

O1161 Piperacillin population pharmacokinetics in 161 critically ill patients undergoing renal replacement therapy, data from the SMARRT study

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Background: Piperacillin pharmacokinetics (PK) in critically ill patients, particularly during renal replacement therapy (RRT), can be severely altered potentially leading to ineffective or toxic concentrations. In this work, we aim to develop a population PK model of piperacillin in this specific patient subset.

Materials/methods: Adult critically ill patients undergoing RRT and receiving piperacillin were included as part of the international SMARRT study. Clinical, demographic and RRT-related covariates were collected at one or two administration occasions. In addition, pre-filter, post-filter, RRT-effluent and urine piperacillin concentrations and amounts were measured. Pmetrics[®] R[®] package to perform non-parametric population PK modelling. Various structural models were compared using Akaike information criterion (AIC). Univariate and multiple linear regressions were then used to explore potent covariate-estimated PK parameters relationships and test their inclusion in the best PK model. Predictive performances of the various models were assessed by bias and imprecision. Internal validation was performed using visual predictive checks (VPCs).

Results: We included 161 patients in 19 sites contributed 1462 pre-filter, 1140 post-filter, 358 RRT-effluent and 64 urines samples during 261 occasions. A three-compartment model best described the data including pre and post-filter concentration data and a peripheral compartment. Three clearance routes were supported, RRT, renal and non-renal/non-RRT. The mean (CV%) estimated volume of distribution, RRT-clearance (CL), urinary CL and non-renal/RRT CL were respectively 19.8L (80.5%), 1.5L/h (76.9%), 0.7L/h (99.5%) and 0.9L/h (62.6%). The attached table displays predictions descriptors, and percentage of observations within the 5-95% percentile VPCs intervals.

Sample type	Population/Individual	VPC	
	Bias	Imprecision	Interval
Post-filter (mg/L)	0.21/-0.1	7.37/0.56	83.2%
Pre-filter (mg/L)	0.95/-0.1	8.33/0.39	88.7%
RRT-effluent (mg)	3.77/-0.21	315/0.45	87.6%
Urine (mg)	5.18/-0.04	221/0.58	68.3%

Conclusions: To the best of our knowledge, this cohort is the largest describing the PK of piperacillin in ICU patients undergoing RRT. The variability in PK parameters was high demonstrating the challenge of effective dosing in this patient group.

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