.
- Trough concentrations are excessive for patients with renal impairment (CrCl <30 mL/min).
- Guidelines should be modified to allow greater flexibility in peak concentrations and to provide guidance for patients with renal impairment.

References