October 2-6 • Washington, DC • www.idweek.org
IDWeek 2019
Advancing Science, Improving Care
P400

Comparison of tolerance and microbiological efficacy of cefepim and piperacillin/tazobactam in combination with vancomycin as empirical antimicrobial therapy of prosthetic joint infection: a propensity-matched cohort study

C. Triffault-Fillit[1,3], E. Mabrut[1,3], K. Corbin[1,3], A. Becker[1,3], E. Braun[1,3], M. Tod[1-3], S. Goutelle[1-3], M.H. Fessy[1-3], C. Dupieux[1-4], F. Laurent[1-4], S. Lustig[1-3], C. Chidiac[1-4], T. Ferry[1-4], F. Valour[1-4], **on behalf of the Lyon BJI study group*** - [1]Hospices Civils de Lyon, [2] UCBL1, [3] CRIOAc Lyon, [4]CIRI

Aim

The use of piperacillin/tazobactam with vancomycin as empirical antimicrobial therapy (EAT) for prosthetic joint infection (PJI) has been associated with an increased risk of acute kidney injury (AKI), leading to propose cefepim as an alternative since 2017 in our reference center. The present study compared microbiological efficacy and tolerance of these two EAT strategies.

Method

All adult patients with PJI empirically treated by vancomycin-cefepim (n=89) were enrolled in an prospective observational study, and matched with historical controls treated by vancomycin-piperacillin/tazobactam (n=89) according to a propensity score including age, baseline renal function and concomitant use of other nephrotoxics. The two groups were compared using Kaplan-Meier curve analysis and non-parametric tests (Fisher exact test and Mann-Whitney U-test) regarding:

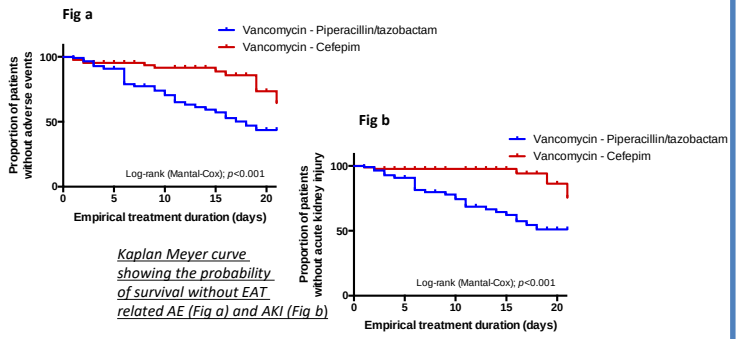
- the proportion efficacious empirical regimen (i.e., at least one of the two molecules active against the identified organism(s) based on *in vitro* susceptibility testing);
- the incidence of empirical therapy-related adverse events (AE), classified according to the Common terminology criteria for AE (CTCAE).

Results

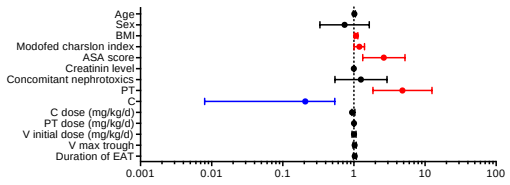
Among the 146 (82.0%) documented infections, the EAT was considered as efficacious in 77 (98.7%) and 65 (98.5%) of the piperacillin-tazobactam and cefepim-treated patients, respectively (p=1.000). The rate of AE, and in particular AKI, was significantly higher in the vancomycin-piperacillin/tazobactam (n=27 [30.3%] and 23 [25.8%%]) compared to the vancomycin-cefepim (n=13 [14.6%] and 6 [6.7%]) group (p=0.019 and <0.001, respectively), leading to a premature EAT discontinuation in 20 (22.5%) and 5 (5.6%) patients (p=0.002). Of note, no significant differences were observed between the two groups regarding sex (91 males; 51.1%), median age (68-year-old; IQR, 59.3-75), main comorbidities, and vancomycin plasmatic overload.

				Piperacillin/tazobactam-vancomycin n=89	Cefepim-vancomycin	*p* -value
Demographics						
	Sex (male)			49 (55.1%)	42 (47.2%)	0.294
	Age (years)			69 (61-77)	67 (58-75)	0.250
Comorbidities						
	BMI (kg/m2)			29.4 (24.0-33.2)	28.4 (24.0-33.2)	0.800
	ASA score			2 (2-3)	2 (2-3)	0.783
	Modified Charlson comorbidity index			3 (2-4)	2 (2-4)	0.291
Baseline renal fonction						
	Creatinin level (umol/L)			60 (51-70)	60 (52-71)	0.955
	Chronic kidney injury			32 (36.0%)	34 (38.2%)	0.877
	Other nephrotoxics			21 (23.6%)	33 (37.1%)	0.072
EAT						
	Betalactam dose (mg/kg/d)			162.2 (133.3-176.5)	76.2 (63.2-89.6)	NA
	Vancomycin initial dose (mg/kg/d)			29.4 (25.0-33.3)	29.4 (25.0-33.3)	0.880
	Vancomycin trough concentration (mg/L)			17.4 (13.0-21.0)	14.4 (10.9-20.8)	0.032
	Duration of EAT (days)			6 (4-14)	13 (5-17)	0.079
	Appropriate EAT			77 (98.7%)	65 (98.5%)	1.000
EAT-related adverse events				27 (30.3%)	13 (14.6%)	0.019
	Delay (days)			8 (6-13.5)	8 (1-16)	0.568
		Grade CTCAE				
			1	11 (40.7%)	8 (61.5%)	0.314
			2	9 (33.3%)	4 (30.8%)	1.000
			3	7 (25.9%)	1 (7.7%)	0.236
	Acute kidney injury			23 (25.8%)	6 (6.7%)	<10 $^{-3}$

Patient characteristics



Kaplan Meyer curve showing the probability of survival without EAT related AE (Fig a) and AKI (Fig b)



Determinants of AKI

Conclusions

The empirical use of vancomycin-cefepim in PJI was microbiologically as efficient as vancomycin-piperacillin/tazobactam, and was associated with a significantly lower incidence of AKI. Adding metronidazole could be discussed in order to fill the anaerobes gap from cefepim spectrum.

* Lyon BJI study group

Lyon Bone and Joint Infection Study Group:
Coordinator: *Tristan Ferry*; **Infectious Diseases Specialists** – *Tristan Ferry, Florent Valour, Thomas Perpoint, Patrick Miailhes, Florence Ader, Sandrine Roux, Agathe Becker, Claire Triffault-Fillit, Anne Conrad, Cécile Pouderoux, Marie-Elodie Langlois, Marielle Perry, Fatiha Daoud, Johanna Lippman, Evelyne Braun, Christian Chidiac*; **Surgeons** – *Sébastien Lustig, Elvire Servien, Cécile Batailler, Romain Gaillard, Stanislas Gunst, Julien Roger, Charles Fiquet, Michel Henri Fessy, Anthony Viste, Philippe Chaudier, Jean Luc Besse, Lucie Louboutin, Gaël Gaudin, Tanguy Ledru, Adrien Van Haecke, Quentin Ode, Marcelle Mercier, Florie Alech-Tournier, Sébastien Martres, Franck Trouillet, Cédric Barrey, Emmanuel Jouanneau, Timothée Jacquesson, Ali Mojallal, Fabien Boucher, Hristo Shipkov, Joseph Chateau, Philippe Céruse, Carine Fuchsmann, Arnaud Gleizal*; **Anesthesiologists** – *Frédéric Aubrun, Mikhail Dziadzko, Caroline Macabéo*; **Microbiologists** – *Frederic Laurent, Laetitia Beraut, Céline Dupieux, Camille Kolenda, Jérôme Josse, Claude-Alexandre Gustave*; **Imaging** – *Fabien Craighero, Loic Boussel, Jean-Baptiste Pialat*; **Nuclear Medicine** – *Isabelle Morelec, Marc Janier, Francesco Giammarile*; **PK/PD specialists** – *Michel Tod, Marie-Claude Gagnieu, Sylvain Goutelle*; **Clinical research assistant and database manager**– *Eugénie Mabrut*

@FerryLyon
@CrioacLyon
http://www.crioac-lyon.fr