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Original Article

Appropriateness of choice and duration of surgical antibiotic prophylaxis and the incidence of surgical site infections: A prospective study

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الملخص

أهداف البحث: تحدث التهابات الموقع الجراحي خلال 30-90 يوماً بعد الجراحة. العلاج الوقائي بالمضادات الحيوية تساعد في تقليل حدوثها حيث يكون السيفازولين هو المضاد الأكثر استخداماً. تنصح التوصيات الحالية بعدم إعطاء المضادات الحيوية بعد الجراحة أو تناولها لمدة قصيرة. هدفت هذه الدراسة إلى تقييم مدى ملاءمة المضادات الحيوية الوقائية لنوع الجراحة وكذلك المدة وتأثيرها في حدوث التهابات موقع الجراحة.

طرق البحث: كانت هذه دراسة استطلاعية قائمة على الملاحظة لجميع البالغين الذين تعرضوا لعمليات جراحية بين يونيو وأكتوبر 2019 لعمليات البطن أو العظام والذين تلقوا مضادات حيوية وقائية. كانت المخرجات الأولية هي مدى توافق مدة المضادات الحيوية الوقائية بعد العملية الجراحية للتوصيات العالمية. تضمنت نقاط النهاية الثانوية مدى ملاءمة اختيار المضادات الحيوية الوقائية ومعدلات حدوث التهابات موقع الجراحة.

النتائج: من بين 98 مريضاً شملهم البحث خضع 59 و 23 و 16 لعملية جراحية في العظام وأعلى البطن وأسفل البطن على التوالي. كانت الفترات المتوسطة للمضادات الحيوية بعد الجراحة أطول في مجموعتي جراحات البطن العلوية والسفلية مقابل مجموعة جراحة العظام (7 مقابل 5 أيام؛ القيمة الاحتمالية=0.03). على هذا النحو كان الامتثال العام للمبادئ التوجيهية من حيث مدة المضادات الحيوية بعد الجراحة 11.2٪ (13.6٪ و 13٪ و 0٪ في كل مجموعة جراحية ، على التوالي ؛ القيمة الاحتمالية=0.3). بالمقابل كان اختيار المضادات الحيوية متوافقاً بشكل كبير مع التوصيات بنسبة 71.4٪ (72.9٪ و 65.2٪ و 75٪ في كل مجموعة جراحية على التوالي؛ القيمة الاحتمالية=0.74). كان هذا مرتبطاً بشكل كبير مع احتمالات أقل لحدوث التهابات موقع الجراحة (نسبية الأرجحية=0.24؛ مجال الثقة 95% 0.09-0.63).

الاستنتاجات: بينما أظهرت هذه الدراسة عدم التوافق مع التوصيات العالمية من حيث المدة إلا أن ملاءمة اختيار المضادات الحيوية كانت عالية وكانت مرتبطة باحتمالية أقل لحدوث التهابات موقع الجراحة. يُنصح الأطباء باتباع التوصيات لتحسين جودة الرعاية للمرضى عبر منع حدوث التهابات الموقع الجراحي وتقليل خطر تطور مقاومة البكتيريا للمضادات الحيوية.

الكلمات المفتاحية: الاتقاء الجراحي بالمضادات الحيوية؛ التهابات الموقع الجراحي؛ القواعد الارشادية؛ بعد الجراحة

Abstract

Objectives: Surgical site infections (SSIs) develop within 30–90 days postoperatively. Antibiotic prophylaxis helps reduce SSI incidence, with cefazolin being the most used agent. Current guidelines recommend against post-operative antibiotic administration or a very short course. This study evaluated the appropriateness of prophylactic antibiotics by surgery type, as well as duration and their impact on SSI incidence.

Methods: This was an observational prospective study of adults admitted between June and October 2019 for abdominal or orthopedic surgery who received prophylactic antibiotics. The primary endpoint was compliance of postoperative prophylactic antibiotic duration with the guidelines. Secondary endpoints included appropriateness of antibiotic choice and SSI rates.

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Results: Of the 98 patients, 59, 23, and 16 had orthopedic, upper abdominal, and lower abdominal surgery, respectively. Median postoperative antibiotic durations were longer in the abdominal surgery group than in the orthopedic surgery group (7 vs. 5 days; $P = 0.03$). Hence, overall compliance with the guidelines in terms of postoperative antibiotic duration was 11.2% (13.6%, 13%, and 0% in each surgery group, respectively; $P = 0.3$). Conversely, antibiotic choice was highly compliant with the guidelines at 71.4% (72.9%, 65.2%, and 75% in each surgery group, respectively; $P = 0.74$). This was significantly associated with a lower risk of SSIs (odds ratio 0.24, 95% confidence 0.09−0.63).

Conclusion: While there was a lack of guidelines compliance in terms of duration, appropriateness of antibiotic choice was high and was associated with a lower likelihood for SSIs. Clinicians are encouraged to follow the guidelines to improve patients' quality of care by preventing SSIs and reducing the risk of antimicrobial resistance development.

Keywords: Guidelines; Postoperative; Surgical antibiotic prophylaxis; Surgical site infections

Introduction

Surgical site infection (SSI) is an infection that occurs after surgery in the part of the body where the surgery took place.[1] SSIs typically occur within 30 days if there are no implants or 90 days in the presence of implants after surgery.[2,3] The Centers for Disease Control and Prevention (CDC) list three types of infections at the surgical site: superficial SSI cutoff, defined as infection that occurs at the exact incision site in the skin area; deep SSI incision, defined as infection that occurs in the muscle under the region of the incision and the tissues that surround the muscles; and organ space, defined as infection that occurs in any region of the body other than the skin, muscle, and adjacent tissue that was involved in the surgery.[3] SSI can manifest as redness, delayed healing of the surgical wound, fever, pain, tenderness, warmth, or inflammation.[4] The most common organisms associated with SSIs include staphylococci, streptococci, and *Pseudomonas aeruginosa*.[5] Patients with SSIs are twice as likely to die, 60% more likely to be admitted to the intensive care unit, and more than five times more likely to be readmitted to the hospital after discharge.[5] The occurrence of SSI is estimated to raise hospital stay by 7−10 days and add more than $3000 to care expenses. In a comparative study of SSI patients versus uninfected patients, the average direct cost of hospitalization was $7531 and $3,844, respectively.[6]

Properly administered prophylactic antimicrobials can reduce the incidence of SSIs.[6] In fact, prophylaxis is not only used for contaminated or dirty surgical operations but is also usually used in all clean-contaminated and some clean surgeries. Unfortunately, there is significant evidence of excessive and unsuitable use of antimicrobials to prevent SSIs. One of the main variables affecting the effectiveness of antimicrobial prophylaxis is the timing of prophylactic antibiotic administration.[7]

The latest antimicrobial prophylaxis in surgery guidelines recommend only a short postoperative course of antimicrobials with either a single dose or no more than 24 h of therapy.[7–9] Cephalosporins (namely cefazolin) are suitable first-line agents for most surgical procedures as they target the most probable organisms while avoiding broad-spectrum coverage that may lead to antimicrobial resistance.[7] Lower abdominal procedures also require additional agents for anaerobic coverage, such as metronidazole. Improper antibiotic prophylaxis (e.g., wrong timing or overconsumption) increases rates of adverse drug reactions, superinfections, development of antimicrobial resistance, and cost of treatment.[10] Unfortunately, some resistant pathogens, such as methicillin-resistant *Staphylococcus aureus* and *Candida* species, are frequently involved in surgical wound diseases.[5] Numerous variables may influence the selection of appropriate antibiotics, such as the most frequent organisms causing wound infection in a particular surgery, as well as the relative expenses of available agents.[11]

A recent study in orthopedic surgery showed that lack of compliance with surgical antimicrobial prophylaxis guidelines is significantly associated with increased rates of SSIs.[12] Additional studies in other surgery types are needed to confirm these findings. Therefore, the purpose of this study was to evaluate the appropriateness of prophylactic antibiotics in terms of antibiotic choice and duration in patients undergoing abdominal and orthopedic surgical operations according to the latest antimicrobial surgical prophylaxis guidelines.

Materials and Methods

Study design and patients

This was a single-center observational prospective study that was conducted at a large tertiary hospital over a 4-month period between June 2019 and October 2019. Patients were screened for eligibility twice weekly on the days on which surgeries are typically scheduled. Figure 1 details the study design and process.

All adult patients (≥18 years) admitted for abdominal or orthopedic operations during the study period who received surgical antibiotic prophylaxis were included in the study. Patients who died or were discharged within 24 h after surgery were excluded.

Study endpoints

The primary endpoint was the rate of compliance of postsurgical antibiotic prophylaxis duration with the latest surgical antimicrobial prophylaxis guidelines.[7–9] Secondary endpoints were the rate of guidelines compliance in terms of antibiotic choice with the respective surgery type, as well as the incidence of SSI. Impact of different factors,

including compliance with the guidelines, on the incidence of SSIs was also assessed.

Data collection

Data were retrieved from the patients' medication chart and electronic medical records. If antibiotics were to be continued for more than 24 h after surgery, the reasons for the prolonged usage were explored. Each patient was reviewed from the time of admission until their discharge from the hospital. The wound classification and SSI criteria were based on the CDC standards.[3] SSI is considered when there is at least one of the following: redness, edema, tenderness, gaping, abscess or purulent discharge, fever (>38 °C), or positive culture of fluid or tissue from the surgical site within 30 days of the operation. Compliance with the guidelines for antimicrobial surgical prophylaxis was evaluated for each patient in terms of selection of proper agents for the operation done and duration of prophylaxis not exceeding 24 h postoperatively.

Statistical analyses

Comparisons were made between the group of patients in which compliance with the guidelines was recorded versus patients where lack of compliance with the guidelines was observed. Continuous variables were assessed for normality using Shapiro–Wilk tests for normality. Given the lack of normal distribution, median and interquartile range were used to represent the continuous variables, which were compared using the Mann–Whitney U test. Categorical variables were expressed as numbers and percentages and compared using the chi-square or Fisher's exact test. Odds ratio (OR) with 95% confidence interval (CI) was calculated to assess the relationship between different factors, including guidelines compliance and incidence of SSIs. Data were analyzed using SPSS version 24.0 (SPSS Inc., Chicago, IL, USA).

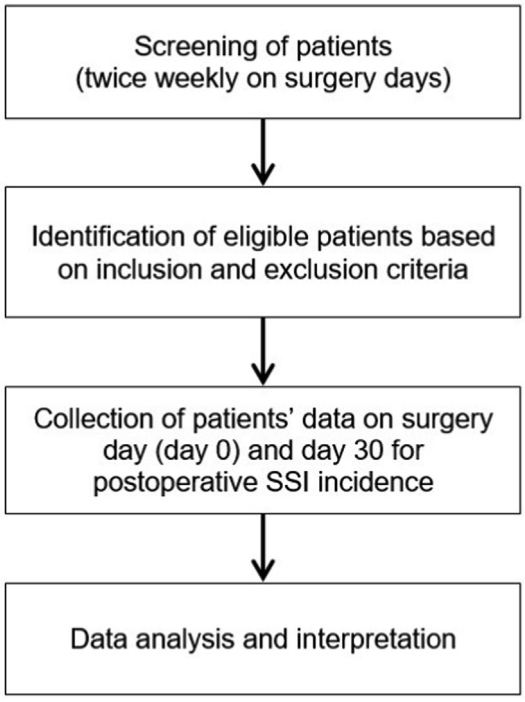

Figure 1: Detailed methodology of the study.

Results

A total of 98 patients who fulfilled the criteria were included in the study. Table 1 lists the baseline characteristics of patients. The median age was 52.5 years, and the majority (60.2%) were males. Cefazolin was the most common antibiotic used in orthopedic and upper abdominal procedures (72.9% and 43.5%, respectively), whereas metronidazole was the most common antibiotic in lower abdominal procedures (62.5%). Median durations of postoperative antibiotics were 2 days longer in the upper and lower abdominal surgery groups versus the orthopedic surgery group (7 vs. 5 days; $P = 0.03$) with overall duration reaching 14 days in some patients. As such, overall compliance with the guidelines in terms of postoperative antibiotic duration was 11.2% (13.6%, 13%, and 0% in orthopedic, upper abdominal, and lower abdominal surgeries, respectively; $P = 0.3$). Conversely, antibiotic choice showed a higher rate of compliance with the guidelines at 71.4% (72.9%, 65.2%, and 75% in the orthopedic, upper abdominal, and lower abdominal surgeries, respectively; $P = 0.74$). SSIs occurred in 38.1% of patients (37.9%, 47.8%, and 25% in orthopedic, upper abdominal, and lower abdominal surgeries, respectively; $P = 0.35$). Most of the reported SSIs were skin infections (56.8%).

Table 2 shows the ORs for SSI incidence considering different factors. All tested variables did not influence the incidence of SSIs, except compliance with guidelines in terms of antibiotic choice, which showed a lower odds of SSI development when antibiotic choice was appropriate (OR 0.24, 95% CI 0.09–0.63; $P = 0.004$).

Discussion

SSIs are an important cause of morbidity, mortality, and economic burden. They can be either local (e.g., skin or soft tissue infection, meningitis in case of neurologic surgeries, or urinary tract infection in case of urologic surgeries) or systemic (i.e., result in sepsis). SSIs can be prevented by appropriate antimicrobial prophylaxis considering antibiotic choice and duration. Appropriate antibiotic choice was highly prevalent in our study and significantly associated with a lower SSI incidence. However, duration of antibiotic therapy exceeded guideline recommendations. Although not assessed in our study, unnecessary prolonged duration of antibiotic administration can increase the risk of developing antimicrobial resistance, potential superinfections (e.g., *Clostridioides difficile* infection), as well as increased length of stay and high healthcare costs as previously reported.[1,2,6,13–16] It is worth noting that findings from this study can be applicable to any surgical procedure that requires preoperative antibiotic prophylaxis.

Clinical guidelines are developed by a panel of experts based on careful evaluation of all available evidence and most recent data on the diagnosis, management, and

Table 1: Baseline and clinical characteristics of patients.

Characteristic	Total (n = 98)	Orthopedic (n = 59)	Upper abdominal (n = 23)	Lower abdominal (n = 16)	*P* value
Age	52.5 (28–65)	62 (29–71)	50 (35–62)	32.5 (20–49)	0.004
Sex (male)	59 (60.2)	40 (67.8)	10 (43.5)	9 (56.3)	0.122
Antibiotic received[a]					0.003
• Cefazolin	56 (57.1)	43 (72.9)	10 (43.5)	3 (18.8)	
• Cefuroxime	12 (12.2)	3 (5.1)	6 (26.1)	3 (18.8)	
• Metronidazole	20 (20.4)	4 (6.8)	6 (26.1)	10 (62.5)	
• Meropenem	5 (5.1)	4 (6.8)	0 (0)	1 (6.3)	
• Imipenem	2 (2)	1 (1.7)	1 (4.3)	0 (0)	
• Gentamicin	4 (4.1)	2 (3.4)	2 (8.7)	0 (0)	
• Clindamycin	3 (3)	2 (3.4)	0 (0)	1 (6.3)	
• Piperacillin/tazobactam	3 (3)	1 (1.7)	1 (4.3)	1 (6.3)	
• Co-amoxiclav	3 (3.1)	2 (3.4)	0 (0)	1 (6.3)	
• Ciprofloxacin	3 (3.1)	0 (0)	2 (8.7)	1 (6.3)	
Antibiotic duration[b]	6.5 (4.75–7.5)	5 (5–10)	7 (4.5–8)	7 (4.5–7)	0.027
Developed SSI	37 (38.1)	22 (37.9)	11 (47.8)	4 (25)	0.352
Infection type					0.352
• SSTI	21 (56.8)	14 (63.6)	6 (54.5)	1 (25)	
• Other infection	16 (43.2)	8 (36.4)	5 (45.5)	3 (75)	

Data are presented as n (%) or median (interquartile range).
IQR, interquartile range; SSI, surgical site infection; SSTI, skin and soft tissue infection.
[a] Some patients received more than one antibiotic.
[b] Includes total duration of presurgical plus postsurgical durations.

Table 2: Odds ratios for SSI incidence in the presence of different factors.

Factor	OR (95% CI)	*P* value
Age	1.02 (0.99–1.05)	0.110
Sex		
• Male	1.86 (0.77–4.45)	0.170
• Female	Ref	Ref
Surgery type		
• Orthopedic	2.19 (0.28–17.21)	0.456
• Upper abdominal	4.64 (0.54–39.9)	0.162
• Lower abdominal	Ref	Ref
Antibiotic duration	1.08 (0.79–1.46)	0.631
Compliance with antibiotic choice	0.24 (0.09–0.63)	0.004
Compliance with antibiotic duration	1.36 (0.34–5.39)	0.660

prevention of certain diseases.[17] They may also include recommendations based on cost-effectiveness and risk/benefit ratio. The latest guidelines on surgical antimicrobial prophylaxis were developed by the CDC in 2017 preceded by World Health Organization guidelines in 2016 and joint guidelines by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society, and the Society for Healthcare Epidemiology of America in 2013.[7–9] Our study provides evidence that antibiotic choices made on the basis of guideline recommendations result in favorable outcomes. Previous studies have also shown benefit when such guidelines were followed. A study by Walczak et al.[18] demonstrated a lower incidence of SSIs when surgical prophylaxis guidelines were adhered to compared with the non-compliance group (3.3% vs. 8.1%; $P = 0.07$). Similarly, a study in 930 patients showed a cumulative incidence of SSIs of 4.6% when antibiotic prophylaxis was in compliance with the guidelines (relative risk = 0.5, 95% CI 0.1–1.9).[19] Such findings of low SSI rates corroborate our findings but with added statistical significance (OR 0.24, 95% CI 0.09–0.63). By contrast, lack of compliance with surgical antibiotic and venous thromboembolism (VTE) prophylaxis guidelines reportedly increased the risk of both SSIs and VTE, respectively, in a large study involving 3285 orthopedic surgery patients.[12] As expected, cefazolin was the most prescribed antibiotic, particularly for orthopedic and upper abdominal procedures. This compliance with the guidelines helps reduce the risk of developing antimicrobial resistance since cefazolin is not considered a broad-spectrum antibiotic while still covering potential SSI organisms including Gram-positive pathogens (namely *Streptococci*, methicillin-susceptible *S. aureus*, and coagulase-negative staphylococci) and Gram-negative Enterobacterales.

Non-compliance with the guidelines when it comes to surgical antibiotic prophylaxis is a universal issue[20]; hence, expecting compliance with the guidelines may not be sufficient in the absence of an enforced hospital-specific protocol or care bundle, education, and adherence tracking to minimize SSI risk. In our institution, surgical antibiotic prophylaxis use is based on updated constructed local hospital guidelines on antimicrobial therapy, which were developed according to the hospital's antibiogram. The surgical prophylaxis protocol is one part of these guidelines, whereas the other parts include empirical antimicrobial therapy and therapeutic drug monitoring. These hospital

guidelines are updated every 4 years by the antimicrobial stewardship subcommittee.

In a comprehensive review discussing SSIs and reasons for poor compliance, Leaper, et al.[21] listed seven recommendations to improve patient outcomes and reduce SSI rate through compliance with the guidelines. These included tracking compliance with hospital's care bundles and conducting pertinent qualitative research, including the care bundles in the patient's informed consent to ensure transparency of the process, establishing national or regional SSI surveillance programs, continuous updating of the national (or at least hospital) guidelines as new evidence evolves, recognition of compliant surgery teams, logging issues that could otherwise be prevented, and plan effective communication strategies if advice is needed from experienced healthcare providers.

Our study revealed the significance of guidelines compliance and importance of the protocol developed. Nonetheless, it was limited by the small sample size, which was attributed to the short study duration due to time constraints. Also, culture results from patients who developed SSIs were not collected, although the outcomes of SSI treatment were not the scope of this study.

Conclusion

In conclusion, our study showed that compliance with the guidelines in terms of antibiotic choice was associated with a lower likelihood of SSI development. However, lack of compliance was noticed with the duration of antibiotic administration. Therefore, a protocol enforcing short postoperative antibiotic courses and detailing the correct antibiotic to be selected for each surgery type should be developed by responsible multidisciplinary teams involving the surgical and pharmacy departments. Moreover, clinicians are encouraged to follow the updated guidelines and hospital protocols to improve patients' quality of care by preventing SSI incidence and reducing the risk of antimicrobial resistance development.

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Conflict of interest

The authors have no conflict of interest to declare.

Ethical approval

The research protocol was approved by the Medical Research and Ethics Committee, Medical Services Division of the Ministry of Defense and Aviation in KSA (Reference No. REC 288).

Authors contributions

FA: Conceptualization; project administration; methodology; resources; supervision; writing − review and editing. EMF: Data curation; investigation; writing − original draft. AKT: Formal analysis; software; writing − original draft; writing − review and editing. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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