Prosthetic joint infections: new diagnostic and therapeutic strategies

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CHAPTER 6a

Outcome of acute staphylococcal prosthetic joint infection treated with debridement, implant retention and antimicrobial treatment with short duration of rifampicin

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Letter to the editor

A prosthetic joint infection (PJI) is a devastating complication of orthopaedic implant surgery. Cure with retention of an acutely infected prosthesis is possible if antimicrobial therapy is combined with thorough surgical debridement. Current international treatment guidelines for acute staphylococcal PJI advocate at least 12 weeks of combination therapy including rifampicin[1]. The evidence for shorter antimicrobial treatment duration with rifampicin is limited. Often, rifampicin is withheld until antimicrobial susceptibility is known and the postoperative wound is dry. Rifampicin might be most effective during the first days after debridement, the time period in which new biofilm formation on the surface of the implant needs to be prevented. Therefore, over the last 14 years, in our tertiary institution for orthopaedic implant surgery, all patients with an acute staphylococcal PJI who underwent a DAIR (Debridement, Antibiotics and Implant Retention) were treated with only five days of rifampicin in combination with at least 6 weeks of betalactam/glycopeptide antibiotics, both started immediately postoperative.

In this letter, we report the clinical outcome of these patients and assessed whether intraoperative start of rifampicin induced rifampicin resistance in patients who developed a relapse. Oncology patients with an infected megaprosthesis were also included. Patients were excluded if more than one prosthetic joint was infected. PJI was defined according to the IDSA criteria[1]. The criterion for 'acute' infection (three weeks) was extended to two months as DAIR was also performed in patients with longer duration of symptoms. The primary outcome was cure, defined as absence of infection and a stable retained implant for at least six months after stopping antibiotics. Failure was defined as either chronic suppressive antibiotic therapy with implant retention or removal of the implant. Treatment consisted of extensive surgical debridement, rinsing with povidone iodine and pulsed lavage with at least 3 liters of saline. Standard procedure required 3-6 periprosthetic tissue samples to be taken for culture. Empiric antibiotic therapy with a betalactam, an aminoglycoside and rifampicin (600 mg b.d.) was started intraoperative, after debridement. Rifampicin was stopped after five days. After two weeks, intravenous antibiotics were switched to an oral alternative depending on antimicrobial susceptibility testing, flucloxacillin oral absorption test[2] and the clinical response. Total treatment duration of six to twelve weeks depending on clinical response and inflammatory parameters. Follow up was at least one year.

Forty-one patients were included; baseline characteristics are shown in table 1. *Staphylococcus aureus* was involved in 30 cases and coagulase-negative staphylococci (CNS) in 10 cases. One patient had both a *S. aureus* and a CNS. In table 2 cure rates as categorized by affected joint, type of prosthesis and use of immunosuppression are summarized. Overall cure rate was 63%. Notably, patients without a megaprosthesis with a staphylococcal hip PJI (n=18) had a cure rate of 83%. Mean antimicrobial treatment duration in cured patients was 9.7 weeks (median 7.1 weeks). Twelve patients were treated for six weeks; their cure rate was 83%. Mean follow up of cured patients was 392 days (range 97-802 days).

Table 1. Baseline characteristics of 41 patients with acute staphylococcal PJI

	All (n=41)
Demographics	
Age at diagnosis (mean, range)	58 (15-92)
Sex (male, %)	24 (59%)
Implant site (n, %)	
Hip	22 (54%)
Knee	19 (46%)
Revision[#] (n, %)	14 (34%)
Comorbidities (n, %)	
Diabetes mellitus	4 (10%)
Rheumatoid arthritis	9 (22%)
Orthopaedic oncology[$]	14 (34%)
Use of immunosuppressant's^	11 (27%)
Clinical characteristics (n, %)	
Bacteraemia	9 (22%)
Duration of symptoms	
1-7 days	30
8-14 days	6
15-21 days	1
22-29 days	2
29-60 days	2
Microbiology	
Number of cultures taken (median, range)	5 (2-9)
Number of positive cultures per patient[@] (median, range)	4 (0-8)
Microbiology§	
S aureus	31 (76%)
CNS	10 (24%)

[#] patients with revision preceding PJI

^ Use of any of MTX/TNFa-inhibitors/steroids in the months preceding PJI

[$] patients with a tumour prosthesis in situ

[@] Two patients with evident pus but cultures remaining negative

Table 2. Subgroup analyses of outcome of DAIR and 5 days of rifampicin for acute staphylococcal PJI

	n	Complete cure[#]	Functional cure[*]
All patients	41	63%	76%
Patients without tumour prosthesis	27	70%	78%
Hip PJI	18	83%	89%
knee PJI	9	44%	56%
Patients with a megaprosthesis[#]	14	50%	71%
All patients with steroids/anti-TNF/MTX	11	46%	55%

^ acute: symptoms or last operation/revision < 8 weeks.

[#] Complete cure: absence of infection and a stable retained implant for at least six months after stopping antibiotic therapy

[*] Functional cure: stable prosthesis in situ but with chronic suppressive antimicrobial therapy

[#] Mega prosthesis: patients with bone- or soft-tissue tumors

Of the 15 failures, five had a functional (retention of the prosthesis with chronic suppressive therapy). Eight of those failures were caused by the same type of micro-organism as the primary infection (six *S aureus*, two CNS). Rifampicin susceptibility in seven of those latter cases had not changed. In the eighth patient one out of five positive cultures with *S aureus* showed rifampicin resistance.

The high cure rate for staphylococcal hip PJI exceeded those for knee PJI as observed in previous cohort studies.[3,4] Proportion of megaprostheses was higher in knee PJI (53%) compared to hip PJI (18%), which might explain differences in cure rate. The overall cure rate of 63% may be caused by group heterogeneity with respect to underlying disease (i.e. rheumatoid arthritis, bone- and soft-tissue tumors). Also, changing the liner or femoral head was not a routine procedure until three years ago, which might have decreased the likelihood for cure in our patients as well. Antibiotic treatment duration of six weeks was not associated with an increased relapse rate. Allegedly, clinicians are able to select patients who can be treated with a shorter course of antibiotic treatment, based on clinical and laboratory parameters.

The current advocated treatment policy for acute staphylococcal PJI is based on a small randomized trial in which patients were treated with rifampicin combination therapy for at least 12 weeks.[5] Of note, in this underpowered study 50% of the patients had osteosynthesis-associated infection and not a PJI. The drop-out rate due to rifampicin-related adverse events was 33% (6/18). Cure rates with combination therapy were thereafter reported to be 65-90% in observational studies[3-8]. No studies have been published in which short treatment duration with rifampicin was investigated. Our data suggest that prolonged treatment with rifampicin might not be needed as its added bactericidal and biofilm-preventing effect has already taken place in the first few postoperative days.[9] Rifampicin monotherapy and high bacterial loads are well known risk factors for evolving resistance. The absence of development of rifampicin resistance might be explained by the short treatment duration with rifampicin. However, resistance usually develops within two to three days of starting rifampicin monotherapy.[10]

This study adds new insights to the concept of antimicrobial treatment for patients with a staphylococcal PJI. Short-term postoperative treatment with rifampicin resulted in high cure rates in patients with staphylococcal hip PJI. Immediate intraoperative start of combination therapydid not result in rifampicin resistance. Additional prospective studies are warranted to elucidate the optimal duration of rifampicin as part of the antimicrobial therapy in patients with a staphylococcal PJI.

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