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Are gram negative bacilli a threat for prosthetic joint replacements? Experience of a university hospital

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Prosthetic joint infections (PJIs) are rare but the most devastating complications of prosthetic joint replacements. The incidence varies between 0.6% and 2.5% per year with an economic burden of $30,000-$60,000 per patient. PJIs lead to prolonged hospitalization, increased morbidity and mortality, and severe inability of patients (1). The aim of the present study was to evaluate the incidence of PJIs, etiology of infection, and antimicrobial prophylaxis in an orthopedic clinic.

The study was conducted in Erciyes University Hospital between April 2006 and April 2008. It is a tertiary care center in Central Anatolia, Turkey, and has been providing care for a large population in the region. The annual prosthetic joint operation number is approximately 550. Special laminar flow ventilation, without HEPA filtration, has been used in orthopedic operation rooms.

This was a prospective and observational study during a 2-year period, and there was no intervention during this period. All patients with prosthetic joint replacement were included. A designated registered nurse from the hospital's infection control unit regularly assessed all patients who underwent orthopedic procedures. Patients were followed up for 2 years. PJI was diagnosed by clinical and inflammatory markers as described previously (2). The infections were described as early (within 3 months) and delayed (between 3 months and 2 years) manifestation (3). Operations were classified as clean, clean-contaminated, contaminated, and dirty according to the level of bacterial contamination (4). Multi-drug resistance (MDR) was defined as diminished susceptibility to 2 or more antibiotic classes (5).

During the 2-year period, the total number of prosthesis operations was 1122, 717 (64%) of which had primary total hip prosthesis (THP), 395 (35%) primary total knee prosthesis (TKP), and 10 (1%) other prosthesis operations. The median age was 64, ranging from 13 to 99 and the median operation duration was 100 min, ranging from 25 to 400 min. Among these operations, 1110 (99%) were clean and 12 (1%) were dirty. Dirty operations were re-intervention operations for infected prosthesis. AP was given in all clean operations and administered within 15-60 min before the incision. The most frequent antibiotic for AP was cefazolin. However, antibiotic combination or broad-spectrum antibiotic was used in 43% of clean operations. Gentamicin was the most preferred antibiotic in combination. The duration of AP was 24 h in only 4 (0.4%) operations, and 2-5 days in 70% of the operations (Table 1). A total of 27 (2.4%) prosthesis infections was determined and 22 (82%) of them were in the clean operations. The infection rate was 2% in THP and 3% in TKP. No infection was detected in the other prosthesis operations during the study

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Table 1. Prosthesis joint infection and antibiotic prophylaxis in prosthetic joint replacements.

Prosthetic joint replacement	n = 1122	%
Hip	717	64
Knee	395	35
Others	10	1
Age (median, range)	64 (13-99)	
Prosthetic joint replacement	Infection/n	%
Hip	15/717	2
Knee	12/395	3
Others	0/10	0
Total	27/1122	2.4
Antibiotic prophylaxis	n = 1110	
Cefazolin	628	56.6
Cefazolin+gentamicin	298	26.8
Ampicillin/sulbactam+gentamicin	87	7.8
Ampicillin/sulbactam	84	7.6
Cefazolin+ampicillin/sulbactam	4	0.4
Cefazolin+gentamicin+clindamycin	2	0.2
Ampicillin/sulbactam+gentamicin+ clindamycin	2	0.2
Ceftriaxone	2	0.2
Ciprofloxacin	1	0.1
Metronidazol+ ceftriaxone	1	0.1
Cefazolin+ clindamycin	1	0.1
Duration of antibiotic prophylaxis (day)	n = 1110	
1	4	0.4
2-5	772	70
6-10	319	29
>10	15	1.4

period. Infection occurred early in 20 (74%) of the patients and delayed in 7 (26%) of the patients. None of the patients had infection in another source before PJI occurred. Culture was positive in 21 patients and 71.5% of the microorganisms were gram negative bacilli (Table 2). Furthermore, all the isolated microorganisms were MDR bacteria.

In our orthopedic clinic, incidence of prosthesis infection was within the range reported in the literature (1); however, the frequency of causative microorganisms was different from previous reports. Gram-positive bacteria were responsible for nearly 65% of PJIs, whereas gram negative bacilli caused 25% of these infections in the literature (1). Conversely, 71.5% of our causative microorganisms were gram negative and all of the isolates were MDR in our study. Since multiple factors (patient factors, technical aspects of operation, perioperative management, prophylactic antibiotic administration, etc.) affect the microbiology of surgical site infection, prophylactic antibiotic administration is one of the important components of this issue. The critical aspects of

Table 2. Causative bacteria in prosthetic joint infections.

Microorganisms	n (%)
Gram positive bacteria	6 (28.5)
Enterococcus spp.	3
Staphylococcus aureus	2
Coagulase negative staphylococcus	1
Gram negative bacteria	15 (71.5)
Escherichia coli	5
Pseudomonas aeroginosa	1
Acinetobacter baumannii	2
Enterobacter cloacae	2
Klebsiella pneumoniae	2
Klebsiella oxytoca	1
Klebsiella spp.	1
Enterobacter spp.	1

*All microorganisms were multidrug resistant

prophylactic antibiotic administration are defined as giving an appropriate antibiotic, giving an adequate dose, achieving proper timing before incision, and maintaining therapeutic levels of antibiotic throughout the operation. However, AP may have some disadvantages (side effects, antibiotic cost, and induction of antimicrobial resistance) if prolonged antimicrobial or broad spectrum antibiotic is used (6). The recommended duration of AP in orthopedic surgery is not longer than 24 h, and prolongation does not have extra benefit for prevention of surgical site infections (1,7). In this study, AP was administered for 24 h only in 0.4% of all prosthetic operations. Moreover, combination therapy or broad spectrum antibiotic were used in 43% of operations. Although antibiotic resistance is not only related to inappropriate perioperative prophylaxis, it has an important role in the development of resistance to antibiotics.

We followed up patients for 2 years, and so we were not able to record late manifestation of PJI. However, late infections are predominantly acquired by hematogenous seeding and hemotogenous infection only plays a minor role (0.18%-0.6%) in prosthetic joint replacement (1). In this study, 74% of the PJIs were early manifestation and none of our patients had previous or concomitant infection in another source. Unfortunately, infection control practices in the operative room could not be evaluated, and early and delayed infections are usually acquired during implantation of the prosthesis (1). Poor infection control practices can be another reason for MDR gram-negative bacteria in our study.

In conclusion, AP is critical for prevention of surgical site infection. However, postoperative doses do not have any extra benefit, and moreover increase the incidence of MDR pathogens. Cost of these extra doses and antibiotic therapy for MDR pathogens is another important issue for developing countries, which has to be taken into consideration for infection control. On the other hand, surveying nosocomial infections, evaluating the antibiograms of causative pathogens, and informing clinicians of the results are important topics for infection control and reducing the incidence of resistant pathogens.

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