**INTRODUCTION**

Vancomycin (VCM) is a glycopeptide antibiotic generally used for the treatment of gram-positive infections it’s widely prescribed for sepsis

**AIM**

The purpose of this study is to investigate the population pharmacokinetic of VCM in a population of Tunisian patients to identify the covariates that influenced pharmacokinetic parameters and for individualized optimal VCM dosage

**MATERIAL AND METHODS**

**PATIENTS AND PROTOCOL**

- Population pharmacokinetics of VCM was investigated in 202 patients aged from eight month to 64 years (40±20 years), following sepsis.
- Dose of VCM was varied between 0.04 to 6 g per day with median equal to 1.5 g and was administered by intravenous infusion.
- Patients benefited from two plasma samples: T0 immediately before VCM infusion
- Tmax: 60 minute following completion of VCM infusion.
- The serum concentrations of VCM were measured by a fluorescence polarization (Axym® Abbott).
- The population data set comprised 473 concentration measurements

**PHARMACOKINETIC ANALYSIS**

- To assess the VCM pharmacokinetic profile of each patient, individual analysis of the blood concentration data were performed by nonlinear regression using NONMEM VI software (NONMEM Project Group, University of California, San Francisco, USA).
- The population means parameters; between-subject variance and residual variance were estimated using the first order conditional estimation (FOCE) interaction method (residual intraindividual variability and residual variance were estimated using the first order conditional estimation (FOCE) interaction method)
- The following clinical factors were tested for their influence on clearance (CL) and volume of distribution (V): sex; age, weight and creatinine clearance.
- Model comparisons were based on the change in objective function value (OFV).
  - A one compartment population pharmacokinetic model described the VCM concentration-time data.
  - Several pharmacokinetic models (one, two and three-compartment) have been used to describe VCM pharmacokinetic profile. However, in clinical setting the one and two compartment models are the most used
  - A good correlation was obtained between Bayesian-estimated and experimental observation ($R^2 = 0.84, p<0.01$).
  - Estimates of mean pharmacokinetic parameters were shown on the table below.

**RESULTS AND DISCUSSION**

- The structural model was established initially, followed by development of the covariate model.
- Covariate selection revealed that total body weight (TBW) affected V, and creatinine clearance influenced VCM clearance
- In the other studies the covariates cited were age, TBW influenced V or creatinine clearance
- Estimates of mean pharmacokinetic parameters were shown on the table below.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>MEAN</th>
<th>CV%</th>
<th>Median</th>
</tr>
</thead>
<tbody>
<tr>
<td>CL (l/h)</td>
<td>4.09</td>
<td>59.3</td>
<td>320</td>
</tr>
<tr>
<td>V1 (l)</td>
<td>55.10</td>
<td>320</td>
<td></td>
</tr>
<tr>
<td>Ke (h⁻¹)</td>
<td>0.058</td>
<td>-</td>
<td></td>
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</tbody>
</table>

**CONCLUSION**

The models could be used to estimate appropriate VCM dosage guidelines, which are not clearly defined for this high-risk population. Their simple structure should allow easy implementation in clinical software and application to dosage individualizes using Bayesian approach.

**REFERENCES**
