Piperacillin pharmacokinetics and pharmacodynamcis during continuous infusion in critically ill patients

[1]S. Helbig, [1] O.R. Frey, [1]A.C. Röhr, [2]A. Köberer, [2]T. Fuchs, [2]A. Brinkmann
[1]Department of Pharmacy [2]Department of Anesthesia and Intensive Care Medicine General Hospital of Heidenheim

25th ECCMID COPENHAGEN, DENMARK 25-28 APRIL 2015 | ESCMID EUROPEAN SOCIETY OF CLINICAL MICROBIOLOGY AND INFECTIOUS DISEASES

P1130

Introduction and purpose

The purpose of this study was to describe the pharmacokinetics and pharmacodynamics of Piperacillin during continuous infusion in critically ill patients and to determine the frequency in which pharmacodynamic targets are achieved.

Methods

Critically ill patients receiving Piperacillin (+Tazobactam) in 2013 were eligible for this study. A loading dose of 2000mg and individualised maintenance doses, based on renal function and applied renal replacement therapy (RRT), were administered by continuous infusion. Within the first 12-24(48) hours of therapy the first serum level was drawn and measured with validated HPLC-UV methods. Primary target concentration was a steady state concentration of > (16)32-100 mg/l. Overdose was defined by a serum level > 100 mg/l, reflecting a Piperacillin dose > 32g/24h in normal subjects.

Number of patients	Mean age [years]	Mean SAPS II (median; range)	Mean TISS (median; range)	Number of patients on RRT
180 (160m;64f)	71 (75;24-91)	37.2 (37;0-83)	10.4 (10;0-36)	35 (19.4%)
Patients with severe sepsis	**Patients with septic shock**	**ICU mortality**	**Success of therapy**	**Mean duration of therapy**
53 (29.4%)	50 (27.8%)	57 31.7 %	129 (72.1%)	6.5 (6; 2-19)

Table1: patient characteristics and clinical data; data are presented as the median and range or as a number with the percentage in parenthesis

Results

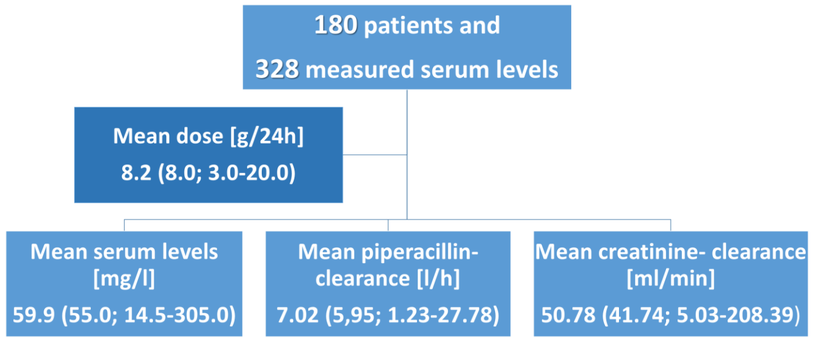

Figure1: Administered daily dose, measured serum levels and pharmacokinetic parameters

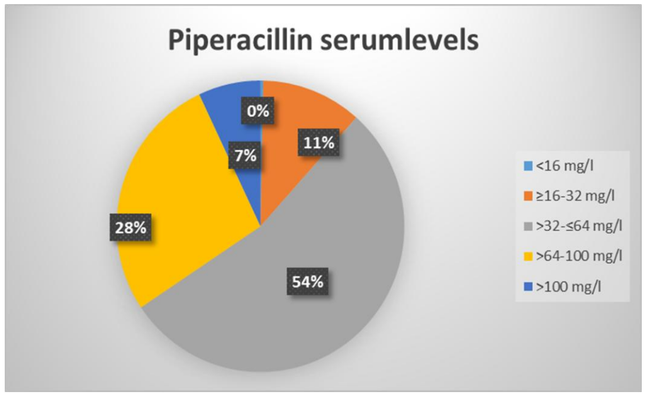

Diagram1: Attained serum levels subdivided in target groups using TDM guided continuous infusion

Dose adjustment after first measurement			Dose adjustment after following measurements		
	Number patients	[%]		Number patients	[%]
Dose maintained	136	75.6	Dose maintained	133	89.8
Dose increased	12	6.6	Dose increased	6	4.1
Dose decreased	32	17.8	Dose decreased	9	6.1

Table2: Need for dose adjustment after first and following TDM levels (presented as a number of patients or percentage)

Conclusion

Piperacillin clearance in critically ill patients shows high variation, requiring a wide range of doses to achieve target levels. By individualising and optimisation of antibiotic dosing, PK/PD targets can be achieved in the majority of patients. Our study suggests that individual dosing strategies, as well as application of Therapeutic Drug Monitoring (TDM), are advisable to avoid the risk of treatment failure or doses dependent toxicity. These methods may also decrease the development of resistance.

Literature

Roberts JA, Ulldemolins M, Roberts MS, Mc Whinney B, Ungerer J, Paterson DL, Lipman J Therapeutic drug monitpring of β-lactams in critically ill patients : proof of concept. Int J Antimicrob Agents 36(2010) 332-339
Ashley C. The Renal drug Handbook, 3rd edition 2009, Radcliff publishing Ltd
De Waele JJ, Carette S, Carlier M, Stove V, Claeys G, Leroux-Roels I, Hoste E, Depuydt P, Decruyenaere J, Verstraete AG Therapeutic drug monitoring – based dose optimisation of piperacillin and meropenem: a randomised controlled trial . Intens Care Med 40 (2014) 380-387
CADDy Calculator to Approximate Drug-Dosing in Dialysis http://www.thecaddy.de/de/caddy/caddy. Accessed April 17, 2015.
Fachinformation Tazobac® (German summary of product characteristics)

klinikumheidenheim