Adverse events (AE) during prosthetic joint infection (PJI) empirical antimicrobial therapy: a five year prospective cohort study

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on behalf of the Lyon BJI study group
Introduction

- PJI incidence 1.5%
- Mortality 4.6%
- Difficult to treat
- High doses of ATB
**Main pathogens**
- Gram positive cocci: SA, CoNS (> 65%), *Streptococcus* (20%),
- Gram negative bacilli: *Enterobacteriaceae* (20%)

**VANCOMYCIN + BROAD SPECTRUM BETA-LACTAMIN**
- 3rd generation cephalosporin
- Piperacillin-Tazobactam

- **PJI incidence**: 1.5%
- **Mortality**: 4.6%
- **Difficult to treat**
- **High doses of ATB**

HAS 2012; RAISIN 2015
Osmon 2013, IDSA Guidelines, Hoyby 2014 ESCMID Guidelines
Introduction

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Tolerance?
Prospective cohort of the reference centre for the management of PJIs, between 2011/2016

**Inclusion criteria**

All adult patients (>18 years) managed for a PJI who received an empirical antimicrobial therapy

**Prosthetic joint infection**

Clinical, morphological, microbiological and therapeutic criteria

**Adverse events**

- Prospective collection of AE occurring on empirical antimicrobial therapy (until 21st day)
- Retrospective collection of the AE characteristics
- Classification according to the National Cancer Institute (CTCAE)
Results

567 patients

333 Empirical antibiotherapy

Male: 168 (51%)
Median age: 70 yo (59-79)
ASA score: 2 (2-3)
PJI:
- Hip (54%) and Knee (43%)
- Early (65%)
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Main combinations
- VANCOMYCIN + PIPERACILLIN/TAZOBACTAM 123 (37%)
- VANCOMYCIN + 3rd GENERATION CEPHALOSPORIN 33 (10%)
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42 Adverse events (12.6%)
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42 Adverse events (12.6%)

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ASA score: 2 (2-3)
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- Early (65%)
Results: Adverse event risk factors

OR (univariate analysis):

Demographic characteristics are not significant

**Kaplan Meier:**

- Vancomycin: 3.7 (1.8-7.2)
- VAN-PT combination therapy: 6.9 (2.1-22.9)
- VAN + PT: 4.1 (2.1-8.2)

Log rank (Mantel-Cox); p<0.001
OR (univariate analysis):

Demographic characteristics are not significant

Results: Acute kidney injury risk factors

Kaplan Meier:

Log rank (Mantel-Cox); p<0.001

Delay from empirical antimicrobial therapy initiation (days)
Results: Acute kidney injury risk factors

OR (univariate analysis):

Demographic characteristics are not significant

Vancomycin overdose
8 (33.3%) patients → AKI
Not related to AKI occurrence
→ High adverse event rate during the empirical antimicrobial therapy (12.6%)
→ Toxicity of the vancomycin – piperacillin/tazobactam combination
Conclusions

- High adverse event rate during the empirical antimicrobial therapy (12.6%)
- Toxicity of the vancomycin – piperacillin/tazobactam combination

**VANCYMYCIN + BROAD SPECTRUM BETA-LACTAMIN**
- 3rd generation cephalosporin
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CARBAPENEM ?

Sousa et al., Acta Orthop Belg, 2010; Moran et al., Journal of Infection, 2007
Conclusions

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**VANCOMYCIN + BROAD SPECTRUM BETA-LACTAMIN**
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**CEFEPIME ?**
- Very broad spectrum
- Tolerance
- Anaerobes

**CARBAPENEM ?**
- Dysbiosis
- Resistance

**METRONIDAZOLE ?**

Navalkele et al. CID 2017; Jeon et al., International Journal of Antimicrobial Agents, 2017
→ High adverse event rate during the empirical antimicrobial therapy (12.6%)
→ Toxicity of the vancomycin – piperacillin/tazobactam combination

→ Is this broad spectrum beta-lactam necessary every time?
→ Couldn’t we « target » according to the time to occurrence of PJI?
Aknowledgement : Lyon BJI study group

- **Coordinator** – Tristan Ferry
- **Anesthesiologists** – Frédéric Aubrun, Isabelle Bobineau, Caroline Macabéo
- **Microbiologists** – Frederic Laurent, François Vandenesch, Jean-Philippe Rasigade, Céline Dupieux
- **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
- **Prevention of infection** – Solweig Gerbier-Colomban, Thomas Benet
- **Clinical research assistant** – Eugénie Mabrut

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