

Review Article

Current perspectives on surgical antibiotic prophylaxis: guideline recommendations, prescribing patterns, antimicrobial resistance and future directions

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ABSTRACT

Surgical antibiotic prophylaxis is an essential component of peri-operative infection prevention and plays an important role in reducing surgical site infections. Although guidelines and evidence-based approaches have been agreed upon on an international level, there is still a great deal of variation between healthcare institutions in the way that they prescribe, which can result in antimicrobial resistance, higher healthcare costs and morbidity among patients. This review highlights existing guidance for the use of surgical antibiotic prophylaxis (SAP), reviews the current antibiotic use trends, explores typical prescribing errors and adherence to guidelines, and explores their impact on AMR and clinical outcomes. A literature review was undertaken using international guidelines, peer-reviewed publications, surveillance reports and systematic reviews with a particular focus on antibiotic selection, timing of antibiotic prophylaxis, Duration of antibiotic prophylaxis, interventions to support antimicrobial stewardship and antibiotic prescribing practices in tertiary care, and emerging strategies to optimize SAP. There is evidence that proper implementation of the SAP guidelines lessens the risk of surgical site infections (SSIs). Inappropriate practices, such as the use of broad-spectrum antibiotics, delayed treatment and extended antibiotic coverage after surgery, however, are still common and lead to greater AMR, healthcare costs, and poor clinical outcomes. Rational antibiotic use can be achieved with antimicrobial stewardship initiatives, prescription audits, clinical pharmacist involvement, and/or electronic decision-support systems. While SAP continues to play a key role in preventing SSIs, it must be implemented in accordance with evidence-based recommendations. Enhancing antimicrobial stewardship, optimizing prescribing and implementing supportive technologies can optimize SAP, limit AMR, and improve surgical patient outcomes.

Keywords: Surgical antibiotic prophylaxis, Surgical site infection, Antimicrobial resistance, Prescribing patterns, Guideline adherence, Antimicrobial stewardship, Perioperative antibiotics

INTRODUCTION

Surgical site infections (SSIs) are still one of the most frequent healthcare-associated infections (HAIs) worldwide and are still a significant source of postoperative morbidity, long hospital stay, healthcare costs, and mortality.¹ SSIs develop when pathogenic microorganisms enter the surgical wound, involving the incision site, deep tissues, and/or organ spaces of the

surgical procedure. Although surgical techniques, sterilisation practices, and perioperative care have improved substantially, SSIs still remain a significant burden in the health-care system worldwide.^{1,2} SSIs have been linked to longer hospital stay, higher use of health services, rehospitalization, and lower quality of life for surgical patients.³ Surgical antibiotic prophylaxis (SAP) refers to using antibiotics before the surgery becomes contaminated to prevent postoperative infection.⁴

Appropriate SAP administration has been demonstrated to significantly decrease the occurrence of SSIs if the appropriate antibiotic is started at the right time, dose and antibiotic category.⁵

SAP is recommended as an important element of SSI prevention by the World Health Organization (WHO) in many different surgical interventions.⁶ Although there are guidelines available, there is significant variation in antibiotic prescribing practices reported in tertiary care hospitals across the globe.⁷ Prescribing issues such as the inappropriate use of antibiotics, delayed antibiotic use, and extended post-operative use are continued concerns that can impact patients' outcomes.⁸ In addition, overuse and unnecessary antibiotic administration is one of the important factors in the development of antimicrobial resistance, which is now a significant public health threat worldwide.⁹ Thus, it is important to be aware of what the current guidelines are, how these are being used and what this means for antimicrobial resistance in order to optimise surgical antibiotic prophylaxis and maximise patient benefit.

PRINCIPLES AND GUIDELINE RECOMMENDATIONS

SAP is the use of antibiotics before surgery to decrease the number of microorganisms entering the body during surgery, lowering the risk for SSI. Because the goal of SAP is prevention, rather than treatment, sufficient antimicrobial levels must be achieved in serum and tissues at the time of surgical incision and maintained during the procedure when necessary.⁴ The current international consensus for deciding the use of SAP is the type of surgical procedure, level of wound contamination, risk factors of the patient and the consequences of postoperative infection. The following procedures are classed as clean contaminated procedures, contaminated procedures or clean procedures involving prosthetic material or implants and so require antibiotic prophylaxis.¹⁰ However, routine prophylactic antibiotic use is not recommended for uncomplicated clean surgical procedures which do not involve the use of a prosthesis because potential harm (such as adverse drug reactions and antimicrobial resistance) may be greater than potential benefit.¹¹

Antibiotic selection is an important part of successful prophylaxis. The selected agent should have a good safety profile, minimal ecological impact and cover the microorganisms most likely to be found in the operative field. In many surgical operations, the first generation of cephalosporins in particular (cefazolin) are still the drugs of choice for their effectiveness against common skin flora and their pharmacokinetic properties, as well as for being cost-effective.⁴ Timing of antibiotic use plays an important role in the effectiveness of the prophylaxis. The recommendation for most prophylactic antibiotics now is to give them within 60 minutes before the skin is cut open, so as the antibiotic is in the tissues at its best concentration

when bacteria are at their peak. If the antibiotic is one that needs several hours to be fully distributed in the body, like vancomycin and fluoroquinolones, it should be administered within 120 minutes of incision to ensure optimal distribution prior to surgery starting.¹² The guidelines also suggest intraoperative redosing when the procedure lasts for more than 2 half-lives of the given antibiotic or there is significant blood loss to ensure that there remain adequate levels of the antimicrobial during surgery.¹⁰

In addition to the antibiotic used, patient-specific and procedure-specific factors are also important in the effectiveness of postoperative antibiotic prophylaxis. Advanced age, diabetes mellitus, obesity, immunocompromise and malnutrition, long hospitalization before surgery have been found to be independent risk factors for the development of surgical site infections. So, a prudent assessment of infection risk must be performed when deciding on a strategy for antibiotic prophylaxis.¹³ Along with patient factors, the type of surgical wound is an important factor to consider when deciding whether or not to give prophylactic antibiotics. Surgical procedures have traditionally been classified as clean, clean-contaminated, contaminated, or dirty/infected. The likelihood of post-operative infection also increases with each of these categories and the level of antibiotic prophylaxis recommended varies by this risk. Prophylaxis may be especially useful in clean-contaminated and contaminated procedures where there is a much greater risk of microbial exposure.¹⁴

Also, the use of narrow-spectrum antibiotics, when possible, should be considered. Use of these broad-spectrum agents can also disrupt normal microbial flora and increase the risk of the establishment of multi-drug-resistant organisms, without offering any extra protection against SSIs. For this reason, international guidelines recommend the most narrow-spectrum antibiotic coverage that is likely to be effective for the pathogens likely to be present in the surgical procedure.¹⁵ It has also become an important factor in contemporary surgery, namely by weight dosing. Antibiotics may not reach a sufficient level of efficacy in the tissues when given in standard doses to obese patients, which can decrease the efficacy of the antibiotic for disease prevention. Based on this, a few guidelines suggest using larger doses of certain antibiotics such as cefazolin, for patients with increased body weight, to provide optimal antimicrobial exposure during surgery.¹⁶ There has been recent evidence that reinforces the need to embed surgical antibiotic prophylaxis as part of an infection prevention package. Appropriate antisepsis of skin, maintenance of normothermia, glycaemic control, and sterile surgical technique are all factors which act synergistically with antibiotic prophylaxis and help to minimise the risks of SSI. Thus, SAP must be considered as part of a holistic perioperative infection prevention program, not as an isolated measure.⁶

PRESCRIBING PATTERNS OF SURGICAL ANTIBIOTIC PROPHYLAXIS

Commonly prescribed antibiotics

The choice of antibiotic for use as a prophylactic depends on the institution and the surgical specialty, and worldwide, cephalosporins are the most commonly used antibiotics due to their activity against the most common surgical pathogens and favourable safety profile.¹⁷ Many clean and clean-contaminated surgeries have been recommended to use cefazolin as the first choice of prophylactic antibiotic agent because of its broad activity against gram positive skin flora, low cost, and favorable pharmacokinetic characteristics.¹⁸ Guideline recommendations favor the use of cefazolin, but some LMIC countries have noted high rates of broad-spectrum prophylactic use, including ceftriaxone, cefoperazone-sulbactam, piperacillin-tazobactam and fluoroquinolones for routine prophylaxis.¹⁹

Variations in prescribing practices

There is a significant variance in the prescription of SAP across countries, hospitals, surgical departments and even individual surgeons which are related to local policies, antimicrobial availability and preferences of the clinicians.²⁰ There have been several observational studies that have shown significant deviations from recommended antibiotics, dosage, treatment timing, and/or duration of antibiotic prophylaxis.⁵ These variations can lead to differential protection from surgical site infection and can contribute to exposure to unnecessary antibiotics.¹

Timing of antibiotic administration in clinical practice

Compliance with the timing recommendations for prophylactic antibiotic administration is suboptimal in many healthcare settings, and is one of the most important determinants to achieve the effectiveness of SAP.²¹ There are reports of antibiotics being given too early or after surgery has been performed, thus not achieving high enough concentrations in the tissues when bacterial exposure is highest.²²

Duration of prophylaxis and extended antibiotic use

A common concern for prescribers globally is continued antibiotic use for unnecessary periods after recommended postoperative antibiotic use.⁸ There are indications that prolonging prophylaxis for more than 24 hours does not significantly decrease SSI rates in most surgical procedures, but may lead to antimicrobial resistance, infection with *Clostridioides difficile* and antibiotic adverse effects.⁶ Tertiary care hospitals in developing nations frequently continue to use antibiotics for longer than recommended, and consideration of the prevention of SSI often trumps adherence to the most evidence-based recommendations.²³

Procedure-specific prescribing trends

The use of surgical antibiotic prophylaxis in prescriptions varies with the type of surgery. Prophylactic indications vary among different disease surgical procedures such as orthopedic surgery, cardiothoracic surgery, neurosurgery, colorectal surgery, gynecologic surgery, and urologic surgery, depending on the microorganisms expected and the risk of postoperative infection.²⁴ In orthopedic and cardiovascular surgery where the use of prosthetic material is involved, prophylactic antibiotics are routinely given due to the high morbidity rate of implant-associated infection, which may require revision surgery or extended antibiotic treatment.²⁵ On the other hand, most colorectal surgeries require wider antibiotic coverage due to the presence of both aerobic and anaerobic gut flora and antibiotic selection is especially critical.²⁶

Influence of local microbial epidemiology

In many tertiary care hospitals, the trends in antimicrobial resistance are significant determinants of drug choices for prescription. In areas with high resistance rates of commonly seen pathogens, surgeons might choose to use alternatives to guideline-recommended drugs.²⁷ Over the last few years, the emergence of methicillin-resistant *Staphylococcus aureus* (MRSA), extended-spectrum beta-lactamase (ESBL) producing organisms, and multi-drug-resistant Gram-negative bacteria (MDR-GNB) has led some institutions to adjust their antibiotic protocols, depending on their local epidemiology.²⁸

Patterns observed in tertiary care hospitals

The compliance with the existing SAP guidelines has been consistently reported by studies conducted in tertiary care hospitals with different levels of compliance. In a large fraction of cases antibiotic therapy may be successfully prescribed, though it is common to have problems with the timing and length of courses.²⁹ Although there has been a continuous campaign for early stoppages of antibiotic therapy, several studies that have been performed in many surgical departments have shown that prolonged postoperative prophylaxis is one of the most frequent patterns of inappropriate antibiotic use.³⁰ In addition, periodic review of prescriptions and institutional audits have been proven to be effective in achieving compliance with SAP guideline-recommended practices and decrease in unnecessary antibiotic exposure.³¹

GUIDELINE ADHERENCE AND PRESCRIBING ERRORS

Importance of guideline adherence

To achieve the greatest efficacy of surgical antibiotic prophylaxis without undue antibiotic exposure, it is important to follow evidence-based guidelines for SAP. There are recommendations from international organisations such as the WHO, ASHP, CDC and NICE

on the indication, selection, timing, dose and duration of antibiotic use as a prophylactic to ensure optimal surgical outcomes and prevent SSI.⁶ Standardised prescribing in surgical settings is crucial to reduce SSI rates, shorten hospital stays and decrease healthcare costs, as several studies have shown.³² Although there are detailed recommendations, adherence to them is still suboptimal in many health care institutions around the world and there is significant variation between surgical specialties and health care systems.²⁰

Appropriate and inappropriate prescribing

Appropriate SAP prescribing is the use of the right antibiotic, correct dosage, appropriate time window, and recommended length of therapy for the surgical procedure performed.³³ Examples of inappropriate prescribing include antibiotic use without a proper indication, prescribe unnecessarily broad-spectrum antibiotics, delayed antibiotic use, inappropriate dose or prolonged antibiotic use after surgery.³⁰ These may render the prophylactic ineffective, exacerbate adverse drug reactions, lead to greater health resource use and promote antibiotic resistance.³⁴

Antibiotic selection errors

An extremely common error reported is prescribing broad-spectrum antibiotics as opposed to narrow-spectrum antibiotics as recommended by guidelines.³⁵ In tertiary care centres, the use of third generation cephalosporins, carbapenems and combination therapies for routine surgical prophylaxis has been documented, but there is little evidence of their superiority over the recommended first line agents (cefazolin).³⁶ The overuse of broad-spectrum antibiotics can create a selective pressure which can lead to the development of multidrug-resistant organisms in healthcare centers.³⁷

Timing-related prescribing errors

One of the most frequent problems in clinical practice is still the time interval between antibiotic administration and surgery started, which should not exceed the recommended duration.²¹ Administering too early before surgery could lead to insufficient tissue levels at the time of incision, and if administered too late, it could cause the surgical wound to be exposed to microbes during the most critical period of microbial exposure.¹⁸ Errors related to time have been found in several audits as one of the most common causes of lack of adherence to SAP guidelines in tertiary care hospitals.²⁹

Duration-related prescribing errors

Inappropriate duration of therapy is one of the most commonly reported SAP prescribing errors, globally. According to current evidence-based guidelines, antibiotics for surgery should be discontinued within the first 24 hours after the surgery, since there is no evidence that this would confer extra protection against SSIs.³⁸ In

spite of these recommendations, postoperative antibiotics are frequently prescribed for more than a few days due to potential for wound infection, surgeon preference or institutional practice of prescribing antibiotics.⁸ Multiple studies have shown that there is no statistically significant reduction in the incidence of SSI with extended prophylaxis, but a higher risk of developing an adverse drug reaction, *Clostridioides difficile* infection (CDI) or antimicrobial resistance.³⁹ As a result, the inappropriate use of antibiotics for longer than recommended is now known to be a primary focus for antimicrobial stewardship in surgery.⁴⁰

Overuse and underuse of prophylactic antibiotics

The indiscriminate use of prophylactic antibiotics continues to be a problem in both developed and underdeveloped health care systems. Common examples include administration of broad-spectrum antibiotics when more narrow-spectrum antibiotic should be administered, use of multiple antibiotic combinations when there is no evidence for their use, and unnecessarily prolonging postoperative prophylaxis.²⁷ If antibiotics are used too much, it leads to selection of microbes, induces antimicrobial resistance and leads to higher cost of healthcare without better clinical outcomes.⁴¹ In contrast, there was underuse of prophylactic antibiotics in that patients may not have received SAP or received it in an inadequate dose, which may make them more vulnerable to postoperative infections.⁴² SSI has been linked to failure to offer adequate prophylaxis during high-risk surgical procedures, as does extended hospitalization and further treatment needs.⁴³

Factors associated with non-compliance

There are a number of reasons for poor compliance with SAP guidelines in clinical practice. Inadequate knowledge of the new recommendations is also an important barrier between healthcare professionals involved in the peri-operative care.⁴⁴ Absence of standardised protocols, poorly established monitoring systems and ineffective antimicrobial stewardship support programmes may also play a role in inappropriate prescribing practices.⁴⁵ The different prescribers' preferences and concerns about potential postoperative infections may also vary prescribing practices and may lead to variation from the guidelines.⁴⁶ Availability of antibiotics is also not always consistent in resource-limited settings, and regular (public) audits of prescribing may not occur, thus further compromising compliance with evidence-based SAP practices.⁴⁷

Strategies to improve guideline adherence

AMS programs have become one of the most successful methods to enhance adherence to SAP guidelines and to maximize the use of antibiotics in surgery.⁴⁸ Adherence to recommendations concerning antibiotic selection, timing and duration has been shown to be significantly improved through educational interventions, dissemination of

institutional protocols and regular feedback to surgeons.³⁰ Using electronic prescribing systems and clinical decision support tools to give automated reminders about what antibiotic to use, how and when to, and when to stop it may further improve antibiotic use, and thus compliance.⁴⁹ Prescription audits and surveillance programs are also valuable quality improvement tools as they allow healthcare institutions to detect deficiencies in prescription and monitor adherence and undertake targeted corrective actions.⁵⁰ Overall, these interventions help to ensure rational antibiotic use, the reduction of inappropriate antibiotic use and play a role in patient outcomes and the prevention of the development and spread of antimicrobial resistance.

ANTIMICROBIAL RESISTANCE AND CLINICAL IMPACT

Surgical antibiotic prophylaxis and antimicrobial resistance

Antimicrobial resistance (AMR) is one of the biggest public health challenges in the world, and is undermining the effectiveness of antibiotics, which have been proven to be very effective in preventing and treating infectious diseases.⁵¹ The misuse of SAP is an important factor in the emergence and transmission of drug-resistant microorganisms in health-care facilities.³⁷ When patients are exposed to antibiotics that are not necessary, the pressure of the antibiotic will cause resistant bacterial strains to grow and susceptible strains to die out.⁵² This has led to irrational prophylactic use of antibiotics which is a significant driver of the global burden of drug-resistant infections and health-care-associated infections.⁵³

Emergence of multidrug-resistant organisms

Multidrug-resistant organisms (MDROs) have been reported in increasing numbers in healthcare facilities across the globe, including some attributed to a lack of antibiotic use oversight and inappropriate antibiotic use for prophylaxis.⁵⁴ Methicillin-resistant *Staphylococcus aureus* (MRSA) is one of the most significant resistant pathogens seen in surgical patients and linked to increased morbidity, longer hospital stays, and greater treatment expense.⁵⁵ Likewise, there has been a tremendous rise in the prevalence of extended-spectrum β -lactamase (ESBL)-producing Enterobacterales (EPE) in the last 2 decades, which diminishes the use of widely prescribed cephalosporins and other β -lactam antibiotics.⁵⁶ In addition to this, the presence of carbapenem-resistant Enterobacterales (CRE) and multidrug-resistant *Pseudomonas aeruginosa* (MDR PA) makes the management of postoperative infections more challenging and a concern for healthcare systems around the world.⁵⁷

Clinical consequences of antimicrobial resistance

It has been found that infections with resistant organisms are linked to increased clinical failure, when compared to infections by susceptible organisms.⁵⁸ Those infected with

a resistant microorganism may need to stay in hospital for longer, undergo further testing and receive more costly and potentially toxic antimicrobial agents.⁵⁹ A potential increase in antimicrobial resistance may also lead to failure of treatment, surgical complications, admission to an intensive care unit and death in surgical patients.⁶⁰ Moreover, resistant postoperative infections often require long treatments of antimicrobials, which can lead to further resistance development and result in an escalating use of antimicrobials.⁶¹

Economic burden of antimicrobial resistance

The impact of AMR on the economy is not just on the individual patient, but also on healthcare systems and national economies and is significant.⁵² Research has shown that with resistant infections, there is an increase in hospital costs because of longer hospital stays, extra laboratory testing, isolation and the use of antimicrobial agents.⁶² Global estimates suggest that if action is not taken to address AMR, then it could kill millions of people each year and cause trillions of dollars in economic losses.⁶³

Public health implications

Many of the advances achieved in modern medical practice, such as complex surgery, organ transplantation, cancer chemotherapy and intensive care management (ICM) depend on antimicrobial susceptibility, and this has become increasingly a problem due to the emergence of antimicrobial resistance (AMR).⁶⁴ One of the best ways to minimize unnecessary antibiotic exposure and decrease the development of antibiotic-resistant microorganisms is to optimize surgical antibiotic prophylaxis, in line with evidence-based practice (EBP) guidelines.³⁸ This means rational prescribing, ongoing monitoring of antimicrobial resistance and effective antimicrobial stewardship programs must be adopted to maintain the effectiveness of antimicrobials and achieve best possible surgical outcomes in the future.⁶⁵

ANTIMICROBIAL STEWARDSHIP AND FUTURE DIRECTIONS

Antimicrobial stewardship programs

Antimicrobial stewardship programs (ASPs) are coordinated interventions aimed at optimizing the use of antimicrobial agents, patient outcomes, decreasing the spread of antimicrobial resistance, and maximizing the utilization of healthcare resources.⁴⁰ In a surgical context, ASPs are important in ensuring compliance with evidence-based guidelines on: antibiotic selection; timing of antibiotic use; antibiotic dose; and duration of SAP.⁴⁵ Implementation of stewardship interventions has been shown to be effective in increasing compliance with guidelines for antibiotic prescribing and to decrease inappropriate use of antibiotics and health care costs in several studies.²⁷

Role of clinical pharmacists in surgical antibiotic prophylaxis

The importance of clinical pharmacists to antimicrobial stewardship team is growing due to their knowledge of antimicrobial therapy and medication management.⁶⁶ The interventions by the pharmacist have been shown to increase adherence to SAP guidelines and to decrease prescribing errors, such as reviewing antibiotic prescriptions, monitoring prophylactic regimens and providing evidence-based recommendations.⁶⁷ The contribution of clinical pharmacists to perioperative care may help with the right antibiotic choice, the optimisation of dose regimens and the timely termination of antibiotic prophylaxis.³⁰

Audit and feedback strategies

Audit and feedback mechanisms are effective approaches to quality improvement which can support the achievement of the SAP guidelines and the identification of prescribing deficits in surgical departments.⁶⁸ The routine examination of prescribing practices allows healthcare providers to track the patterns of antibiotic use, assess adherence, and set up interventions as needed.⁵⁰ Structured audit and feedback programs have been shown to lead to important changes in antibiotic prescribing in several studies, especially regarding the duration and timing of antibiotic prophylaxis.²⁰

Electronic prescribing and clinical decision support systems

Health information technology (HIT) innovations have introduced new possibilities for optimizing surgical antibiotic prophylaxis via computer-assisted surgical antibiotic prescribing systems and clinical decision support tools (CDSTs).⁴⁹ Based on procedure-specific guidelines, electronic systems can make real time recommendations for antibiotic selection, dosage, time of administration and when to stop antibiotics.⁶⁹ Automated reminders and integrated prescribing alerts have been found to minimise medication errors and prophylactic protocols.⁷⁰

Precision medicine and future innovations

In the future, the increasing availability of microbiological surveillance data, pharmacokinetic modelling and genomic technologies is likely to revolutionise the future of surgical antibiotic prophylaxis.⁷¹ The use of patient-specific risk assessment, local resistance patterns, and individualized antimicrobial selection along with the aim of maximizing the effectiveness of future prophylactic strategies will minimize unnecessary antibiotic exposure.⁷² The ability for AI and machine-learning algorithms to predict infection risk, determine high-risk patients, and suggest optimal prophylactic regimens, using real-time clinical data, could also aid clinical decision-making.⁷³

Future research directions

Future studies should consider the effectiveness of procedure-specific approaches to prophylaxis, implementation optimisation of prophylaxis in special patient groups and the long-term effects of stewardship interventions on trends of antimicrobial resistance.¹ More multicenter studies are required to identify barriers to guideline adherence and to develop effective interventions to implement across different healthcare settings.⁵ Also, ongoing antimicrobial resistance surveillance is important to guarantee that future SAP recommendations are effective against new antimicrobial resistances.⁷⁴

CONCLUSION

Properly used, surgical antibiotic prophylaxis is an excellent means to prevent surgical site infection and enhance the outcomes of surgery. It is important to use the dosages and timing of antibiotics, adhering to evidence-based guidelines, in order to enhance its benefits and reduce any negative impact. Although international guidelines are available, inappropriate antibiotic choice, late administration, and unnecessary and inadequate antibiotic cover for the postoperative period continue to be common problems, leading to higher costs of care, side effects and antimicrobial resistance. To enhance antimicrobial stewardship programs, frequent prescribing audits, and greater collaborative efforts between surgeons, pharmacists, microbiologists, and infection-control practitioners are all crucial for better SAP practices. Other innovations such as electronic decision support systems and AI-driven tools could complement the effective use of medicines. Overall, improved guideline adherence and evidence-based antibiotic use are crucial for reducing surgical site infections, preserving antimicrobial effectiveness, and enhancing the safety and quality of surgical care.

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