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Review

Antibiotic prophylaxis in orthopaedic surgery: A review of evidence and best practices

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Abstract

The use of prophylactic antibiotics in Orthopaedic and Trauma surgery is well-established. Superficial and periprosthetic joint infections are dreaded complications that increase morbidity, disability, and mortality. Despite the various guidelines and the wide employment of antibiotics, there is still controversy about their optimal use. The main factors that have to be taken into account are the choice of the most effective antibiotic, the timing of administration, and the duration of the treatment. This review deepens into the evidence behind commonly argued topics in antibiotic prophylaxis and highlights the fundamental aspects that lead our current practice.

Keywords

Antibiotics; prophylaxis; surgical site infection; orthopaedics

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Introduction

Infection is one of the most disastrous complications in Orthopaedic surgery. It is associated with increased morbidity, disability, and mortality.[1] The use of antibiotics against infections, which was once considered a panacea, remains an integral part of Orthopaedic practice as it has been proved that antibiotic prophylaxis is effective in reducing the incidence of surgical site infection (SSI) subsequent to arthroplasty from roughly 4% to 1%. SSIs can result in extended hospital stays, increased healthcare expenses, and patient discomfort.[2]

Infection control methods have been extensively disseminated, but guidelines are frequently disregarded. The World Health Organization (WHO) has recommended a 19-item surgical safety checklist to reduce complications before any surgical procedure, which includes prophylactic antibiotics.[3] Nevertheless, the antibiotic resistance that has arisen due to inconsiderate use presents a major threat and the WHO has warned about a new era in which trivial infections and minor injuries will once again threaten human life.[4]

Despite the widespread acceptance of antibiotic prophylaxis in Orthopaedic surgery, significant variability in practice patterns persists.[5] Discrepancies in adherence to guidelines, debates over the most effective antibiotic choices, and concerns about the optimal timing and duration of administration highlight a need for clarity.[6] This review aims to compile the latest research and guidelines to support evidence-based practices in Orthopaedic antibiotic prophylaxis, addressing areas of controversy and emphasizing the need for consistency and compliance in clinical practice.

Risk factors for infection in Orthopaedic surgery

Infections in orthopaedics remain a significant concern, as SSIs can significantly affect patient recovery and healthcare costs.[7] Advances in surgical techniques and the increased use of implants, while improving outcomes, have also increased the risk of SSIs.[8] Factors such as diabetes mellitus and hypertension are well-established risk factors, with diabetic patients being six times more likely to develop infections.[9] Hypertension has similarly been linked to higher SSI risk.[10] Additionally, the influence of age on infection rates is debated; while younger patients may face lower risks, older adults often experience higher susceptibility due to weaker immune system and existing chronic comorbidities.[11] Surgical factors, including the type of incision, also play a crucial role; fresh, open wounds present the highest risk, while clean, sterile incisions are associated with the lowest infection rates.[12]

Moreover, complex and prolonged surgeries increase the likelihood of SSIs, highlighting the need for surgical precision and strict adherence to infection control protocols.[13] Operating room conditions, such as proper air filtration and use of laminar flow systems, contribute to maintaining a sterile environment. Finally, the presence of multidrug-resistant organisms adds another complicated burden, making targeted antibiotic prophylaxis essential. Despite extensive research, inconsistency in identifying specific SSI risk factors remains a challenge.[14] Improving our understanding of these variables can result in more effective preventative strategies and decreased SSI rates in Orthopaedic patients, thus improving outcomes and reducing healthcare costs.

Surgical site infection

Orthopaedic procedures, such as joint replacement or fracture fixation, include bone and soft tissue manipulation, and often implantation of prosthetic devices. These procedures are threatened by the likelihood of surgical site infections, which can result in serious complications such as implant failure, septic arthritis, and osteomyelitis. This risk is mitigated by antibiotic prophylaxis, which prevents the colonization and subsequent infection of the surgical site by bacteria introduced during surgery.[15]

Airborne organisms and patient microbiota are the most prevalent causes of SSIs, frequently acquired in the operating theater. Staphylococcus aureus and coagulase-negative staphylococci such as Staphylococcus epidermidis are the most common infectious agents.[2]

It has been demonstrated that the overall incidence of SSI following hip fracture surgery is approximately 5%, with roughly one-third of these cases involving a deep infection.[16] Within a year, approximately fifty percent of patients who develop an SSI after hip fracture surgery will pass away.[17] Around twenty-three percent of revisions after total knee arthroplasty (TKA) and between 7% and 13% of revisions after total hip arthroplasty (THA) in elective surgery is caused by infection with the mortality rates associated with prosthetic joint infection (PJI) ranging between 2% and 18%.[18,19,20]

Timing of antibiotic administration

The minimum inhibitory concentration (MIC) of antibiotic levels must be exceeded throughout the duration of the operation for prophylaxis to be effective against bacterial growth.[21] The majority of studies support that prophylactic antibiotics should be administered 30–60 minutes prior to skin incision. Antibiotic concentrations in blood and bone usually arise within 20 and 60 minutes, respectively, and must be maintained until skin closure above the MIC.[22] When antibiotics are administered after tourniquet application, prophylaxis is probably ineffective. Therefore, the extremity remains without high antibiotic prophylaxis for an extended period of time. To prevent this unfortunate circumstance, the antibiotics should be administered at least 10 minutes prior to the incision and tourniquet inflation; they should have a sufficient half-life to maintain MIC throughout the procedure, and they should be effective against the most common pathogenic organisms.[23]

Generally, the initial two hours following an incision or contamination are the most crucial for preserving antibiotic concentration and the antibiotics should ideally be administered within an hour of the incision; however, some authors argue that the administration within two hours is acceptable.[24] Surgical site infection incidence increases two- to six-fold when we fail to provide antibiotic prophylaxis during this 2-hour timeframe.[25]

In the case of an open fracture, where contamination precedes treatment, it is not plausible to administer antibiotics to the surgical site prior to exposure to likely pathogens. The standard recommendation for patients with an open fracture is to administer antibiotics within three hours; nonetheless, in a retrospective study conducted by Lack et al., an interval of >66 min was identified between fracture and antibiotic administration as a major independent risk factor for surgical site infection in Gustilo-Anderson Grade III fractures. Urgent antibiotic prophylaxis and soft-tissue coverage within five days were independently correlated with a lower rate of deep infection; the timing of early surgical debridement had no effect on subsequent infection rates.[26]

Another parameter that might additionally impact the administration time frame is the type of antibiotic applied. For instance, vancomycin, which can be administered to patients with a β-lactam allergy, those colonized with MRSA, and those hospitalized in departments experiencing recent MRSA outbreaks, should be dispensed over a period of minimum 60 minutes due to the potential risk of anaphylactic adverse effects.[27] On this particular topic, no definitive recommendation can be implemented; however, the efficacy of antibiotic therapy has been demonstrated, and it should be administered as soon as possible.

Choice of antibiotics

The selection of antibiotic prophylaxis in Orthopaedic and Trauma surgery should prioritize cost-effectiveness, safety, and broad-spectrum coverage. While there is substantial evidence supporting the general use of prophylaxis, there is no clear consensus favoring one specific antibiotic over another. The most common pathogens causing SSIs are Gram-positive organisms, particularly Staphylococcus aureus and Staphylococcus epidermidis, both of which are part of the skin's natural flora. Therefore, β-lactam antibiotics, such as cephalosporins and penicillin derivatives like cloxacillin, are frequently used.[19] Among these, cefazolin has been the standard choice in Orthopaedic and Trauma surgeries, including arthro-

Table 1. Antibiotic Selection and Indications in Orthopaedic Surgery

Antibiotic Class	Common Agents	Coverage	Advantages	Limitations	Indications
1st Generation Cephalosporins	Cefazolin	Gram-positive, limited Gram-negative	High safety profile, good bone penetration	Limited coverage for Gram-negative, ineffective against 90% of coagulase-negative staphylococci	Standard for orthopaedic and trauma surgeries, including arthroplasty
2nd Generation Cephalosporins	Cefuroxime	Broader Gram-negative, maintains Gram-positive coverage	Better Gram-negative coverage than 1st generation	Less effective against a wider range of Gram-negative organisms	Broader Gram-negative coverage
3rd Generation Cephalosporins	Ceftriaxone	Gram-negative, some Gram-positive	Broader spectrum	Associated with Clostridium difficile infections, leading to reduced use	Maybe in open fractures
Penicillin Derivatives	Cloxacillin, Flucloxacillin	Gram-positive (Staph. aureus)	Good safety profile	Ineffective against MRSA and 90% of coagulase-negative staphylococci	Commonly used in orthopaedic trauma
Macrolides / Lincosamides	Clindamycin	Gram-positive, anaerobes	Excellent bone penetration	Ineffective against aerobic Gram-negative bacteria	Alternative for β-lactam allergic patients, suitable for Grade I and II open fractures
Glycopeptides	Teicoplanin, Vancomycin	Gram-positive (MRSA, MSSA)	Effective against MRSA, good bone penetration	Risk of resistance with vancomycin, potential nephrotoxicity	Used in β-lactam allergic patients, added to bone cement in arthroplasty
Fluoroquinolones	Ciprofloxacin	Broad-spectrum (Gram-positive and negative)	Excellent oral bioavailability	High resistance risk, Clostridium difficile risk	Not used as first-line due to resistance risk
Beta-lactam Combinations	Co-amoxiclav	Broad-spectrum (Gram-positive, negative, anaerobes)	Effective for open fractures		Recommended for open fractures
Local Antibiotics	Gentamicin (in PMMA)	Broad-spectrum (local high concentration)	Effective local delivery, minimizes systemic side effects	Systemic coverage is limited	Used in bone cement, beads for open fractures

plasty, due to its proven efficacy.[21]

Second-generation cephalosporins, like cefuroxime, are increasingly favored for their broader spectrum compared to first-generation cephalosporins. They provide enhanced coverage against Gram-negative organisms while maintaining efficacy against key Gram-positive pathogens. This makes them a suitable alternative for prophylaxis in certain surgical settings, particularly where Gram-negative coverage is a concern.[28,29]

Cephalosporins, in general, have a favorable safety profile, excellent penetration into bone and muscle tissues, and are recommended by the American Academy of Orthopaedic Surgeons (AAOS) for arthroplasty patients.[30] However, they are less effective against a wider range of Gram-negative bacteria and only cover about 10% of coagulase-negative staphylococci.[31] Concerns over third-generation cephalosporins' association with Clostridium difficile infections have led to their reduced use as first-line prophylactic agents, particularly in the United Kingdom, where about half of NHS hospitals have transitioned to flucloxacillin to target Staphylococcus aureus.[32,33]

For patients with a β-lactam allergy, alternatives such as clindamycin are effective against Gram-positive and anaerobic bacteria, though they lack efficacy against Gram-negative organisms, making them unsuitable for higher-grade open fractures.[34] Vancomycin and teicoplanin are effective antibiotics for Gram-positive bacteria, including MRSA and MSSA, making them suitable options for patients with β-lactam allergies.[11] However, vancomycin requires cautious use due to concerns over resistance and potential nephrotoxicity, limiting its recommendation for routine systemic administration.[35,36,37] In specific clinical contexts, such as arthroplasty and contaminated open fractures, vancomycin can be utilized locally. It can be added to bone cement for arthroplasty prophylaxis, used in antibiotic nanoparticles to prevent infections in open fractures, and employed in spinal surgeries or ACL reconstructions by soaking the graft in a vancomycin solution.[5,38,39] These localized approaches aim to deliver high antimicrobial concentrations directly to the surgical site while minimizing systemic side effects. Similarly, gentamicin-loaded bone cement is commonly used to provide effective local antibiotic delivery in procedures at high risk of infection.[38,40]

The decision to use dual antibiotic prophylaxis against periprosthetic joint infections (PJIs) remains controversial due to potential risks like acute kidney injury. Thus, considerations regarding antibiotic resistance, cost-effectiveness, and patient-specific factors should guide the choice of prophylactic regimens.[41] In clinical practice, antibiotics targeting Gram-negative organisms are reserved for high-risk joint replacements, provided the patient's renal function allows it. Quinolones, despite their broad-spectrum coverage and good oral bioavailability, are avoided as first-line agents due to increased resistance risks and Clostridium difficile concerns.[5] For open fractures, co-amoxiclav, a combination of amoxicillin and clavulanic acid, remains a favored option due to its wide coverage of Gram-positive, Gram-negative, and anaerobic bacteria.[5]

Duration of antibiotic prophylaxis

The controversy over antibiotic chemoprophylaxis duration in Orthopaedic surgery arises from inconsistent guidelines recommending anywhere from a single dose to 14 days. This variation results from insufficient high-quality evidence, as decisions are frequently influenced by expert opinion and institutional practices rather than reliable clinical data.[23,42,43] Overall, there is a trend toward a decrease in the necessary doses of prophylactic antibiotics. The American Academy of Orthopaedic Surgeons (AAOS) recommends that chemoprophylaxis should not exceed 24 hours[14], and even stricter, the 2017 U.S. Centers for Disease Control and Prevention (CDC) guideline advises against administering antibiotic prophylaxis after surgical site closure in clean or clean-contaminated operations. In the orthopaedic setting, this includes procedures such as elective joint replacements without existing infections (clean) and minimally invasive surgeries with minor exposure to sterile areas (clean-contaminated), to prevent antibiotic overuse and resistance.[44] Williams and Gustilo found no difference in the infection rate between those who received prophylaxis for one and three days, in a retrospective study of patients undergoing total hip and knee arthroplasty.[45] A randomized controlled trial (RCT) reinforced the previous results, as no difference in the incidence of SSI between patients who received prophylaxis for 24 hours or seven days after THA or TKA was observed.[46]

In both elective and trauma surgery, evidence suggests that a single dose of antibiotic prophylaxis may be adequate;[47,48] however, the recommendation to shorten prophylaxis remains controversial, especially in high-risk situations like surgeries involving wound drainage or prosthetic implants, where the consequences of a SSI could be severe. Patients with total hip or knee arthroplasties who were not given extended oral antibiotic prophylaxis were up to five times more likely to develop periprosthetic joint infection (PJI), according to a retrospective analysis.[49] Long-term use was linked to drug-resistant pathogens, drug-induced hepatic/nephropathy, and burdensome healthcare costs.[1] The optimal duration of postoperative antibiotics is not yet clearly established, although the majority of reports indicate that prophylactic antibiotics administered for more than 24 hours postoperatively provide virtually no extra benefit.[50,51,52,53]

The authors' experience and everyday clinical practice contain the application of antibiotics for 24 hours in soft tissue procedures and for 48 hours when implantation of prostheses is performed. This clinical practice has led to significantly low infection rates, without severe side effects for many years. An individualized approach is of paramount importance, though.

Conclusion

Without a doubt, the utilization of surgical prophylactic antibiotics is of great importance in everyday orthopaedic practice. Regarding the timing, choice, and duration of prophylactic antibiotics in Orthopaedic surgery, general guidelines exist but an ongoing debate is also present. As a general rule, we could summarize that the current trend and the authors' proposal are to administer mainly cephalosporins (first or second-generation), but also vancomycin, clindamycin or penicillin-derivatives as prophylactic antibiotics 30 minutes to one hour prior to skin incision, preferably via intravenous infusion for 24 hours to three days postoperatively, depending on the type of the procedure and the patient characteristics. Exact antibiotic selection should be decided depending on cost, availability, allergies and local microbiology characteristics. A dual antibiotic scheme could be considered in selected cases.

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