HOSPITAL FOR SPECIAL SURGERY

Assessing the Role of Daptomycin as Antibiotic Therapy for Staphylococcal Prosthetic Joint Infection

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Abstract

Background: Optimal antibiotic therapy following surgery for prosthetic joint infection (PJI) depends on potency, toxicity, convenience, and cost. Daptomycin, a potent, convenient, and low-toxicity antibiotic, is FDA-approved for the treatment of skin and soft tissue infections, but its role in treatment of PJI is less clear. We reviewed our experience with daptomycin in the treatment of staphylococcal PJI.
Methods: A retrospective cohort of staphylococcal hip and knee PJI treated with daptomycin after debridement (I&D) or 2-stage exchange was identified by query of hospital coding records from 2009 to 2014, with subsequent chart review. All cases met Musculoskeletal Infection Society International Consensus criteria for PJI; all staphylococcal species were included. The primary endpoint was defined in debrided joints as retention of the prosthesis at 2-year followup, and for two-stage exchanges, as prosthesis retention for 2 years from reimplantation. Descriptive statistics were completed using the Fisher's exact test for categorical variables and the Mann-Whitney U test for continuous variables.
Results: 241 patients with staphylococcal PJI were identified: 148 two-stages (112 [75%] had success at 2 years) and 95 I&Ds (44 [47%] had success at 2 years. 28 (19%) two-stages and 9 (10%) of debridements received daptomycin, of which 20 two-stages (72%) and 6 debridements (66%) reached a successful 2-year outcome. In univariate analysis, there was no association between success and receipt of daptomycin in patients with staphylococcal PJI (two-stages, p=0.71; debridement, p=0.63). There were no associations noted between outcome and age, sex, or BMI.
Conclusion: Daptomycin appeared no better or worse than comparator antibiotics in a relatively large retrospective cohort of staphylococcal hip and knee PJI patients, regardless of surgical strategy. Given its favorable convenience and toxicity profile, it is an attractive antibiotic choice for staphylococcal PJI despite its high cost.

Background & Aims

- Daptomycin for prosthetic joint infection (PJI)
  - Daptomycin used as early as 2005 to treat PJI (Hayden et al., 2005)
  - Several more small retrospective abstracts/ publications
  - Post-Marketing real-world studies - US and European Cubicin Outcomes Registry and Experience (CORE and EU-CORE)
  - Reports of the emergence of daptomycin-resistant strains of *Staphylococcus* – both in animal models and during clinical use
  - Pharmacokinetic studies
    - Conflicting data regarding biofilm penetration
    - *In vivo* study - Rapid penetration into bone (Rosa et al., 2014).
- **We reviewed our experience with daptomycin in the treatment of staphylococcal PJI.**

Methods

Retrospective cohort study
Data source: Hospital for Special Surgery (HSS) Infection Database
Inclusion:
2009-2014
Hip & knee PJI treated with daptomycin after DAIR or 2-stage exchange
All cases met Musculoskeletal Infection Society (MSIS) International Consensus criteria for PJI
All staphylococcal species were included
Primary Outcome:
For DAIR, retention of the prosthesis at 2-year follow-up
For two-stage exchanges, prosthesis retention for 2 years from reimplantation.
Analysis:
Fisher's exact test for categorical variables
Mann-Whitney U test for continuous variables.

Results

- 241 patients with staphylococcal PJI
  - 112 MSSA, 37 MRSA, 92 coagulase negative
- In univariate analysis, there was no association between success and receipt of daptomycin in patients with staphylococcal PJI
  - Two-stage, p=0.71; DAIR, p=0.63
- There were no associations noted between outcome and age, sex, BMI, species, age of prosthesis or duration of symptoms prior to surgical treatment.
- Daptomycin-resistance strains were not detected in patient who did not reach the primary outcomes
- Discontinuation of daptomycin due to adverse events occurred in 2 patients
  - Both patients developed eosinophilic pneumonitis
  - Both patients recovered after daptomycin was discontinued
  - Both patients had undergone 2-stage exchange and both reached the primary endpoint after being changed to an alternative antibiotic regimen
- One patient in the two-stage exchange group died on POD#3 of asystolic cardiac arrest.
  - Daptomycin was not thought to be responsible
- Treatment-limiting CPK elevation or clinical rhabdomyolysis was not observed in any patients

All patients with staphylococcal PJI

	Success	Failure
Two-stage	112 (76%)	36
DAIR	44 (46%)	51
Total	156 (64%)	87

Daptomycin-treated patients

	Success	Failure
Two-stage	20 (71%)	8
DAIR	6 (67%)	3
Total	26 (70%)	11

Discussion

- **Daptomycin was well tolerated in our cohort: there were two patients with daptomycin-induced eosinophilic pneumonitis, and none with rhabdomyolysis**
  - Risk for eosinophilic pneumonitis in patients treated with daptomycin is not well studied
  - A review of the literature and the US FDA Adverse Event Reporting System database in 2012 revealed 7 definite, 13 probable, and 38 possible cases of daptomycin-induced eosinophilic pneumonia
  - A 2018 review of PubMed found 32 case reports that met the formal diagnostic criteria for eosinophilic pneumonitis
  - Combined CORE/EU-CORE – (>11,000 patients) – reported eosinophilic pneumonitis in only .03% of patients (Seaton et al.,2016).
- **Future areas of study**
  - Effect of adjunctive rifampin on daptomycin efficacy
    - Improving outcomes
    - Preventing emergence of daptomycin non-susceptible strains
  - Role in the treatment of other gram positive infections – including *Enterococcus*, *Streptococcus* spp. and *C. acnes*
  - Utility of daptomycin in spacers and beads

Conclusion

Daptomycin appeared similarly effective to comparator antibiotics in a large retrospective cohort of staphylococcal hip and knee PJI patients, regardless of surgical strategy.

References

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