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Prolonged infusion without TDM



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DALI – PK/PD target attainment

	p-value	Odds ratio	95% CI	
			Lower	Upper
Age (per year)	.656	1.005	.984	1.025
Interval start AB -sampling (/day)	.101	1.073	.986	1.168
APACHE II score (/point)	.425	.985	.949	1.022
SOFA score (/point)	.733	1.014	.935	1.100
Cockroft-Gault CL _{CR} (/mL/min)	.000	.988	.982	.994
Ratio antibiotic dose to DD _{ICU}	.338	1.003	.997	1.009
Trauma as an admission diagnosis	.056	.385	.145	1.024
Surgery in the previous 24h	.068	.475	.214	1.057
Extended/continuous infusion used (vs. intermittent infusion)	.000	3.964	1.859	8.453
Prophylaxis indication	.834	1.079	.527	2.212



Prolonged infusion



GHENT UNIVERSITY

Roberts, JA. Int J Antimicrob Agents 2010 2:156-163

Tissue concentrations and Cl



Obstacles to TDM-based dosing

- MIC availability and duration
- TDM availability
- Knowledge gaps
 - Lack of clear targets for beta-lactam antibiotics
 - Uncertainties about tissue concentrations



We don't have a clue...

Table 4. List of PK/PD targets for dose adjustment adopted by selected ICUs





Wong, G. J Antimicrob Chemother 2014 5:1416-1423

Assays for TDM



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ARTICLE INFO

ABSTRACT

Article history: Received 28 January 2015 Accepted 22 June 2015

Keywords:

In some patient groups, including critically ill patients, the pharmacokinetics of β-lactam antibiotics may be profoundly disturbed due to pathophysiological changes in distribution and elimination. Therapeutic drug monitoring (TDM) is a strategy that may help to optimise dosing. The aim of this review was to identify and analyse the published literature on the methods used for β -lactam quantification in TDM programmes. Sixteen reports described methods for the simultaneous determination of three or more



Carlier, M. Int J Antimicrob Agents 2015 4:367-375



journal homepage: http://www.elsevier.com/locate/ijantimicag

Contents lists available at ScienceDirect

Assays for therapeutic drug monitoring of β-lactam antibiotics:

Assays for TDM - wishlist

- Limited sample preparation
- Stable in pre-analytic phase
- Broad range of concentrations
- Validated methods
- Fast

Mostly in-house methods (meropenem and piperacillin) Many published methods fail Other matrices – beware!





Prolonged infusion without TDM

- Optimized therapy necessary
- Factors associated with low concentrations known
- Increased dose for selected patients
- TDM sounds attractive but hasn't proved anything
- Many issues with assays

• Targets unclear – no consensus





Thank you for your attention

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