Poster

[P25-2] P25-2: Anti-infective drugs (2): Beta-lactams

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[P25-2-3] Simultaneous determination of nine beta-lactam antibiotics in human plasma by an ultrafast hydrophilic-interaction chromatography —tandem mass spectrometry

Birgit C. P. Koch[1], Alan Abdulla[2], Soma Bahmanya[3], Rixt A. Wijma[4], Bart C.H. van Der Nagel[5] (1.Erasmus MC, 2.Erasmus MC, 3.Erasmus MC, 4.Erasmus MC, 5.Erasmus MC)

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Background

Dosing strategies that ensures optimal antibiotic exposures should be considered essential in critically ill patients to increase the chances of effective treatment. Given the variability in exposures across critically ill patients, an “one-dose-fits-all” approach is undesirable. However, therapeutic drug monitoring (TDM) of β-lactam antibiotics is rarely performed, most often related to difficult sample preparation and long analysis times. We describe an ultrafast Hydrophilic-Interaction Chromatography (HILIC) based UPLC-MS/MS method for the simultaneous determination of amoxicillin, benzylpenicillin, cefotaxime, cefuroxime, ceftazidime, flucloxacillin, imipenem, meropenem and piperacillin in human plasma.

Methods

The UPLC system (Dionex Ultimate) was connected to a triple Quadrupole mass spectrometer (Thermo TSQ Vantage with HESI-probe). An electro-spray ionization (ESI) source interface operating in positive-ion mode was used for the selective reaction monitoring (SRM) analysis. The ion source settings were: capillary temperature, 250 ˚C; vaporizer temperature, 400 ˚C; spray voltage, 3000 V, auxiliary gas, nitrogen (3.4 L/min); nebulizer gas, nitrogen (8.6 L/min); and collision gas, argon (0.2 Pa). The method was validated according to the Food and Drug Administration (FDA) guidance on bioanalytical method validation.

Results

Accuracy ranged from 0.3-18.3%, and precision ranged from 0.8-4.7% within runs and from 1.0-16.5% between runs. The responses were linear in the assayed range and determination coefficient values were at least 0.990. LLOQ and ULOQ were found to be sufficient to cover the therapeutic range for all antibiotics. Matrix effect was investigated through the addition of the analytes to blank matrix extracts. No significant ion suppression and carryover was observed. Auto-samples stability was tested for all analytes, the QC levels were found to be stable for at least 24h. The retention times ranged from 0.85 to 4.80 minutes, and the total assay run time is 5.20 minutes. This method was successfully applied in a large pharmacokinetic study performed in the Intensive Care setting.

Conclusions

Our method is simple, sensitive and the feasibility of the analytical procedure was demonstrated in a clinical study and routine clinical practice. Moreover, the analysis of several β-lactam antibiotics in a single protocol is beneficial in light of the combined use of multiple antibiotics in clinical practice.