INTRODUCTION

- A new service has been introduced that allows patients to be given antibiotic treatment with intravenous teicoplanin in an outpatient setting.
- Teicoplanin has a long elimination half-life, it can be administered three times a week.
- Current doses are determined empirically as there are no published guidelines

AIMS

- To describe the PopPK of teicoplanin in outpatients who are receiving thrice weekly IV therapy
- To identify clinical factors that influence the pharmacokinetics of teicoplanin in this population
- To develop dosage guidelines for future use

METHODS

Dosage regimen and blood sampling
- Loading doses of 15 - 25 mg/kg/day were given for three days followed by 15-25 mg/kg on Mondays, Wednesdays and Fridays.
- Troughs were withdrawn Monday mornings (72 hours after the last dose).
- Teicoplanin doses were adjusted to maintain troughs of 20 - 30 mg/L (deep seated infections) or 10 - 20 mg/L (bacteremia or soft tissue infections)
- Concentrations were measured by fluorescence polarisation immunoassay

Data analysis
- NONMEM V with FOCE interaction (1). 1 and 2-compartment models were tested, interindividual variability (IV) was assumed to be log-additive; additive, proportional, combined residual error models compared.
- Covariates: age; weight (TBW); ideal body weight (IBW); height; serum creatinine concentration; creatinine clearance using the Cockcroft-Gault equation (2) with TBW (CCI) or IBW (C(I)C) and the Salazar-Corcoran equation CCLB (4). Scatterplots were examined using Xpose version 3.0 (4).
- Model comparison: change in OFV (3.84 significant) scatterplots and IV and residual variability.

Development of dosage guidelines
- Typical trough profiles were simulated for patients weighing 40, 50, 60, 70, 80, 90, 100, 120 kg with creatinine CL of 20, 25, 30, 35, 40, 50, 60, 70, 80, 100, 120 ml/min.
- Loading regimens that achieved troughs of 20-30 mg/L were identified and used to construct dosage guidelines

RESULTS

Table 1. Clinical characteristics of the patients (n = 93).  

<table>
<thead>
<tr>
<th>Clinical characteristic</th>
<th>Median (range)/Number</th>
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<tbody>
<tr>
<td>Male / Female</td>
<td>55 / 39</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63 (15-94)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>73 (45-146)</td>
</tr>
<tr>
<td>&gt; 20 % above IBW</td>
<td>46</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.68 (1.37-1.93)</td>
</tr>
<tr>
<td>Creatinine (µmol/l)</td>
<td>95 (58-308)</td>
</tr>
<tr>
<td>CCl/min</td>
<td>53 (16-136)</td>
</tr>
<tr>
<td>CCLB/min</td>
<td>64 (16-195)</td>
</tr>
<tr>
<td>CCB/min</td>
<td>22.6 (5.33-77)</td>
</tr>
</tbody>
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Model development – Basic model
- 1-cpt model with proportional residual error
- Clearance = 0.537 L/hr (IV 42%)
- Volume = 99.5 L (IV 51%)
- Residual variability = 12%

SUMMARY

- Routine TDM data were collected from patients receiving a new approach to intravenous antibiotic therapy with teicoplanin.
- A population model was developed that related teicoplanin clearance to creatinine clearance (based on total body weight) and volume of distribution to total body weight.
- Dosage guidelines were developed based on weight and estimated creatinine clearance.

CONCLUSIONS

- Teicoplanin dosage regimens for patients receiving thrice-weekly therapy should be based on estimated creatinine clearance and weight, not just weight.
- Further work is underway to evaluate the model and to develop the dosage guidelines in a separate group of patients receiving the same treatment approach. The guidelines will then be introduced into clinical practice.

REFERENCES