Temocillin quantification in human serum using a high performance liquid chromatography-tandem mass spectrometry

P. Ngougni Pokem1,3, A.C. Miranda Bastos1,2,3, P.M. Tulken1,3, F. Van Bambeke1,3, A. Capron4

Louvain Drug Research Institute: (1) Pharmacologie cellulaire et moléculaire, (2) Clinical Pharmacy Research Group, (3) Center for Clinical Pharmacy, Cliniques Universitaires Saint-Luc: (4) Department of Clinical Chemistry, Université Catholique de Louvain, Brussels, Belgium.

Contact: francoise.vanbambeke@uclouvain.be

Introduction

Temocillin (TMO) is a beta-lactam antibiotic that has recently seen both its usage and associated research increased, due to its remarkable resistance to beta-lactamases. [1] Measuring TMO serum concentrations can be clinically useful for optimal patient management. A method using HPLC coupled to a UV detector has recently been developed and validated [2]. Yet, UV detection being not specific, interferences could occur when assaying TMO in the serum of patients taking multiple medications.

Aim of the study

To develop and validate a new HPLC method coupled to MS-MS detection for the analysis of temocillin in human serum.

Methods

Methanol protein precipitation was used as the extraction method.
- TMO calibration standards: 1 to 500µg/mL.
- TMO quality standards: 5 to 450µg/mL.
- Internal standard: Ticarcillin (TIC) - final concentration 160µg/mL.

Results

**Linearity**

<table>
<thead>
<tr>
<th>TMO theoretical concentration µg/mL</th>
<th>Mean estimated concentration µg/mL</th>
<th>intra-day (n=5) Precision (CV%)</th>
<th>inter-day (n=15) Accuracy (MRPE %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LLOQ 1 1.07</td>
<td>1.07</td>
<td>15.73</td>
<td>13.09</td>
</tr>
<tr>
<td>LQC 5 5.48</td>
<td>5.17</td>
<td>13.02</td>
<td>7.05</td>
</tr>
<tr>
<td>MQC 250 259.19</td>
<td>7.21</td>
<td>6.75</td>
<td>3.67</td>
</tr>
<tr>
<td>HQC 450 460.18</td>
<td>7.14</td>
<td>11.68</td>
<td>2.26</td>
</tr>
</tbody>
</table>

**Precision and Accuracy**

- LLOQ: CV<20%, intra-day: CV<15%, inter-day: CV<15%
- LQC: MRPE<20%, intra-day: MRPE<15%, inter-day: MRPE<15%
- Method is precise

Recovery and Precision

<table>
<thead>
<tr>
<th>TMO theoretical concentration µg/mL</th>
<th>Mean % recovery (n=5)</th>
<th>Standard deviation</th>
<th>Coefficient of variation (CV%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LQC 5 85.80</td>
<td>6.90</td>
<td>8.04</td>
<td></td>
</tr>
<tr>
<td>MQC 250 90.86</td>
<td>6.86</td>
<td>7.54</td>
<td></td>
</tr>
<tr>
<td>HQC 450 99.40</td>
<td>7.50</td>
<td>7.55</td>
<td></td>
</tr>
</tbody>
</table>

**Carry-over**

- Carry-over % of LLOQ
- Carry-over is in the acceptable range

References


Conclusion

This is the first report describing the quantification of temocillin by HPLC-MS/MS. This method proved fast, specific, and sensitive enough for determining temocillin levels in serum. It could be used for both pharmacokinetic studies and therapeutic monitoring purposes and should avoid any interference with other medications taken by the patients.