ORIGINAL ARTICLE

Improving Compliance with Timely Intraoperative Redosing of Antimicrobials in Surgical Prophylaxis

Gina Riggi, PharmD;[1] Mayela Castillo, PharmD;[1] Margaret Fernandez, PharmD;[1] Andrew Wawrzyniak, PhD;[2,3] Michael Vigoda, MD, MBA;[4] Scott Eber, MD;[4] David Lubarsky, MD, MBA;[4] Lilian M. Abbo, MD[3]

BACKGROUND. Appropriate use of antimicrobials for surgical prophylaxis is an important patient safety issue. Antimicrobial levels should be present during the duration of the surgical procedure until incision site closure. For prolonged surgical procedures in which the tissue concentration of the prophylactic antimicrobial may decrease to below the necessary minimum inhibitory concentration, intraoperative redosing of antimicrobials may be crucial.

OBJECTIVE. To evaluate compliance of appropriate intraoperative antimicrobial surgical prophylaxis using real-time intraoperative antimicrobial dosing reminders at a large teaching hospital.

METHODS. A retrospective review of electronic records (March 2009–October 2012) was performed. Patients were included if they were at least 18 years of age and underwent a procedure requiring antimicrobial surgical prophylaxis. Compliance was determined by comparing 3 time intervals: baseline (March 2009–March 2010); intervention period 1 (IP-1; April 1, 2010–April 30, 2012), and intervention period 2 (IP-2; May 1, 2012–October 31, 2012). Interventions included a hospital-wide standardized protocol comprising an automated intraoperative paging system to notify when antimicrobials should be redosed.

RESULTS. A total of 7,461 of 75,230 surgical procedures required intraoperative redosing of antimicrobials and were analyzed. Patient mean age (± standard deviation) was 45 ± 19 years, and 62.6% were female. The most common procedures that required prophylaxis were solid organ transplantation, neurosurgical procedures, and orthopedic procedures. Baseline compliance (n = 2,183) was 15.8%; compliance significantly improved to 65.3% during IP-1 (n = 4,486; $P < .001$). The compliance rate improved to 76.7% during IP-2 ($P < .001$ compared with no reminder).

CONCLUSIONS. Compliance with redosing of intraoperative antimicrobials was improved with the combined approach of guidelines, education to healthcare providers, and real-time automated paging system.

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Prevention of surgical site infections (SSIs) requires multidisciplinary approaches that include optimized surgical techniques, preparation of the instrumentation, use of sterile barriers, and appropriate antimicrobial prophylaxis.[1] In the United States, the Joint Commission and the Centers for Medicare and Medicaid have mandated the implementation of national inpatient quality measures, including the Surgical Care Improvement Project,[2,3] to reduce the risk of SSI and optimize the use of perioperative antimicrobials in surgical prophylaxis. These quality measures are good but not perfect.[4] They have economic repercussions in hospital reimbursement and also represent important opportunities for antimicrobial stewardship programs to optimize the use of antimicrobials in surgical prophylaxis.

Antimicrobial surgical prophylaxis aims to achieve adequate serum and tissue drug levels to exceed the minimum inhibitory concentration (MIC) for the most likely organisms to be encountered during surgery.[5] The selection of an appropriate antimicrobial is also an important decision. This selection depends on the identification of the most likely pathogens that are associated with a specific surgical procedure and selecting drugs with a minimal adverse effect profile.[3] The timing of antimicrobial prophylaxis is considered to be optimal if it is administered between 30 and 60 minutes before the incision.[5] Antimicrobial levels should be present for the duration of the surgical procedure until incision site closure.[5] For prolonged surgical procedures in which the tissue concentration of the prophylactic antimicrobial may decreases to below the necessary MICs, intraoperative redosing of antimicrobials is as crucial as their initial administration.[1] National guidelines recommend redosing antimicrobials intraoperatively for procedures lasting longer than 2 half-lives

Affiliations: 1. Department of Pharmacy, Jackson Memorial Hospital, Miami, Florida; 2. School of Nursing and Health Studies, University of Miami Miller School of Medicine, Miami, Florida; 3. Department of Medicine, Division of Infectious Diseases, University of Miami Miller School of Medicine, Miami, Florida; 4. Department of Anesthesiology, University of Miami Miller School of Medicine, Miami, Florida.

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of the prophylactic agent or when intraoperative blood loss is greater than 1.5 L.[5-7] Theoretically, appropriate preoperative and intraoperative dosing of antimicrobials should reduce unnecessary doses of postoperative antimicrobials with a potential decrease in SSIs. In clinical practice, surgical and anesthesiology teams in the operating room usually determine the need for intraoperative redosing of antimicrobials.

The purpose of this study was to report baseline and follow-up compliance after the implementation of a perioperative surgical prophylaxis bundle that included real-time intraoperative antimicrobial dosing reminders at a single large teaching hospital.

METHODS

Retrospective review of electronic anesthesiology records was performed at a 1,500–licensed bed tertiary care teaching hospital in Miami, Florida. The retrospective review was prompted by a drug use evaluation (DUE) performed in 2009 to assess baseline compliance with our hospital's antimicrobial surgical prophylaxis protocol. The DUE revealed poor compliance with antimicrobial prophylaxis guidelines. As a quality improvement project, a combination of multidisciplinary interventions was subsequently implemented that was directed at intraoperative antimicrobial redosing for surgical prophylaxis. In addition, multiple changes have occurred in preventing SSIs at our institution, including the use of chlorhexidine gluconate preoperative baths, shampoos for craniectomies, and changes in intraoperative skin preparation that could have reduced SSI rates. Therefore, we cannot attribute any changes in SSI rates to our interventions alone, and SSI rates are not reported in this study.

Electronic Reminder System

The hospital performs approximately 15,000 surgical procedures annually. Approximately 20% of these procedures meet requirements for antimicrobial intraoperative redosing based on the duration of the procedure. On average, there are 24 operating rooms (ORs) running simultaneously, with peak days of 28 sites running cases; however, the number of cases on the weekends vary. Approximately 16 redosing reminder pages are sent daily to healthcare providers. In 2010, the Department of Anesthesiology and the Antimicrobial Stewardship Program developed intraoperative real-time alerts to remind the anesthesiology team if intraoperative redosing of an antimicrobial was required. The real-time alert was based on the timing of preoperative antimicrobial administration (as recorded in the anesthesia electronic medical record), the selected preoperative antimicrobial, and the duration of the surgical procedure. The coding for the alert used redosing guidelines based on the half-life of the preoperative antimicrobial. The certified registered nurse anesthetists (CRNAs) received an alphanumeric page alert 30 minutes before the antimicrobial dose was due. The CRNA or resident must document in the anesthesia electronic medical record that the intraoperative dose was administered within 15 minutes of receiving the reminder; otherwise, the attending anesthesiologist received a notification on their alphanumeric pager 15 minutes before the intraoperative dose was due.

The electronic paging system identified the appropriate CRNA, anesthesiology resident, and attending anesthesiologist to page according to the daily OR schedule that was programmed to capture the individual to be paged. The timing of paging depended on the initial antibiotics administered for each specific case and duration. The pharmacy department provides the anesthesia department with an OR tray before each procedure with the appropriate antibiotics. In the event that more antimicrobials are needed for an extended case, the antimicrobials are readily available in the OR automatic dispensing machine. A drawback of the paging system was that anesthesia residents did not initially carry an alphanumeric pager, and if a resident was on the surgical case, they were dependent on being reminded by the attending anesthesiologist, who received a second alphanumeric page 15 minutes before the dose was due. This may have affected overall redosing compliance.

The alert included all surgical procedures regardless of the anticipated duration requiring interventions. The paging system was programmed to trigger a page based on real-time duration of the procedure and the timing of the last antimicrobial given and not a preset duration of the surgical procedure. The paging system is unable to capture the expected blood loss. We cannot estimate the number of patients who would be redosed on the basis of expected blood loss, because it varies in each specific procedure.

The code for the automated program was developed by the center for informatics and perioperative medicine of the Department of Anesthesia and written in Microsoft Access language; it runs near real-time on the background of our anesthesia information management system. The director for the Informatics Division was in charge of developing and implementing the program with our database analyst. A paging program called "note page" also allowed us to run multiple physician notification programs, including the antibiotic reminder. Implementation of the study did not incur any additional cost, because we used local resources.

Compliance with antimicrobial intraoperative redosing was evaluated during 3 time periods (Table 1). During the baseline compliance period (March 1, 2009–March 31, 2010), compliance with antimicrobial redosing without a standardized protocol or reminder was determined. During intervention period 1 (IP-1; April 1, 2010–April 30, 2012), bundled interventions included all of the following: hospital-wide antimicrobial surgical prophylaxis standardized protocol, education to the anesthesiology and surgical staff, and an automated intraoperative paging system with direct feedback to attending anesthesiologists when noncompliance occurred. Feedback in IP-1 consisted of an e-mail to the attending anesthesiologist with the noncompliance details; the chairman of the anesthesiology department was also copied on these

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TABLE 1. Time Periods and Intervention Strategies

Time period description	Time span	Intervention strategies
Baseline data	March 1, 2009–March 31, 2010	No interventions
Intervention period 1	April 1, 2010–April 30, 2012	Hospital-wide antimicrobial surgical prophylaxis standardized protocol; education to the anesthesiology and surgical staff; automated intraoperative paging system; direct feedback to attending anesthesiologists when noncompliance occurred
Intervention period 2	May 1, 2012–October 31, 2012	Updated hospital-wide antimicrobial surgical prophylaxis standardized protocol; education to the anesthesiology and surgical staff; automated intraoperative paging system

e-mails. During intervention period 2 (IP-2; May 1–October 31, 2012), standardized surgical prophylaxis protocols were updated, and the computer-generated intraoperative paging system continued but without feedback to the physicians.

Clinical Data Collection

Patients were included if they were 18 years of age and older; underwent surgery between March 1, 2009, and October 31, 2012, at our hospital; and required redosing of an intraoperative antimicrobial based on the preoperative antimicrobial selected and duration of the surgical procedure. Redosing times were standardized on the basis of the half-life of the antimicrobials per protocol (Table 2). Antimicrobial redosing in the event of excessive intraoperative blood loss was left up to the discretion of the physician and was not be captured in the results. Data collected included demographic characteristics, allergies, weight, surgical service, type of surgical procedure, presurgical antimicrobial, date of surgery, surgery start time, anesthesia start time, surgery end time, anesthesia end time, surgical attending, anesthesia attending, preoperative antimicrobial, intraoperative antimicrobial, time antimicrobial administered preoperatively, time antimicrobial administered intraoperatively, and time of pager reminder(s).

TABLE 2. Standardized Time for Intraoperative Antimicrobial Redosing Based on the Length of the Procedure at Jackson Memorial Hospital

Antimicrobial	Time to redose intraoperatively, minutes
Cefoxitin	180
Ampicillin	240
Ampicillin-sulbactam	240
Cefazolin	240
Cefuroxime	240
Clindamycin	240
Meropenem	240
Metronidazole	240
Piperacillin-tazobactam	240
Cefepime	360
Gentamicin	360
Tobramycin	360
Ciprofloxacin	480
Vancomycin	720

The primary outcome was to compare compliance rates during each time period. Compliance with intraoperative antimicrobial dosing was defined as doses given either 30 minutes before or 30 minutes after the time the antimicrobial was due as reflected by the alphanumeric paging system. This time window was chosen to take into account the possibility of paging system delays or human charting delays. Secondary outcomes were to identify barriers in compliance and opportunities for improvement in antimicrobial surgical prophylaxis. The study was approved by the Institutional Review Board.

For the main analysis, proportions of on-time redosing were compared between the 3 reminder periods using Pearson χ^2. A 3-way log-linear analysis was then performed to compare proportions of on-time dosing between reminder periods and between each antibiotic type.

RESULTS

A total of 50,583 patients were administered antimicrobials for surgical prophylaxis during the study period. Intraoperative antimicrobial redosing on the basis of our inclusion criteria was indicated in 7,461 patients (14.8%), and these patients were included in the analysis. Mean age ($\pm$ standard deviation) was 45 $\pm$ 19 years, and 63% of patients were female. On average, there were 16 redosing reminder pages sent to providers each day. This number varied widely (approximately 30 per weekday to 1–2 per day during the weekend), because each case could have multiple providers involved, including the anesthesia attending and resident/CRNA in the OR.

The most common surgical procedures requiring intraoperative redosing of antimicrobials were neurosurgical procedures, orthopedic procedures, and solid organ transplantation. Compliance rates were compared between baseline, IP-1, and IP-2 to determine the effect of a reminder on antimicrobial intraoperative redosing. Compliance during baseline (n = 2183) was 15.8% and significantly improved to 65.3% during IP-1 (n = 4,486); compliance then significantly

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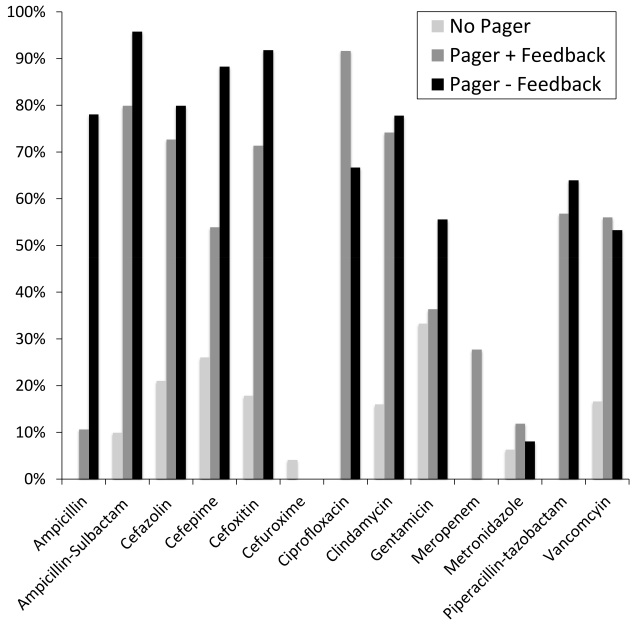

FIGURE 1. Successful redosing between reminder condition and antibiotic type.

increased to 76.7% during IP-2 compared with baseline and IP-1 (χ^2 [2] = 1,665.40, $P < .001$).

A 3-way log-linear analysis to compare proportions of on-time redosing between the 3 reminder periods and between antibiotic types was found to be significant. There was an interaction between presence of reminder pages, antibiotic, and whether redosing occurred on time (χ^2 [24] = 209.46, $P < .001$; Figure 1).

DISCUSSION

Our study shows that most clinicians accepted changes to their clinical practice, but they often need to be reminded in order to improve compliance. Baseline compliance in our study was 15.8%, suggesting that many practitioners were not aware that an intraoperative dose was indicated or that it was overlooked during the procedure. During the intervention periods, compliance increased to 65.3% and 76.7%. This continuous increase suggests that strategies were successful and that the constant reminders allowed practitioners to recall that an intraoperative antimicrobial dose was indicated. We were not able to identify specific variables (eg, specific type of procedure or attending anesthesiologist) that accounted for the 35% noncompliance at the end of IP-1. To increase compliance after receiving these results, we increased education to the staff and improved mandatory use of our institutional surgical antimicrobial prophylaxis order form in all preoperative and holding areas. The optimal type of education according to our results is a combination of a protocol with an automated reminder system. The period of feedback may have changed the compliance of those practitioners who were found to be noncompliant with the automated system.

There is not a clear explanation as to why compliance further improved without feedback. We assume that, during IP-1, some early adopters of the intervention used the paging system and feedback to improve their compliance. Then, during IP-2, it is possible that late adopters were engaged with the paging system regardless of feedback and became used to the intervention. In addition, it was likely that the constant reminders led to increases in the compliance of intraoperative redosing throughout both periods. Specific variables were not identified to suggest that certain prescribers were consistently noncompliant.

Noncompliance with intraoperative antimicrobial redosing is an international issue. Koopman et al[8] examined the adequacy of end-of-procedure cefazolin blood concentrations in 57 patients who underwent elective procedures. In that study, timing of the dose was a critical determinant in adequate antimicrobial concentrations. Although there was a 74% compliance rate based on the Centers for Medicare and Medicaid Services guidelines, noncompliance was associated with inadequate cefazolin concentrations at the end of the surgical procedure. Intraoperative antimicrobial redosing for surgical prophylaxis is currently not part of the core measures. It is recommended but not mandated in national surgical prophylaxis guidelines, which may be one of the reasons why compliance is usually low.[1,8,9]

Timely intraoperative redosing has been found to reduce SSI rates in a randomized controlled trial focusing on cardiac surgical patients[6] and also in a multicenter, prospective observational study that included cardiac, hysterectomy, and hip and knee arthroplasty procedures.[10] In the study by Steinberg et al,[10] 690 (21%) of 1,062 patients who underwent a cardiac surgical procedure that lasted at least 4 hours received intraoperative redosing. The rate of SSIs among patients who did not receive an intraoperative dose of cefazolin was 5.5% compared with a SSI rate of 1.8% among patients who did receive an intraoperative dose of cefazolin (odds ratio, 3.08 [95% confidence interval, 0.74–12.90]; $P = .06$).[11]

The use of computerized reminder systems has been studied with positive outcomes. St. Jacques et al[1] used a computerized reminder system directed at antibiotic intraoperative redosing. Timely intraoperative antibiotic redosing increased from 20% to 57% ($P < .001$) after the implementation of a reminder system. Computerized reminder systems are an effective tool to assist in appropriate intraoperative redosing of prophylactic antibiotics during lengthy surgical procedures. Zanetti et al[6] assessed the impact of an automated intraoperative alert to redose prophylactic antibiotics in prolonged cardiac operations. They found that the use of an automated reminder system was associated with a significant increase in the rate of appropriate intraoperative dosing of prophylactic antibiotics. Compliance was 40% (55 of 136) in the control group and 68% (93 of 137) in the automated intraoperative alert group ($P < .01$). Our study has demon-

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strated similar results with the use of electronic pager reminders with real-time feedback at the point of care. Prescribers were receptive to real-time feedback in the appropriate redosing of intraoperative antimicrobials with sustained changes over time.

Limitations to our study include that it was retrospective and was conducted in a single center. We were not able to capture intraoperative redosing on the basis of intraoperative blood loss, because the automated system was programmed on the basis of time and selection of preoperative antibiotic agent, and it is not possible to electronically predetermine the amount of blood to be lost in a surgical procedure.

Despite some limitations, our study was conducted in a very large teaching hospital. Although each hospital would need to evaluate their current practices and available resources to implement a similar intervention, our study did not incur any additional costs to our daily operations and could be applicable to other community and academic hospitals to improve compliance with the selection, timing, and intraoperative redosing of antimicrobials for surgical prophylaxis. For those institutions in which a single practitioner is performing anesthesia, this reminder system would be valuable to capture the opportunity to redose antibiotics. Additional studies in this area may include evaluating the impact of intraoperative redosing in reducing SSIs and reducing the postoperative doses of prophylactic antimicrobials.

The rate of compliance with antimicrobial intraoperative redosing was improved by the implementation of several strategies, including the development of a new antimicrobial surgical prophylaxis protocol, targeted education to healthcare providers, and the introduction of an automated paging system. Our results demonstrate that compliance with intraoperative redosing of antimicrobials can be accomplished with electronic reminders at the point of care and that healthcare providers are receptive to real-time feedback optimizing quality of care.

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Address correspondence to Lilian M. Abbo, MD, University of Miami Miller School of Medicine, 1120 Northwest 14th Street, Suite 851, Miami, FL 33136 (labbo@med.miami.edu).

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