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Major Article

Implementation of a multifaceted program to sustainably improve appropriate intraoperative antibiotic redosing

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Key Words:
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Surgical site infection
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Background: National guidelines recommend intraoperative redosing of prophylactic antibiotics at defined intervals to reduce the risk of surgical site infections. Compliance with these guidelines is poor.

Methods: A quality improvement project—including education, progress reports, and automated redosing reminders in the anesthesia electronic health record—was implemented at a large university-affiliated hospital to increase rates of intraoperative antibiotic redosing for surgeries lasting more than 4 hours.

A retrospective, observational study was then conducted. The primary outcome was the compliance rate with intraoperative antibiotic redosing criteria for all surgeries lasting more than 4 hours in the pre- and post-project period. The effect of the intervention was assessed by an interrupted time-series Poisson regression model.

Results: A total of 13,695 surgical procedures were evaluated. Time-series analysis demonstrated that the project was associated with significant improvement of compliance rates (incidence rate ratio [IRR]: 1.16; $P = .002$) with no significant change in underlying improvement trend (IRR: 1.00; $P = .22$).

Discussion: Few peer-reviewed manuscripts describe effective methods to ensure appropriate antibiotic redosing during prolonged surgeries. We demonstrated that a multipronged approach was very effective at producing immediate and sustained improvements in guideline compliance.

Conclusions: Implementation of a multifaceted intervention improved rates of guideline-concordant redosing of intraoperative prophylactic antibiotics.

Surgical site infections (SSIs)—defined as infections that occur after surgery in the part of the body where the surgery took place—are reported to occur in almost 3% of the surgical procedures performed annually in the United States.[1] SSIs are expensive and morbid complications, annually costing our healthcare system between $15.8 and $57.2 billion dollars to treat, while adding an additional 4 million hospital days and causing 8,000 deaths per year.[2-7] When administered correctly, perioperative prophylactic antibiotics (PPAs) have repeatedly been shown to decrease the rate of SSIs.[8] However, selection of inappropriate antibiotics, mistiming of initial dose, or failure to appropriately redose PPAs intraoperatively can all negate this benefit and lead to increased SSI rates, healthcare costs, and risk of resistant infections.[2,8-10]

In 2013, evidence-based clinical practice guidelines for antimicrobial prophylaxis in surgery were published in the *American Journal*

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of Health-System Pharmacy.[11] Notably, these guidelines recommended intraoperative antibiotic redosing intervals during surgical procedures based on population pharmacokinetics of each drug. Redosing of antimicrobials with a short half-life was recommended at an interval of approximately 2 times the half-life of the agent in patients with normal renal function.

The University of Iowa Hospital and Clinics is a 761-bed tertiary care center that performs more than 31,000 major surgical operations per year, including over 250 colorectal surgeries, nearly 650 total abdominal hysterectomies, and over 850 knee or hip total arthroplasties. For all elective surgeries, a member of the surgical team places an initial order for a PPA through an electronic health record (EHR) system. The EHR inpatient care module has been pre-programmed with clinical decision support tools, according to surgical case type, that include guideline-concordant antibiotic recommendations. The pharmacy delivers the ordered PPA to the patient bedside preoperatively, and an anesthesia provider administers the PPA. Using this system, our hospital, like many other institutions, managed to achieve very high compliance with mandated Center for Medicaid and Medicare Services Surgical Care Improvement Project measures for initial antibiotic dosing. However, an internal audit for guideline-concordant intraoperative antibiotic *redosing* at our institution revealed low baseline compliance with the 2013 guidelines. A 2014 manual chart review of 1,931 surgeries at our hospital showed that guideline-compliant redosing occurred in only 17% of cases. This low percentage approximates the dismal values published by other institutions that have audited their intraoperative antibiotic redosing rates.[10,12,13]

Therefore, anesthesia and pharmacy providers at the University of Iowa initiated a quality improvement project to increase compliance with published PPA *intraoperative redosing* recommendations for surgical procedures lasting more than 4 hours.

METHODS

Intervention

This project was determined to not be human subjects research, and a waiver of institutional review board oversight was granted.

First, a guideline-based[11] intraoperative Antibiotic Administration Guide was created and distributed to anesthesia providers (available on request by emailing the corresponding author). One side of the guide listed recommendations for antibiotic choice by surgical category; the other side listed redosing recommendations. The guide was reviewed and approved by various hospital pharmacy and antibiotic stewardship committees prior to implementation.

Next, an aggressive campaign was conducted to inform all perioperative personnel about the project to improve evidence-based antibiotic redosing. Multiple educational sessions were held for anesthesia providers, surgeons, nurses, and pharmacists who work regularly in the operating room. The Antibiotic Administration Guide was also placed on a reference section of the EHR so all providers had easy access to it. All surgical service chiefs were also notified and asked to support the project.

In addition, an electronic reminder was created within the anesthesia record of the EHR that alerts providers 15 minutes before the scheduled antibiotic redosing time. This interval was designed to allow providers a 30-minute window to order, receive from the pharmacy, and administer the appropriate antibiotic redose.

Finally, the Department of Anesthesia used the prophylactic antibiotic redosing data as a trackable metric and reported monthly to hospital leadership to encourage peer accountability and feedback.

Data Source and Variable Definitions

Data obtained from the EHR data warehouse included patient identification, body weight, most recent serum creatinine level, operating room location, surgeon(s), surgical procedure, anesthesia provider(s), anesthesia start and stop times, surgical start and stop times, antibiotic dose and route, date and time of antibiotic administration, and time(s) of antibiotic redosing. The time between antibiotic doses was then calculated, and each patient-antibiotic event was graded as either "pass" or "fail." The case was classified as a "fail" if either of the following scenarios occurred: 1) the antibiotic redose was administered more than 15 minutes after the guideline-recommended interval; or 2) based on the length of the procedure and antibiotic given, the number of doses expected to occur (based on redosing interval) did not match the number of doses given (observed vs expected mismatch). All other cases were classified as a "pass."

To maintain consistency with national guidelines[11] (which do not explicitly recommend adjusting the dosing interval of antibiotics based on serum creatinine level), renal function was not used to determine "appropriate" timing of antibiotic redose in either the intraoperative antibiotic administration guide or the computerized report of redosing compliance. Therefore, for the purposes of this report, cases in which an antibiotic was purposely not redosed due to provider concerns about exacerbating renal dysfunction *were* included in the report and categorized as a "fail."

Patients who received ertapenem, gentamicin, vancomycin, ceftriaxone, or quinolone derivatives were included in the analysis and always triggered a "pass" categorization, because there is no national guideline recommendation to redose these antibiotics intraoperatively.

Statistical Methods

To analyze the effect of the multifaceted quality improvement interventions, while accounting for pre- and post-intervention trends, seasonality, and autocorrelation, we used a quasi-experimental interrupted time-series analysis. The number of surgical procedures that lasted more than 4 hours and received appropriate redosing was modeled as count data by Poisson regression model, while incorporating baseline trend and trend change after the intervention. The number of qualified surgical procedures was included in the model as an offset variable (denominator). A dummy variable to indicate before and after the completion of intervention was also included in the model to detect immediate change with an intervention. We also considered possible seasonality by including annual harmonic function as a potential independent variable. Slopes of trends and immediate change were calculated as incidence rate ratios (IRRs). Model diagnostics, including residual plots, were considered to ensure the model appropriateness, and autocorrelation was assessed using the Durbin-Watson statistic and inspections of autocorrelation function plots. Using a significance level of less than .05, 95% confidence intervals (CIs) and 2-sided *P* values were also calculated. All statistical calculations were performed using R version 3.4.3 software (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

The initial draft of the intraoperative Antibiotic Administration Guide was presented in January 2014 and finalized in October 2015 after a significant bureaucratic process involving feedback from

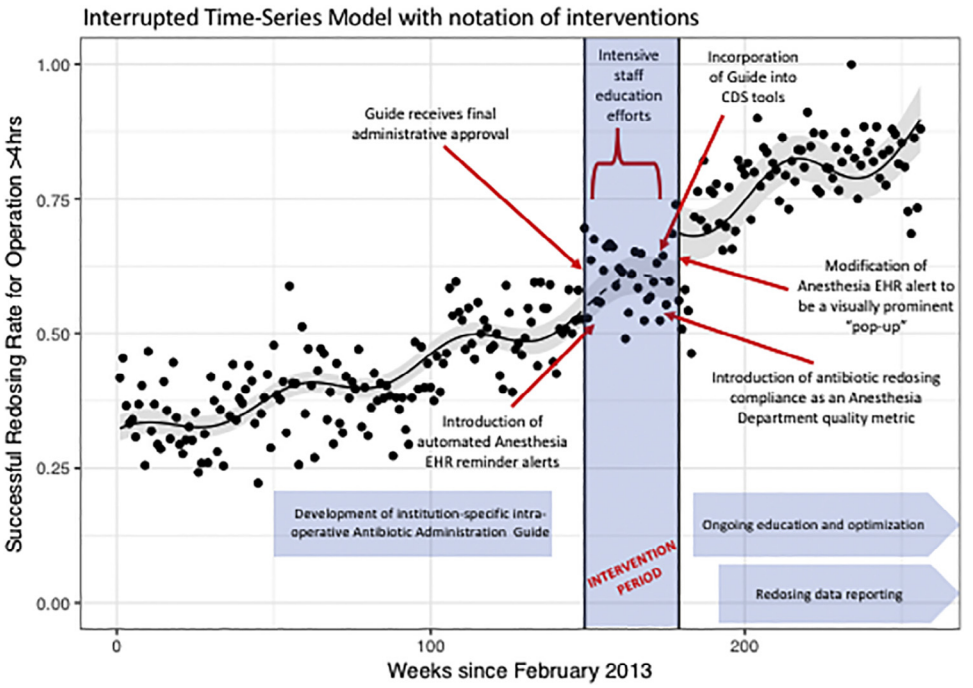

Fig 1. Interrupted time-series analysis with notation of interventions. National consensus guidelines for perioperative prophylactic antibiotic redosing were released in February 2013. An improving trend in antibiotic redosing rates is noted from this time prior to initiation of a multifaceted quality improvement project at the University of Iowa Hospital and Clinics. The quality improvement project began in the final months of 2015 and was primarily undertaken in the date ranges listed as "Intervention Period." The project centered around interprofessional education, monthly provider progress reports, introduction of redosing compliance as a tracked quality metric, and automated reminders in an anesthesia EHR. It displayed a clear additive effect by improving perioperative prophylactic antibiotic redosing compliance rates by approximately 15% without compromising the baseline improvement trend.
CDS = clinical decision support; EHR = electronic health record.

multiple stakeholders and approvals from relevant hospital committees. Most educational presentations to staff took place from December 2015 to March 2016, and introduction of the guide to clinical practice occurred in January 2016. The EHR reminder tool was initially created in late 2015, but it was revised in September 2016 to appear as a more prominent pop-up that appeared in the middle of the anesthetic record.

A total of 13,695 surgical procedures lasting more than 4 hours were performed between February 2013 (when national consensus antibiotic redosing guidelines were released[11]) and December 2017. The interrupted time-series model (Fig 1) showed that there was already an improving trend prior to our multifaceted intervention (IRR: 1.004 per week [95% CI: 1.003–1.004]; $P < .001$). At the end of the multifaceted intervention implementations, we observed significant increase in appropriate redosing rates (IRR: 1.158 [95% CI: 1.056–1.268]; $P = .002$). No statistically significant change of the slope was observed after the intervention (IRR: 0.999 [95% CI: 0.997–1.001]; $P = .22$). There was also weak but statistically significant first-order harmonic seasonality ($P = .01$).

DISCUSSION

Despite the presence of consensus practice guidelines, how to appropriately redose PPAs is actually somewhat controversial. Current guidelines are based on a variety of small trials and retrospective pharmacodynamics studies, suggesting that antibiotic concentration at skin closure is an independent risk factor for the development of an SSI.[1] Redosing an antibiotic based on its pharmacologic half-life is presumed to help ensure adequate levels at the time of skin closure. However, the guidelines do not make explicit accommodations for patient renal function, and if strictly instituted could lead to the potential for antibiotic overdose and toxicity. For example, the recommended redosing interval for ampicillin-sulbactam is every 2 hours, based on an estimated population half-life of 1 hour. Therefore, in a surgical procedure lasting more than 8 hours, the total dose of antibiotic could exceed the 24-hour maximum dose recommendations.[14] A manual audit of patient-antibiotic event "failures" in our report showed that 75% of such cases were for a PPA with a recommended 2-hour redosing interval. This suggests that redosing criteria were often not met because of an active decision (by the surgeon or anesthesia provider) to withhold a drug with a short half-life.

Other reports in the medical literature describe interventions to increase compliance with recommended perioperative antibiotic prescribing practices, but these other reports mostly focus on the timing of the initial dose of PPA.[10,15-28] A limited number of reports focus on ensuring appropriate PPA redosing in prolonged surgeries[1]; those that do document only modest improvements in the redosing rate.[12,13] We demonstrated that our multidisciplinary and multifaceted approach was effective at producing immediate and sustained improvements in guideline compliance, and the magnitude of benefit was much greater than in previous reports. Despite the fact that we observed an improving trend prior to our intervention, the intervention displayed a clear additive effect by improving PPA redosing compliance rates by approximately 15% without compromising the baseline improvement trend. By the end of the observation period, our compliance rates had improved to approximately 80%, and in only about 1.2% of cases lasting more than 4 hours had antibiotics been inappropriately not redosed without an apparent justification (such as concerns about drug toxicity with every-2-hour dosing or active skin closure/placement of a wound dressing).

Assigning anesthesia providers the responsibility for PPA administration has repeatedly been shown to increase compliance with

published guidelines and to potentially reduce SSI rates.[10,15,17,18] However, previous reports also suggest that anesthesia providers as a group are largely unfamiliar with relevant guidelines, lack education in antibiotic selection and dosing, or lack access to PPAs in the operating room.[10,15] Therefore, automated anesthesia EHR-based reminders and decision tools have been evaluated for an effect on provider practice. In previous studies, use of EHR messaging systems to assist anesthesia providers in achieving timely PPA administration resulted in 92%–99% compliance with initial dosing recommendations[10] but only 58%–73% compliance with evidence-based intraoperative redosing recommendations.[12,13] Our experience demonstrates that combining EHR-based interventions with education and incentive models may help further improve compliance rates.

Strengths of our study include use of a multifaceted and bundled approach that has not been used in previously reported redosing compliance improvement studies. In addition, the large number of included surgical procedures at our institution allowed us to perform interrupted time-series analysis with weekly data. It also allowed us to assess the significance of the intervention while accounting for multiple chronological factors, such as trends and seasonality. Interrupted time-series analysis is generally considered one of the most robust and reliable methods among various quasi-experimental designs.

One limitation of our study is that we could not completely eliminate the possibility of other external effects. However, the timing of intercept change strongly suggests that the intervention had a meaningful effect, and we did not identify any major change in national practice guidelines or external quality incentives. Second, we did not have a comparison group without intervention as a control, because all cases with indication for redosing were included in the intervention by the nature of the quality improvement project. However, we think that the similar or even greater effect size of our report compared to previously reported studies strongly suggests that our intervention was effective even without a control group.

Barriers to implementation of this project included the need for specialized programmers to create automated electronic reminders in the EHR and to create the antibiotic redosing report to measure performance; a widespread baseline lack of awareness among anesthesia providers of national guidelines for antibiotic redosing; and bureaucratic delays in achieving institutional approval of the intraoperative Antibiotic Administration Guide.

CONCLUSION

In this multidisciplinary quality improvement project at a large tertiary academic hospital, we demonstrated that multifaceted interventions—including aggressive education of surgeons, anesthesia providers, and ancillary operating room staff; EHR-based reminder tools; and a quality report card—can effectively and sustainably improve the rates of guideline-concordant antibiotic redosing. Further studies are ongoing to determine whether this has had an effect on clinically meaningful outcomes, such as SSIs.

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