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RESEARCH NOTE

Treatment of acute post-surgical infection of joint arthroplasty

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ABSTRACT

The best antibiotic regimen for acute prosthetic joint infection, treated without removal of the implant, has not been well-defined. This study describes the use of a protocol based on oral rifampicin combinations to treat 47 cases that were followed prospectively for a 2-year period. The regimen used most commonly was levofloxacin 500 mg/24 h plus rifampicin 600 mg/24 h for a mean duration of 2.7 ± 1 months. The cure rate was 76.9%, and the only independent risk-factor associated with treatment failure was infection caused by methicillin-resistant *Staphylococcus aureus* or *Enterococcus* spp. (OR 17.6, p 0.003). Overall, the results suggested that use of oral antibiotics, including rifampicin, for 2–3 months was a good treatment option.

Keywords Acute prosthetic joint infection, antibiotic regimen, levofloxacin, rifampicin, treatment

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Acute post-surgical prosthetic infection can be treated successfully by open debridément and prolonged intravenous antimicrobial therapy. However, it has not yet been established which

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antibiotic, or combination of antibiotics, is the most appropriate choice, or for how long treatment should be administered. This study presents the results of a treatment protocol based on open debridément and leaving the prosthesis in place. In addition, independent variables associated with treatment failure are analysed.

Acute deep post-surgical infection was considered when infection appeared within the first 3 months after arthroplasty and the patient had inflammatory signs, increased levels of C-reactive protein, and yielded pathogenic microorganisms from deep samples, and/or pus was present. Once samples were taken, treatment with a broad-spectrum parenteral antibiotic was commenced, with treatment modified subsequently according to the organism's antibiogram, giving priority to oral combinations containing rifampicin. Oral dosages of levofloxacin, clindamycin and rifampicin were 500 mg/24 h, 300 mg/8 h and 600 mg/24 h, respectively. The intravenous dosage of teicoplanin was 10 mg/kg/24 h. Antibiotic treatment was continued until resolution of clinical signs and normalisation of CRP levels (< 1 mg/dL).

Patients were followed for a minimum of 24 months. Outcome was evaluated according to the following definitions: (i) *cured*, when the patient was asymptomatic, the prosthesis was functioning well, and the CRP level was < 1 mg/mL, or when the patient developed a non-septic complication that required prosthesis replacement and cultures of deep tissues were negative; (ii) *failure*, when inflammatory signs and high CRP levels remained during treatment, or reappeared after completing treatment; and (iii) *non-evaluable*, when the patient died before treatment was completed.

Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL, USA). For univariate analyses, categorical variables were compared using the chi-square test or Fisher's exact test, and quantitative variables were compared using the Students *t*-test or ANOVA. A logistic regression model was used to identify independent variables associated with treatment failure. Variables included in the statistical analysis were age, co-morbidity, type of prosthesis, route of administration and duration of antimicrobial treatment, and the aetiological agent. Statistical significance was defined as a two-tailed p value < 0.05.

During the study period, 47 patients were investigated. The mean age (SD) was 76.1 (10) years, 23 patients were male and 24 were female. Twenty-one cases involved a hemiarthroplasty (HA), 11 involved a total hip arthroplasty (THA), and 15 involved a total knee arthroplasty (TKA). The mean time from arthroplasty to the diagnosis of infection was 25.7 (16.8) days. Eight patients (seven HA and one THA) died within a few days of being diagnosed and were thus non-evaluable.

The mean (SD) duration of antimicrobial treatment was 2.7 (1) months, with 30 patients treated by the oral route and nine treated intravenously. Outcome according to the type of implant and aetiology is summarised in Table 1. The duration and efficacy of the three antimicrobial regimens used most frequently are shown in Table 2. The duration of antibiotic treatment was similar for all microorganisms.

Table 1. Patient outcome according to aetiological agent and type of implant

	Hemiarthroplasty (n = 21)		Total hip arthroplasty (n = 11)		Total knee arthroplasty (n = 15)	
Microorganism	**Evaluable[a]**	**Cured (%)**	**Evaluable[a]**	**Cured (%)**	**Evaluable[a]**	**Cured (%)**
Gram-positive cocci	10	8 (80)	9	8 (88.9)	12	6 (50)
Staphylococcus aureus	4	4 (100)	1	1 (100)	6	2 (33.3)
Methicillin-susceptible	3	3 (100)	1	1 (100)	3	2 (75)
Methicillin-resistant	1	1	–	–	3	0
Coagulase-negative staphylococci	3	3 (100)	6	6 (100)	5	3 (60)
Methicillin-susceptible	–	–	3	3	2	1 (50)
Methicillin-resistant	3	3	3	3	3	2 (75)
Streptococcus viridans	1	1 (100)[b]	1	1 (100)	1	1 (100)
Enterococcus spp.	2	0 (0)	1	0 (0)	–	–
Gram-negative bacilli	3	3 (100)[c]	–	–	1	1 (100)
Culture-negative	1	1 (100)	1	1 (100)	2	2 (100)[b]
Total	14	12 (85.7)	10	9 (90)	15	9 (60)

[a]Patients who completed antimicrobial therapy.
[b]One patient developed an aseptic loosening after 24 months.
[c]One patient had a prosthesis luxation after 6 months and cultures were negative.

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Table 2. Patient outcome according to antimicrobial treatment

Antimicrobial	Mean duration (SD) in months	No. cured/No. evaluable[a] (%)	Microorganisms (number cured/number treated)					
			CNS (MR)	SAU (MR)	STR	ENT	GNB	CN
Lev + Rif	2.5 (1.1)	12/13 (92.3)	5/6 (1)	5/5	1/1	–	–	1/1
Clin + Rif	3 (1.3)	7[2]/10 (70)	4/4 (4)	1/3 (1)	2/3	–	–	–
Tei (alone or in combination)	2.8 (1)	5[b]/8 (62.5)	2/2 (2)	0/1 (1)	–	0/2	–	3/3
Other regimens	2.5 (0.7)	6[c]/8 (75)	1/1 (1)	1/2 (2)	–	0/1	4/4	–
Total		30/39 (76.9)	12(6)/13(8)	7(1)/11(4)	3/4	0/3	4/4	4/4

SD, standard deviation; Lev, levofloxacin; Rif, rifampicin; Clin, clindamycin; Tei, teicoplanin; CNS, coagulase-negative staphylococci; SAU, *Staphylococcus aureus*; MR, methicillin-resistant; STR, *Streptococcus* spp.; ENT, *Enterococcus* spp.; GNB, Gram-negative bacilli; CN, culture-negative.
[a]Evaluable, patients who completed antimicrobial therapy.
[b]One patient developed an aseptic loosening.
[c]One patient had a prosthesis luxation after 6 months and cultures were negative.

Thirty (76.9%) of the 39 evaluable patients were classified as cured; 27 maintained the prosthesis in place with good mechanical results after follow-up for 24 months, and the prosthesis was removed because of non-septic complications in three cases. Nine patients were classified as treatment failure (23.1%). The only independent factor associated with failure in the multivariate analysis was infection caused by *Enterococcus* spp. or methicillin-resistant *Staphylococcus aureus* (MRSA) (OR 17.6, 95% CI 1.3–238.3, p 0.003).

Open debridément combined with administration of intravenous β-lactam agents for 4–6 weeks has been reported to have a success rate of < 50% with *S. aureus* infections [1–3], but a combination of rifampicin with other antibiotics has been demonstrated in recent years to have a higher success rate [4–7]. The protocol used in the present study for treatment of acute post-surgical prosthetic infection gave priority to levofloxacin plus rifampicin. Levofloxacin was preferred over ciprofloxacin because of: (i) its better therapeutic index as a consequence of a lower MIC for *S. aureus* and a high serum concentration (higher bioavailability); (ii) the advantages of once-daily administration; and (iii) its bactericidal activity against staphylococci in a non-growing state [8], which probably makes it more active against bacteria living in a biofilm, especially when combined with rifampicin.

The results suggested that rifampicin 600 mg/24 h was as effective as the regimen of 450 mg/12 h used previously [7]. Rifampicin is a concentration-dependent antibiotic, and the best pharmacodynamic parameter related to its activity is C_{max}/MIC [9]. Rifampicin as a 600-mg mono-dose is easier to administer and could also result in a higher C_{max}/MIC than a dose of 450 mg/12 h. The results in Table 2 show that the once-daily regimen of levofloxacin plus rifampicin had the highest cure rate of 92.3%.

The only independent risk-factor for failure was infection caused by MRSA or *Enterococcus* spp. (OR 17.6, 95% CI 1.3–238.3). Previous experience with high doses and prolonged courses (6–9 months) of co-trimoxazole for infections caused by MRSA showed a 50% and 62% success rate with THP and TKP infections, respectively [10]. However, 20% of patients stopped treatment because of adverse events. Other active antimicrobial agents with good preliminary results, such as linezolid [11–13], should also be investigated.

Although the logistic regression model showed that the type of implant was not a factor associated with treatment failure, the cure rate was lower in patients with a TKA (60% vs. 90% and 85.7% for THA and PHA, respectively). This was probably associated with the fact that MRSA was isolated more frequently from knee prosthesis infections than from other infections. However, previous studies have reported a high failure rate in the treatment of knee prosthesis infections [3,14], indicating that this aspect deserves further investigation.

In conclusion, the results of this study suggest that acute post-surgical infection of joint arthroplasty caused by methicillin- and fluoroquinolone-susceptible staphylococci or streptococci can be treated with open debridément and the use of oral antimicrobial agents for a 2–3-month period. Infections caused by MRSA or *Enterococcus* spp. were associated with a high rate of treatment failure, making it necessary to evaluate new agents active against these pathogens.

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RESEARCH NOTE

Clinical significance of isolated *Staphylococcus aureus* central venous catheter tip cultures

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ABSTRACT

This retrospective cohort study examined the clinical significance of isolated *Staphylococcus aureus* central venous catheter (CVC) tip cultures (i.e., positive tip cultures without concomitant positive blood cultures). Subsequent *S. aureus* bacteraemia was found in nine (12%) of 77 patients at a median time of 4 days after CVC removal. A high co-morbidity score and no effective antibiotic treatment within 48 h of CVC removal were independent risk-factors for septic complications following multivariate analysis. A matched case-control study that compared the above cohort with patients with CVC tip cultures negative for *S. aureus* supported the significance of these findings.

Keywords Bacteraemia, central venous catheter, risk-factors, significance, *Staphylococcus aureus*, tip cultures

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Few data exist concerning the clinical significance of central venous catheter (CVC) tip cultures that are positive for *Staphylococus aureus* in patients who have no blood cultures collected around the time of CVC removal, or whose

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