Intensive Care Medicine Experimental
a SpringerOpen Journal

POSTER PRESENTATION Open Access

Optimizing the dosing regimen of linezolid in critically ill septic patients undergoing continuous hemodiafiltration using a pharmacokinetic/ pharmacodynamic analysis and monte carlo simulation

H Barrasa González[1*], A Martín López[1], A Isla Ruiz[2], A Rodríguez Gascón[2], A Soraluce Olañeta[2], E Asín Prieto[2], A Canut Blasco[1], JA Sánchez Izquierdo[3], B Fernández Miret[1], A Vallejo De la Cueva[1], FJ Maynar Moliner[1]

From ESICM LIVES 2015
Berlin, Germany. 3-7 October 2015

Introduction

Pharmacokinetic (PK) of drugs in critically ill patients could vary from the general population. Patients undergoing hemodiafiltration (HDF) could present lower linezolid (LZ) concentration than expected. The pharmacokinetic/pharmacodynamic analysis (PK/ PD) is a useful tool to optimize dosing regimens of antibiotic therapy.

Objectives

To evaluate the efficacy and safety of LZ for the treatment of infections caused by gram-positive microorganisms (GPM) in the Intensive Care Unit (ICU) patients undergoing HDF using a PK/PD analysis and Monte Carlo simulation (MCS).

Methods

Study developed in three tertiary hospitals in patients with severe sepsis, HDF and treatment with LZ (600mg q12h). 8 each patient blood (prefilter and postfilter) and ultrafiltrate samples were taken. Concentrations of linezolid were determined by HPLC-UV. PK analysis and MCS were performed using Phoenix WinNonlin Version 6.3 (Pharsight) and Oracle Crystal Ball programs to assess the probability of successful treatment (PST) [area under the curve (AUC24)/MIC> 100 for different MICs], the probability of C_{min}>2 mg/L and the risk of overexposure (RO) [C_{min}> 10 mg /L and/or AUC24> 400 mg * h/L] at doses of 600mg q12 and q8h. Patients were grouped by liver and renal function considering impaired liver function (ILF) the elevation> 2 times transaminase and/or elevated bilirubin and severe renal dysfunction (SRD) the presence of CrCl < 15 ml/min. Group (G) 0: both normal, G1: ILF or SRD, G2: both. Quantitative variables were expressed as mean and standard deviation (SD), qualitative as percentages. α significance level of 0,05.

Results

26 patients were included. The AUC 24 (mg * h / L) was: G0 111 (SD 39), G1 155 (SD 79) and G2 246 (SD64), the C_{min} (mg/L) was: G0 1,5 (SD 1,2), G1 2,5 (SD 1,8) and G2 4,6 (SD 2) and the clearance (Cl) (L/h) was: G0 12 (SD 4), G1 10,1 (SD 5,9) and G2 8,9 (SD 5,1). The PST was 96, 81, 38 and 0% for GPM with MICs of 0,5, 1, 2 and 4 mg/L. In the MCS, 600 mg 12qh ensures PST> 80% for MIC ≤1mg/L in the presence of some dysfunction (G1 and G2), increasing to> 90% for all groups with 600 mg q8h without RO. In the G2, the current dose assures PST> 70% for MIC of 2, increasing to >90% with 600mg q8h but with high RO (> 30%). No amount is effective for MIC ≥4 mg/L. The probability of C_{min} >2 mg/L was 23, 33 and 85% for G0, G1 and G2 respectively, increasing to 60% in G0 and G1 with 600 mg q8h (see summary table in Figure 1).

[1]Osakidetza, Vitoria, Spain
Full list of author information is available at the end of the article

SpringerOpen
© 2015 Barrasa González et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (http://creativecommons.org/licenses/by/4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Efficacy							
% AUC/CMI>100		GO (no dysfunction)		G1 (SRD or ILF)		G2 (SRD and ILF)	
		q12h	q8h	q12h	q8h	q12h	q8h
MIC	0,25	100	100	100	100	100	100
	0,5	98,31	100	100	100	100	100
	1	55,24	89,93	74,23	93,64	99,6	100
	2	3,1	23,79	21,66	52,74	74,73	98,66
	4	0,01	0,42	1,23	8,89	2,19	32,78
	8	0	0	0	0,22	0	0,05
Cmin>2		23,17	60,86	33,45	60,53	84,6	99,25
Safety							
Cmin>10			3,92		12,87		32,57
AUC>400			0,3		9,14		33,09

Figure 1

Conclusions

In patients with RRT, 600 mg q12h guarantees PST >80% for MIC ≤1 in the presence of SRD and/or ILF. For this MIC, 600 mg q8h guarantees high PST in all patients and increases the probability of Cmin> 2. For MGP with MIC of 2, only in the presence of both dysfunctions is possible achieving the PK/PD target.

Grant Acknowledgment

Pfizer sponsored this study.

Authors' details
[1]Osakidetza, Vitoria, Spain. [2]University of the Basque Country, Vitoria, Spain. [3]Doce de Octubre Hospital, Madrid, Spain.

Published: 1 October 2015

doi:10.1186/2197-425X-3-S1-A395
Cite this article as: Barrasa González *et al.*: Optimizing the dosing regimen of linezolid in critically ill septic patients undergoing continuous hemodiafiltration using a pharmacokinetic/pharmacodynamic analysis and monte carlo simulation. *Intensive Care Medicine Experimental* 2015 **3**(Suppl 1):A395.

Submit your manuscript to a SpringerOpen journal and benefit from:

- ► Convenient online submission
- ► Rigorous peer review
- ► Immediate publication on acceptance
- ► Open access: articles freely available online
- ► High visibility within the field
- ► Retaining the copyright to your article

Submit your next manuscript at ► springeropen.com