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Expanded Gram-Negative Antimicrobial Prophylaxis Reduces Surgical Site Infections in Hip Arthroplasty

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A B S T R A C T

Background: A first-generation cephalosporin is the recommended antibiotic prophylaxis for implants. However, this standard does not address the increasing prevalence and virulence of gram-negative pathogens infecting patients. We found that gram-negative bacilli caused 30% of our surgical site infections (SSIs) following hip procedures, whereas only 10% of knee SSIs were caused by gram-negative bacilli. To address this, we instituted Expanded Gram-Negative Antimicrobial Prophylaxis (EGNAP) for our hip arthroplasty patients. The purpose of this study is to measure the effect of EGNAP on the SSI rates following primary total hip arthroplasty.
Methods: The study consisted of 10,084 total patients. Before July 2012, all patients were administered 1 g of cefazolin. After July 2012, our protocol was adjusted by adding the EGNAP with either gentamicin or aztreonam to hip patients (group 1) and not to the knee arthroplasty patients (group 2).
Results: Group 1 consisted of the 5389 primary hip arthroplasty patients. Of these patients, 4122 (before July 2012) did not receive weight-based high-dose gentamicin and 1267 (after July 2012) did. Before the introduction of EGNAP, group 1 SSI rate was 1.19% (49/4122). After July 2012 when EGNAP was added, the overall group 1 SSI rate decreased to 0.55% (7/1267) ($P = .05$). During the study period, there was not a significant difference in SSI rate of knee arthroplasty (group 2): 1.08% vs 1.02% ($P = .999$).
Conclusions: The addition of EGNAP for hip arthroplasty is a safe and effective method to decrease SSIs.
Level of Evidence: III. Case-control study.

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Prophylactic antibiotics are an effective means of decreasing the likelihood of surgical site infections (SSIs) following total joint arthroplasty. The early 1960s saw several published studies demonstrating the ability of antibiotics given within 1 hour of incision to reduce SSIs following implant surgery. These early studies advocated the use of first-generation cephalosporins including cefazolin [1,2]. Since that time, there has been little or no change in the standard antibiotic prophylactic regimen consisting of intravenous cefazolin given within 1 hour of incision or tourniquet inflation [3]. However, the types and virulence of infecting pathogens have evolved since the protocol was developed. Over the last 50 years, there has been an increase in the proportion of SSIs caused by gram-negative bacilli (GNB) [4,5]. At our institution, 30% of SSIs following hip arthroplasty were caused by GNB, and of these isolates, 44% were resistant to cefazolin [6]. In addition, GNB resistance to cefazolin is increasing on a national basis [4–6].

Recent recommendations for antimicrobial prophylaxis in surgery issued by the American Society of Health-System Pharmacists state that "Individual health systems must consider local resistance patterns of organisms and overall SSI rates when adopting these recommendations." [7]. This recommendation is based on an important principle of antibiotic stewardship—basing selection of antimicrobial agents on both the narrowest spectrum and adequate activity against the pathogens which may be encountered.

With increasing resistant isolates of GNB in our SSIs, it became clear that our standard antibiotic prophylactic protocol was no longer sufficient. To expand gram-negative antimicrobial prophylaxis, we added weight-based high-dose gentamicin (or aztreonam if patient had contraindications to gentamicin) to our prophylactic antibiotic protocol for hip arthroplasty. Incorporating gentamicin into our protocol required reengineering the process of administering preoperative antibiotics. We addressed the difficulty of calculating weight-based doses using complex formulas in the busy preoperative time period by partnering with the pharmacy and anesthesia to develop 7 nomogram-based standard doses. Initially, these doses were based on height, weight, and creatinine and eventually simplified to strictly weight based. The anesthesiologists are responsible for determining and administering the correct gentamicin doses (Appendix A). This protocol was

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begun in July 2012. The purpose of this study is to measure the effect of this new antibiotic protocol on the SSI rates following hip arthroplasty.

Methods

This study was conducted at a university-affiliated, single-specialty, orthopedic hospital. Data from all 10,084 primary total hip and knee arthroplasty patients from January 2009 through December 2013 were collected. The Centers for Disease Control and Prevention's National Healthcare Safety Network criteria were used by our infection control department to define SSIs. Before July 2012, all patients were administered 1 g of cefazolin. This patient group represented the study's control. After July 2012, our protocol was adjusted by adding gram-negative coverage with either weight-based gentamicin or aztreonam to hip patients only. Patients undergoing primary hip arthroplasty were given 1 g of cefazolin and gentamicin with a weight-based dosing protocol (Appendix A). Those >75 years of age, who weighed >120 kg, or with myasthenia gravis were given 2 g of aztreonam instead of gentamicin. Patients with a penicillin allergy were given a weight-based dose of vancomycin as well as gentamicin or aztreonam as indicated above. Knee and hip arthroplasty patients received a weight-based dose of vancomycin if their nares were colonized by methicillin-resistant *Staphyloccus aureus* or if they were allergic to penicillin. Otherwise, knee arthroplasty patients received standard 1 g of cefazolin. Vancomycin coverage for patients with nasal methicillin-resistant *S aureus* and the use of chlorhexidine wipes the evening before surgery began in 2009. All 10,084 study patients received this treatment. The only difference in the control and treatment groups was the addition of Expanded Gram-Negative Antimicrobial Prophylaxis (EGNAP) in the treatment group. We also tracked the rate of nephrotoxicity using the Risk Injury Failure Loss and End Stage Kidney Disease (RIFLE) criteria for the first 1590 patients who received gentamicin in the EGNAP group.

A list of all patients undergoing these surgical procedures was merged with an SSI database to identify confirmed SSI cases and their cultures. Patients were evaluated for type (gram + or gram −) and location (superficial vs deep) of the infecting organism. Data analysis was performed using Statistical Analysis System (SAS, Cary, NC); *P* values were calculated with a 2-sided Fisher exact test.

Results

The study consisted of 10,084 cases. Of these cases, we identified 106 SSIs equaling an infection rate of 1.05%. Total hip arthroplasty and total knee arthroplasty accounted for 5389 and 4695 cases, respectively. The hip arthroplasty patients (5389 cases) comprised group 1. Of these patients, 4122 (before July 2012) did not receive weight-based high-dose gentamicin and 1267 (after July 2012) did. Before the introduction of EGNAP (gentamicin or aztreonam), the group 1 SSI rate was 1.19% (49/4122). After July 2012 when gentamicin or aztreonam was included as part of the prophylactic protocol, the overall group 1 SSI rate decreased to 0.55% (7/1267) ($P = .05$) (Diagram 1). Group 1 SSIs caused by GNB decreased from 0.32% (13/4122) to 0.00% (0/1267) ($P = .048$). Not only did the addition of gentamicin or aztreonam decrease GNB SSIs, but there was also a significant decrease in gram-positive bacteria SSIs. The SSI rate of gram-positive bacteria fell from 1.01% (41/4122) to 0.47% (6/1267) ($P = .05$) (Table 1).

In comparison to the substantial reduction of SSIs in hip arthroplasty, there was not a significant difference in SSI rate of knee arthroplasty (group 2). Before July 2012, the overall SSI rate with standard cefazolin prophylaxis was (36/3321) 1.08% compared with 1.02% (14/1374) ($P = .999$) for cases after July 2012 (Table 1). A review of 1590 patients who received the weight-based high-dose gentamicin demonstrated no cases of ototoxicity and no increase in the rate of nephrotoxicity compared with the preintervention group [8]. (Table 2)

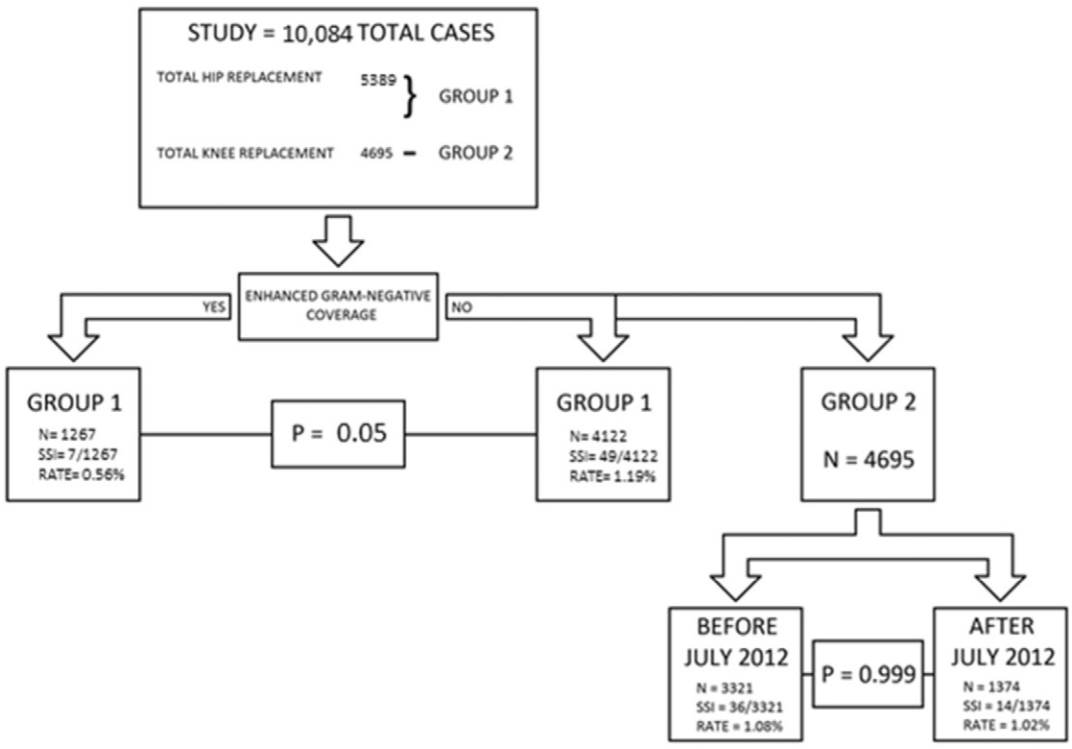

Diagram 1. SSI prevalence by organism.