Clin Orthop Relat Res (2014) 472:227–231
DOI 10.1007/s11999-013-3029-0

Clinical Orthopaedics and Related Research®
A Publication of The Association of Bone and Joint Surgeons®

SYMPOSIUM: 2013 KNEE SOCIETY PROCEEDINGS

Targeted Use of Vancomycin as Perioperative Prophylaxis Reduces Periprosthetic Joint Infection in Revision TKA

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Published online: 4 May 2013

Abstract

Background The role of vancomycin in surgical antimicrobial prophylaxis and high-risk patients who are most likely to benefit remains unclear.

Questions/purposes We determined the impact of targeted use of vancomycin on (1) the incidence of periprosthetic joint infection (PJI); and (2) the incidence of PJI from methicillin-resistant organisms in patients undergoing revision total knee arthroplasty (TKA) at our institution.

Methods In an effort to reduce PJI rates, we added vancomycin to cefazolin as surgical antimicrobial prophylaxis for patients undergoing revision TKA in October 2010. Internal data indicated a high rate of PJI in revision TKA and in particular PJI resulting from methicillin-resistant organisms, including methicillin-resistant *Staphylococcus aureus* (MRSA) and methicillin-resistant *Staphylococcus epidermidis* (MRSE). We retrospectively reviewed infection control surveillance data on 414 revision TKAs performed between July 2008 and June 2012 (fiscal years 2009–2012).

Results The overall rate of PJI in fiscal years 2009–2010 among 190 patients undergoing revision TKA was 7.89%. After the change in surgical antimicrobial prophylaxis, there was a significant reduction in PJI among patients undergoing revision TKA in fiscal years 2011–2012 to 3.13% ($p = 0.046$). In particular, we observed a reduction in PJI resulting from methicillin-resistant organisms over this same time period, from 4.21% to 0.89% ($p = 0.049$).

Conclusions Targeted use of vancomycin in patients undergoing revision TKA was effective in reducing the rate of PJI and PJI resulting from methicillin-resistant organisms in an institution with a high baseline rate of PJI due to MRSA and MRSE. Identification of high-risk subgroups of patients within a surgical population can help target infection prevention strategies to those who are most likely to benefit and thus minimize potential risks (eg, selection of resistant organisms, adverse drug events) associated with broader application of such an intervention.

Level of Evidence Level III, therapeutic study. See the Guidelines for Authors for a complete description of levels of evidence.

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Introduction

Periprosthetic joint infection (PJI) is one of the most challenging complications of TKA, resulting both in increased morbidity and increased healthcare costs [6, 7, 12]. One of the most important components of surgical site infection prevention is surgical antimicrobial prophylaxis, a key element of the Surgical Care Improvement Project (SCIP) infection prevention measures [4]. The American Academy of Orthopaedic Surgeons recommends the use of cefazolin or cefuroxime for antimicrobial prophylaxis before knee arthroplasty and suggests vancomycin as an alternative only in patients with a β-lactam allergy or those with known colonization with methicillin-resistant *Staphylococcus aureus* (MRSA) or in facilities with recent MRSA outbreaks [1]. The 2008 Society for Healthcare Epidemiology/Infectious Diseases Society of America Guidelines on Strategies to Prevent Surgical Site Infections in Acute Care Hospitals also do not recommend routine use of vancomycin and suggest reserving its use for selected scenarios: outbreak of surgical site infection resulting from MRSA, high endemic rates of surgical site infections resulting from MRSA, high-risk patients including cardiothoracic surgical patients and elderly diabetics, and high-risk surgical procedures involving an implant [2].

The specific patient populations including those at high risk for MRSA who may benefit from vancomycin in surgical antimicrobial prophylaxis have not been clearly defined and data to support these recommendations are limited. When compared with β-lactam antibiotics, vancomycin has not been clearly shown to be superior for prevention of surgical site infection [3]; however, most of these studies were published before the emergence of community-acquired MRSA. No definitions for high endemic rates of MRSA surgical site infection have been clearly established. High-risk surgical procedures involving an implant that are most likely to benefit from vancomycin have not been identified. In an era of increasing multidrug-resistant organisms, specifically MRSA and methicillin-resistant *Staphylococcus epidermidis* (MRSE), it is important to define specific surgical populations who are most likely to benefit from use of vancomycin in surgical antimicrobial prophylaxis while minimizing harm of selecting for antimicrobial resistance.

As part of routine infection control surveillance for surgical site infections, we observed that the overall rate of PJI in fiscal year 2009 at our hospital was 3.09% with a disproportionately higher rate of infections among revision TKA (8.79%) compared with primary TKA (0.86%) ($p = 0.0008$). In particular, we noted that the majority of PJI among patients undergoing revision TKA was the result of infections with MRSA or MRSE. In response to these findings, our Infectious Diseases and Infection Control programs recommended a modification to our surgical antimicrobial prophylaxis to include the addition of vancomycin to cefazolin for all patients undergoing revision TKA beginning in July 2009. Patients undergoing primary TKA continued to receive cefazolin alone. This change in prophylaxis was fully implemented in October 2010.

The objectives of this study were to determine the impact of targeted use of vancomycin among patients undergoing revision TKA on (1) the incidence of PJI in patients undergoing revision TKA; and (2) the incidence of PJI in revision TKA resulting from methicillin-resistant organisms.

Patients and Methods

We retrospectively reviewed prospectively collected infection control surveillance data on 1446 TKAs performed between July 2008 and June 2012 (fiscal years 2009–2012) at our institution. There were 31 infections (2.1%) identified during this time period by the Department of Hospital Epidemiology and Infection Control. All cases were defined using Centers for Disease Control and Prevention (CDC) National Health Safety Network (NHSN) criteria for surgical site infection, which includes infections occurring within 1 year of surgery if an implant was inserted and the infection appears related to the operative procedure [5]. All PJI cases were confirmed by an infectious diseases specialist and the attending surgeon. Patients diagnosed with PJI at outside hospitals were included if the index procedure was performed at the University of California, San Francisco (UCSF). For those patients presenting to outside institutions, we relied on infection control practitioners at outside hospitals to identify patients and notify our institution; these cases were confirmed by review of pertinent medical records. PJI data are reported on a quarterly basis to the Infection Control Committee and Quality Improvement Executive Committee. PJI rates for TKA are also reported on a monthly basis to the CDC NHSN and are reported on an annual basis to the Centers for Medicare & Medicaid Services and to the California Department of Public Health and are also publicly available (http://www.cdph.ca.gov/programs/hai/Pages/SurgicalSiteInfections-Report.aspx).

Review of our data at the end of fiscal year 2009 indicated a particularly high rate of infections among patients undergoing revision TKA at 8.79%. Of the eight PJIs among 91 patients undergoing revision TKA during this time period, five were the result of methicillin-resistant organisms (three MRSA, two MRSE), and the overall rate of PJI resulting from methicillin-resistant organisms was 5.49%. In contrast, the overall rate of infection among primary TKA was 0.86%, and the rate of PJI resulting from

methicillin-resistant organisms was 0.43%. Based on the results of the mentioned review, in July 2009, the Department of Hospital Epidemiology and Infection Control and Infectious Diseases Management Program recommended the addition of vancomycin to cefazolin as surgical antimicrobial prophylaxis for all patients undergoing revision TKA. A 1-g dose of vancomycin was recommended for patients < 80 kg and a 1.5-g dose was recommended for those patients ≥ 80 kg. To avoid hypotension associated with histamine release, vancomycin was infused over at least 60 minutes and started in the preoperative area within 120 minutes before incision, consistent with SCIP guidelines [4]. One dose of each drug was given preoperatively as described unless the patient met criteria for redosing of antibiotics based on duration of surgery [4]. A single dose of each drug was also given within 24 hours postoperatively.

We prospectively monitored PJI rates among patients undergoing revision TKA after introduction of the change in antimicrobial prophylaxis. PJI rates were reported by fiscal year by the Department of Hospital Epidemiology and Infection Control, which includes data from July of any given year to June of the next year. Owing to a number of logistical issues regarding administration of vancomycin that were resolved with attention from a multidisciplinary team, full implementation of the change in prophylaxis did not occur until October 2010. Given the prolonged time period required for full implementation of the change in prophylaxis, we used fiscal years 2009–2010 PJI rates as our baseline rates for comparison to fiscal years 2011–2012. PJI rates were followed prospectively through December 1, 2012, as part of routine infection control surveillance.

We used Fisher's exact test to determine if the rate of PJI was different between the two groups. A p value < 0.05 was considered statistically significant.

Results

There was an overall decline in PJI rates between fiscal years 2009–2012 (Table 1). After the change in surgical antimicrobial prophylaxis, there was a significant reduction in PJI rates among patients undergoing revision TKA from 7.89% (15 of 190) in fiscal years 2009–2010 to 3.13% (7 of 224) in fiscal years 2011–2012 ($p = 0.046$). In particular, we observed a reduction in PJI among patients undergoing revision TKA resulting from methicillin-resistant organisms over this same time period, from 4.21% (8 of 190) to 0.89% (2 of 224) ($p = 0.049$). Of 15 PJIs identified in fiscal years 2009–2010, 8 (53%) were the result of methicillin-resistant organisms (5 MRSA, 3 MRSE). Of 7 PJIs identified in fiscal years 2011–2012, 2 (29%) were the result of methicillin-resistant organisms (0 MRSA, 2 MRSE). The vancomycin minimum inhibitory concentration (MIC) of these two MRSE isolated after the intervention were susceptible with MICs of 1 to 2 μg/mL.

There was one patient with vancomycin-resistant enterococcus (VRE) in fiscal years 2009–2010 and no patients with VRE in fiscal years 2011–2012. There were no patients with vancomycin-intermediate *S aureus* (VISA) or vancomycin-resistant *S aureus* (VRSA) at any time period in the study. With the exception of one superficial infection resulting from VRE, all other infections were considered to be deep surgical site infections.

Discussion

Consistent with other published findings in the literature [8, 9, 14, 17], we identified revision TKA as a high-risk group for PJI at our institution in fiscal year 2009. In particular, we found a high rate of PJI resulting from methicillin-resistant organisms with over half of infections resulting

Table 1. Prosthetic joint infection (PJI) rates between fiscal years 2009 and 2012

Fiscal year	Total number of procedures	Number of PJIs	PJI rate	Revision procedures	Number of PJIs	PJI rate	Number of PJIs resulting from methicillin-resistant organisms among revision TKA	Percent PJIs from methicillin-resistant organisms among revision TKA
2009 (July 2008 to June 2009)	324	10	3.09%	91	8	8.79%	5	5.49%
2010 (July 2009 to June 2010)	327	8	2.45%	99	7	7.07%	3	3.03%
2011 (July 2010 to June 2011)	378	6	1.59%	118	3	2.54%	0	0.00%
2012 (July 2011 to June 2012)	417	7	1.68%	106	4	3.77%	2	1.89%

from MRSA and MRSE. In response to these findings, we modified our surgical antimicrobial prophylaxis to include the addition of vancomycin to cefazolin for all patients undergoing revision TKA. We conducted this study to evaluate the impact of our intervention, targeted use of vancomycin among patients undergoing revision TKA on (1) the incidence of PJI in patients undergoing revision TKA; and (2) the incidence of PJI in revision TKA resulting from methicillin-resistant organisms.

We acknowledge several limitations of our study. First, this was a retrospective study and it is possible that cases of PJI may have been missed as a result of treatment at outside institutions. Our Department of Hospital Epidemiology and Infection Control strives for rigorous case ascertainment including followup of PJI that have been reported by other institutions as related to index surgery at UCSF. Second, it is possible that concurrent interventions at our institution may have impacted PJI rates. An institution-wide hand hygiene program was implemented in June 2010. However, there was no significant change in our overall rates of PJI among patients undergoing THA during this same timeframe. Because THAs and TKAs are performed by the same surgeons, it is likely that any impact of hand hygiene on reducing infection rates should have been observed in both patients undergoing THA and those undergoing TKA. In May 2011, preoperative mupirocin and chlorhexidine bathing was implemented among patients undergoing revision TKA and required several months for full adoption. However, we began to observe a significant decline in PJI before introduction of this intervention with rates declining to a low of 2.54% by the end of fiscal year 2011. Because infection rates had already decreased substantially by the beginning of fiscal year 2012, it was difficult to assess the relative impact of mupirocin and chlorhexidine and further longitudinal followup is needed. Because the change in antimicrobial prophylaxis was part of a quality improvement initiative, there may have been other unmeasured variables such as an overall increased attention paid to revision TKA that contributed to the reduction in infection rates. Third, this was a single-center study that serves as a tertiary care referral center and our findings may not be generalizable to centers with lower baseline rates of infection resulting from methicillin-resistant organisms. Finally, we did not assess the safety of our intervention with respect to adverse drug reactions as well as the impact on antimicrobial resistance. The absolute numbers of PJI in our study were relatively low making the latter outcome difficult to assess although there were no cases of VISA or VRSA; we observed one case of VRE in the study that occurred before full implementation of the change in prophylaxis.

Our study found that the targeted use of vancomycin and cefazolin among patients undergoing revision TKA significantly reduced rates of PJI in this high-risk patient group and in particular reduced rates of PJI resulting from methicillin-resistant organisms. The role of vancomycin in surgical antimicrobial prophylaxis remains controversial. A meta-analysis of seven randomized trials comparing glycopeptide (including vancomycin) prophylaxis with β-lactam prophylaxis before cardiac surgery found no difference in rates of surgical site infections [3]. There are limited published data on perioperative prophylaxis among patients undergoing total joint arthroplasty with no randomized trials comparing vancomycin with cefazolin as surgical antimicrobial prophylaxis (Table 2). Ritter et al.

Table 2. Outcomes associated with vancomycin or cefazolin for surgical antimicrobial prophylaxis in total joint arthroplasty

Study	Study type	Study population	Prophylaxis	Outcomes
Ritter et al., 1989 [10]	Retrospective February to October 1987	TKA, THA	Vancomycin + gentamicin	No early infections reported
Savarese et al., 1999 [11]	Retrospective	TKA	Vancomycin	2% infection rate
Song et al., 2011 [16]	Prospective 2006–2009	TKA	Cefazolin	1.06% infection rate
Smith et al., 2012 [15]	Retrospective, 2006–2010	TKA, THA	Switch from cefazolin to vancomycin in 2008	↓ PJI from 1.0% to 0.5% ($p = 0.03$) ↓ MRSA PJI from 0.23% to 0.07% ($p = 0.14$)
Sewick et al., 2012 [13]	Retrospective, 2008–2010	TKA, THA	Cefazolin or cefazolin + vancomycin	No difference in overall infection rates (1.4% versus 1.1%, $p = 0.64$) or by THA and TKA subgroups Higher rate of MRSA in cefazolin (0.008%) versus cefazolin + vancomycin (0.002%; $p = 0.02$)

PJI = periprosthetic joint infection; MRSA = methicillin-resistant *Staphylococcus aureus.*

[10] published their experience with use of vancomycin and gentamicin as perioperative prophylaxis for patients undergoing total joint arthroplasty and did not identify any infections among their patients; however, patients were only followed over an 8-month period and this study was performed in the 1980s when there were lower rates of methicillin-resistant organisms. In contrast, Savarese et al. [11] reported on the use of vancomycin prophylaxis among 96 patients undergoing TKA and found a 2% infection rate. More recently, Song et al. [16] reported outcomes associated with cefazolin prophylaxis among patients undergoing TKA in an institution where over 60% of *S aureus* nosocomial isolates were MRSA; their overall rate of PJI was 1.06%, consistent with their national benchmark rates and other reports in the literature. Therefore, they concluded that use of cefazolin alone as prophylaxis was adequate even in an institution with a high prevalence of MRSA infection. However, this study did not evaluate whether the use of vancomycin could reduce rates even further. Smith et al. [15] described their experience with modification of perioperative prophylaxis from cefazolin to vancomycin among all patients undergoing TKA and THA and found a reduction in PJI from 1.0% to 0.5% and MRSA PJI from 0.23% to 0.07%. Another study observed a lower rate of MRSA infections in patients who received both cefazolin and vancomycin compared with cefazolin alone, although the number needed to treat was very high (138 patients), raising the question of how to balance potential risks of the intervention against a benefit of that size [13].

Targeted use of vancomycin in patients undergoing revision TKA was effective in reducing the rate of PJI and PJI resulting from methicillin-resistant organisms at an institution with a high baseline rate of PJI resulting from MRSA and MRSE. The variable outcomes reported in the limited literature on the role of vancomycin in surgical antimicrobial prophylaxis suggest that "one size does not fit all." Our findings illustrate the importance of using an institution's local epidemiology and antibiogram to guide infection prevention interventions. Further study is needed to determine the impact of the use of vancomycin in surgical antimicrobial prophylaxis on selection of antimicrobial-resistant organisms. Identification of high-risk subgroups of patients within a surgical population such as those undergoing revision arthroplasty can help target surgical antimicrobial prophylaxis and other infection prevention strategies to those who are most likely to benefit and minimize potential harms from broader application of such interventions.

Acknowledgments We thank Laurel Gibbs MT, CIC, for her assistance with data collection and validation, Steven Takemoto PhD, for providing assistance with data analysis, and Vanessa Chan MPH, for her help in preparing the manuscript.

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