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## BRIEF OBSERVATION


 AJM Theme Issue: Infectious Disease

# Conservative Treatment of Staphylococcal Prosthetic Joint Infections in Elderly Patients

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**ABSTRACT:**

**BACKGROUND:** We report the outcome of debridement and prosthesis retention plus long-term levofloxacin/rifampicin treatment of prosthetic joint infections.

**METHODS:** Staphylococcal prosthesis joint infections were defined by positive culture of joint aspirate, intraoperative debridement specimens, or sinus tract discharge in the presence of clinical criteria. Patients received long-term oral levofloxacin 500 mg and rifampicin 600 mg once per day. Sixty patients (age 74.6 ± 8.4 years) were included.

**RESULTS:** Coagulase-negative staphylococci were significantly more frequently isolated in the knee (78.6%;  $P = .00001$ ). Of the *Staphylococcus aureus* isolates, 33.3% were methicillin-resistant. Time from arthroplasty to symptoms onset was higher ( $P = .03$ ) in coagulase-negative staphylococci infections. Global failure was 35% (higher for the knee) and ranged from 16.6% to 69.2% ( $P = .0045$ ) in patients with symptoms duration of less than 1 month to more than 6 months. A shorter duration of symptoms ( $P = .001$ ) and time to diagnosis ( $P = .01$ ) were found in cured patients versus patients showing failure. Among those with *S. aureus* infections, a higher failure rate was found with methicillin-resistance.

**CONCLUSIONS:** Efficacy was higher in patients with shorter duration of symptoms, earlier diagnosis, hip infections, and methicillin susceptibility. © 2006 Elsevier Inc. All rights reserved.

**KEYWORDS:** *Staphylococcus aureus*; Coagulase-negative staphylococci; Levofloxacin; Rifampicin; Arthroplasty; Joint infections

Prosthesis retention can be considered in early infections when the prosthesis is not loose and has good functional status. The etiologic microorganism is likely to be susceptible (as staphylococci) to oral antibiotics,<sup>1</sup> and prosthesis removal may be excessively risky,<sup>2</sup> such as in elderly persons.<sup>3</sup>

Prosthesis retention involves early debridement and prolonged antibiotic treatment.<sup>4</sup> If such an approach results in low morbidity with a high success rate, this remains to be elucidated.<sup>5</sup>

We report the results of conservative treatment of pa-

tients with staphylococcal-infected prosthetic joints after total replacement.

## METHODS

### Study Population

Staphylococcal infection developed in patients who underwent total hip or knee arthroplasty. Patients who underwent debridement and prosthesis retention with antibiotic treatment (levofloxacin and rifampicin following our hospital's routine) from November 1998 to March 2004 were included.

### Definitions

Staphylococcal infection was defined by positive culture of debridement specimens, consecutive joint aspirates ( $\geq 2$ ), or

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sinus tract discharge ( $\geq 3$  on different days). At least one of the following criteria should be present: local pain, swelling, C-reactive protein greater than 0.6 mg/dL, and/or erythrocyte sedimentation rate greater than 10 mm in the first hour; radiolucent areas at bone-cement interface, periprosthetic osteolysis or localized periosteal new bone formation in radiography, and/or bone scanning positive, C-reactive protein greater than 0.6 mg/dL, and/or erythrocyte sedimentation rate greater than 10 mm in the first hour (these determinations were not considered if performed 2 weeks after the arthroplasty); and a sinus tract communicating with the prosthesis.

“Treatment success” was defined as the resolution of all signs and symptoms of active infection without prosthesis removal at the end of therapy and at the end of each patient’s follow-up. “Treatment failure” was defined as the lack of response to therapy or recurrence of signs and symptoms and/or sinus tract bacterial isolation during therapy or follow-up.

“Time free of symptoms” was defined as time (in months) from joint replacement to symptoms onset; “symptoms duration” was defined as time (in months) from initiation of symptoms to diagnosis; and “time to diagnosis” was defined as time (in months) from joint replacement to diagnosis, and was the addition of both.

### Antibiotic Treatment

Patients received oral levofloxacin 500 mg and rifampicin 600 mg once per day for at least 6 weeks after resolution of signs and symptoms, and normalization of C-reactive protein for a minimum of 3 months. This treatment was initially prescribed or followed an initial short course ( $< 2$  weeks) of intravenous levofloxacin (500 mg once per day) plus oral rifampin 600 mg once per day.

### Statistical Analysis

The chi-square test was used for comparisons of percentages. The mean time values were compared using the paired Student *t* test or the Mann-Whitney *U* test. A *P* value less than .05 was considered significant.

## RESULTS

### Study Population

Sixty patients (mean age:  $74.6 \pm 8.4$  years) were included, 38 of whom were female (63.3%). Underlying diseases

were rheumatoid arthritis (10 cases), type II diabetes mellitus (7 cases), and mild renal failure (4 cases).

Twenty-eight infections (46.7%) followed knee arthroplasty, and 32 infections (53.3%) followed hip arthroplasty. One year was the minimum follow-up period posttreatment.

Symptoms duration of less than 1 month was reported by 24 patients (40%), 2 to 6 months by 23 patients (38.3%), and more than 6 months by 13 patients (21.7%).

### Microbiologic Findings

Etiologic diagnosis was performed by culture of aspiration samples (19 cases; 31.7%), debridement material (34 cases; 56.7%), and sinus tract discharge (7 cases; 11.7%: 0/24 [0%] for symptoms duration of  $< 1$  month, 4/23 [17.4%] for 2 to 6 months, and 3/13 [23.1%] for  $> 6$  months).

*Staphylococcus aureus* was isolated in 21 cases (35%), and coagulase-negative staphylococci was isolated in 39 cases (65%). All coagulase-negative staphylococci but two (*S. haemolyticus*, *S. warneri*) were *S. epidermidis*. All isolates were levofloxacin-susceptible.

Table 1 shows etiologic and anatomic relationships. In the etiologic relationship, *S. aureus* was more ( $P = .039$ ) prevalent in hip infections (15/21; 71.4%).

From the anatomic perspective, *S. aureus* and coagulase-negative staphylococci accounted for approximately one-half each of all hip infections, whereas coagulase-negative staphylococci were the causative agents in 78.6% of knee joint infections (22/28), and *S. aureus* was the causative agent in 21.4% of knee joint infections (6/28) ( $P = .00001$ ).

No differences were found in *S. aureus* isolation among the three categories of symptoms duration: 37.5% for less than 1 month, 26.1% for 2 to 6 months, and 46.2% for more than 6 months.

### CLINICAL SIGNIFICANCE

- Coagulase-negative staphylococci are more frequent etiologic agents of prosthetic knee joint infections than coagulase-positive staphylococci.
- Unacceptable failure rates of conservative treatment were found in patients with long symptomatic time periods before diagnosis.
- Time free of symptoms (from joint replacement to symptoms onset) was twice as long for coagulase-negative staphylococci than for *Staphylococcus aureus*.
- Methicillin-resistance showed a tendency for treatment failure of *S. aureus* prosthetic joint infections.

**Table 1** Prosthetic Joint Infections by Microorganism and Anatomic Site

	<i>Staphylococcus aureus</i>		Coagulase-negative Staphylococci		Total	
	n	%	n	%	n	%
Knee	6	21.4	22	78.6†	28	100
Hip	15	46.9*	17	53.1	32	100

\**P*  $< .05$  vs knee.

†*P*  $< .05$  vs *S. aureus*.

**Table 2** Treatment Failure Rates for Prosthetic Joint Infections by Anatomic Site, Microorganism, and Duration of Symptoms

No. Failures/No. Patients (%)									
Duration	<i>Staphylococcus aureus</i>			Coagulase-negative Staphylococci			Total		
	Knee	Hip	Total	Knee	Hip	Total	Knee	Hip	Total
≤1 mo	1/4 (25)	0/5	1/9 (11.1)	1/7 (14.2)	2/8 (25.0)	3/15 (20.0)	2/11 (18.2)	2/13 (15.4)	4/24 (16.6)
2-6 mo	1/1 (100)	2/5 (40.0)	3/6 (50.0)	4/9 (44.4)	1/8 (12.5)	5/17 (29.4)	5/10 (50.0)	3/13 (23.1)	8/23 (34.8)
>6 mo	1/1 (100)	3/5 (60.0)	4/6 (66.6)	4/6 (66.6)	1/1 (100)	5/7 (71.4)	5/7 (71.4)	4/6 (66.6)	9/13 (69.2)*
Total	3/6 (50.0)	5/15 (33.3)	8/21 (38.1)	9/22 (40.9)	4/17 (23.5)	13/39 (33.3)	12/28 (42.8)	9/32 (28.1)	21/60 (35.0)

\* $P < .05$  vs ≤1 month.

Seven of 21 *S. aureus* infections (33.3%) were methicillin-resistant *Staphylococcus aureus* (MRSA).

Among *S. aureus* infections, MRSA isolates increased as symptoms duration increased, from 11.1% (1/9) when less than 1 month, to 33.3% (2/6) when 2 to 6 months, and 66.6% (4/6) when more than 6 months, although differences between less than 1 month and more than 6 months of symptoms duration were not significant ( $P = .09$ ).

### Treatment Outcome

Table 2 shows failure rates according to symptoms duration. Differences ( $P = .0045$ ) were found in the failure rate between patients with more than 6 months of symptoms duration (69.2%) and patients with less than 1 month of symptoms duration (16.6%). Differences between these two groups were maintained splitting by hip (66.6% for >6 months vs 15.4% for <1 month;  $P = .088$ ) or knee infections (71.4% for >6 months vs 18.2% for <1 month;  $P = .077$ ). Globally, similar failure rates were obtained in *S. aureus* versus coagulase-negative staphylococci infections (38.1% vs 33.3%), but not ( $P = .23$ ) in knee versus hip infections (42.8% vs 28.1%).

Among those with *S. aureus* infections, more failures ( $P = .08$ ) were obtained for MRSA (5/7; 71.4%) than for methicillin-susceptible isolates (3/14; 21.4%).

### Timings and Outcome

Longer times were found in patients showing failure: longer time free of symptoms ( $2.0 \pm 1.8$  vs  $1.1 \pm 0.9$ ;  $P = .09$ ), longer symptoms duration ( $6.7 \pm 4.3$  vs  $2.5 \pm 2.4$ ;  $P = .001$ ), and longer time to diagnosis ( $7.3 \pm 4.8$  vs  $3.5 \pm 2.9$ ;  $P = .01$ ).

### Timings in Relation to Cause

Table 3 shows these data split by cause. Differences in time free of symptoms between patients showing failure and cure were the result of those infected by coagulase-negative staphylococci (2.6 vs 1.3;  $P = .062$ ), because time free of symptoms was similar (regardless outcome) in the case of *S. aureus* infections (0.8 vs 0.9;  $P = .83$ ). Significantly longer symptoms duration was found in patients with failures for both *S. aureus* (7.4 vs 2.7;  $P = .034$ ) and coagulase-negative staphylococci (6.2 vs 2.5;  $P = .012$ ), whereas longer time to diagnosis was only found in coagulase-negative staphylococci (8.2 vs 3.4;  $P = .018$ ).

As shown in Table 3, time free of symptoms (considering all infections regardless outcome) was twice as long for coagulase-negative staphylococci than for *S. aureus* (1.8 vs 0.9;  $P = .03$ ).

**Table 3** Treatment Outcomes in Prosthetic Joint Infection According to Cause, Time Free of Symptoms, Symptoms Duration, and Time to Diagnosis

	n	Time (Months)		
		Time Free of Symptoms	Symptoms Duration	Time to Diagnosis
<i>Staphylococcus aureus</i>				
Cure	13	0.9 ± 1.3	2.7 ± 2.9	3.6 ± 4.1
Failure	8	0.8 ± 0.4	7.4 ± 4.5†	5.4 ± 3.4
Total	21	0.9 ± 1.1	4.5 ± 4.2	4.1 ± 3.9
Coagulase-negative staphylococci				
Cure	26	1.3 ± 0.7	2.5 ± 2.2	3.4 ± 1.9
Failure	13	2.6 ± 1.9	6.2 ± 4.5†	8.2 ± 5.2†
Total	39	1.7 ± 1.4*	3.8 ± 3.6	5.0 ± 4.0

\* $P < .05$  vs *S. aureus*.

† $P < .05$  vs cure.

**Table 4** Treatment Outcomes in Prosthetic Joint Infection According to Infection Site, Time Free of Symptoms, Symptoms Duration, and Time to Diagnosis

	n	Time (Months)		
		Time Free of Symptoms	Symptoms Duration	Time to Diagnosis
<b>Knee</b>				
Cure	16	1.0 ± 0.7	2.6 ± 2.7	3.1 ± 2.5
Failure	12	2.2 ± 2.2	6.6 ± 4.3*	8.3 ± 5.7*
Total	28	1.5 ± 1.6	4.4 ± 4.0	5.2 ± 4.8
<b>Hip</b>				
Cure	23	1.3 ± 1.1	2.5 ± 2.3	3.8 ± 3.2
Failure	9	1.7 ± 0.8	6.8 ± 4.8*	5.7 ± 2.6*
Total	32	1.4 ± 1.1	3.7 ± 3.7	4.2 ± 3.2

\**P* < .05 vs cure.

### Timings in Relation to Anatomic Site

Table 4 shows data split by infection site. In both knee and hip infections, significantly longer symptoms duration and time to diagnosis were found in patients showing failure versus cure.

### Treatment Duration

Treatment durations in the 39 cured patients were similar in infections caused by *S. aureus* (6.6 ± 1.0) and coagulase-negative staphylococci (6.9 ± 1.0), and in knee infections (7.1 ± 0.9) and hip infections (6.6 ± 1.0). Treatment duration in the 21 patients showing failure were similar in infections caused by *S. aureus* (3.0 ± 1.1) and coagulase-negative staphylococci (2.9 ± 1.4), and in knee (3.2 ± 1.2) and hip infections (2.7 ± 1.3).

### DISCUSSION

Conservative treatment with rifampicin and levofloxacin produced significantly lower failure rates in patients with less than 1 month symptoms duration in comparison with those with more than 6 months (16.6% vs 69.2%), with longer time free of symptoms, symptoms duration, and time to diagnosis in patients showing failure versus cure. This association between longer time to diagnosis and failure reaches statistical significance only in coagulase-negative staphylococci infections, possibly because of a higher time free of symptoms.

A similar failure rate was obtained with both types of Staphylococci in contrast with previous reports.<sup>2</sup> Isolation of MRSA among *S. aureus* infections increased from 11.1% in patients with symptoms duration of less than 1 month to 66.6% in patients with symptoms duration of more than 6 months. A significantly higher failure rate was found among MRSA isolates versus methicillin-susceptible isolates. Both factors (susceptibility to methicillin and symptoms duration) may be related to the prediction of failure.

With respect to infection site, higher failure rates were found in knee versus hip infections (42.8% vs 28.1%) globally and in both staphylococcal types. A higher number of coagulase-negative staphylococci isolates were found in knee infections (78.6% vs 21.4%), with a similar rate of both staphylococci in hip infections, in contrast with other reports.<sup>6</sup>

Infections caused by *S. aureus* and coagulase-negative staphylococci seem to be different entities, at least when considering the differences found in the time free of symptoms and the frequency of their isolation in the hip and knee. In view of the prognosis of patients receiving conservative treatment, longer time of symptoms duration before clinic attendance and longer time to diagnosis have a high impact on outcome.

In patients with more than 6 months of symptoms duration, conservative treatment is far from adequate with failure rates of approximately 70% regardless of coagulase production of the staphylococcal isolate or knee or hip location of the infection.

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