A UPLC-MS/MS assay for the quantification of meropenem and piperacillin concentrations in human plasma.

Veronique Stove, Eric Van de Velde, Mieke Carlier and Alain Verstraete

Background: Meropenem and piperacillin are beta-lactam antibiotics that are widely used to treat severe infections in the intensive care unit. Various chromatographic methods with UV detection have been were developed to measure total plasma concentrations of these antibiotics. The objective of this work was to develop a rapid method for the simultaneous detection of these drugs in human plasma.
Materials and Methods: After blood collection in lithium heparin tubes, samples were quickly centrifuged and plasma was frozen at -20°C until analysis. Plasma samples were spiked with oxacillin as an internal standard and deproteinised using acetonitrile. The supernatant was analysed using ultraperformance-liquid chromatography tandem mass spectrometry (UPLC-MS/MS). The compounds were chromatographically separated on a Waters Acquity UPLC system with a BEH C18 column (1.7 µm, 100 mm × 2.1 mm) kept at 50°C and a gradient elution of water and acetonitrile, both containing 0.1% formic acid. Compounds were detected with a Waters Acquity TQD mass spectrometer operating in positive electrospray ionisation using a compound-specific MRM method. Total run time was 4 minutes.
Results: The method was validated for precision and accuracy. Linearity was established up to a concentration of 80 mg/L (meropenem) and 200 mg/L (piperacillin). The validated method was used to evaluate the bench-top and refrigerator stability of meropenem and piperacillin levels in non-stabilised plasma samples. At room temperature, the stability was checked after 1 hour and 24 hours and showed for both antibiotics a recovery of >95% and 60-65%, respectively. Storage of the plasma sample for 1 hour at room temperature, followed by storage at 4°C for 7 and 23 hours showed a decrease in drug concentration up to 15-20 %.
Conclusion: Our method allows a rapid and simple determination of meropenem and piperacillin plasma concentrations in a single run. Application of this method in routine monitoring of meropenem and piperacillin for the intensive care unit is feasible, but requires a strict control of the pre-analytical phase.

Veronique.Stove@ugent.be
Eric.Vandevelde@ugent.be
Mieke.Carlier@ugent.be
Alain.Verstraete@ugent.be

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