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Antibiotic Prophylaxis in Gustilo-Anderson Grade II Open Fractures: A Literature Review

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ABSTRACT

Introduction: Infection is one of the most important complications of Gustilo-Anderson Grade II open fractures and may result in delayed union, nonunion, osteomyelitis, and functional impairment. Prophylactic antibiotics, combined with prompt surgical debridement, are a key component of treatment. However, the optimal regimen and duration of prophylaxis remain controversial.
Methods: A literature review was conducted using PubMed to identify studies published through December 2022. The search strategy was developed according to the PICO framework, focusing on patients with Grade II open fractures, prophylactic antibiotic administration, alternative regimens, and infection-related outcomes. After screening for articles meeting predefined inclusion and exclusion criteria, 8 articles were included. Data were synthesized narratively.
Results: First-generation cephalosporins, particularly intravenous cefazolin, were the most consistently recommended first-line prophylactic agents for Grade II open fractures. Clindamycin was the preferred alternative for patients with penicillin allergy. Early antibiotic administration, ideally within 1 hour of presentation, was associated with better infection prevention. Prophylaxis beyond 24 hours after definitive wound closure did not show additional benefit. Evidence supporting the routine use of aminoglycosides, fluoroquinolones, or other broad-spectrum agents was limited and inconsistent.
Conclusion: Current evidence supports early short-course intravenous cefazolin as the preferred prophylactic regimen for Gustilo-Anderson Grade II open fractures, with clindamycin as an appropriate alternative for patients with penicillin allergy. Prolonged antibiotic administration beyond 24 hours is not supported by the available evidence.

Keywords: anti-bacterial agents; fractures, open; anti-infective agents, local; surgical wound infection; osteomyelitis.

INTRODUCTION

An open fracture is defined as a fracture in which the bone and/or fracture hematoma is exposed to the external environment through a traumatic violation of the soft tissues.[1] Open fractures of the lower extremities are most commonly caused by motor vehicle accidents, which account for 34.1% of cases.[2] These injuries are associated with substantial morbidity and mortality, with wound infection representing one of the most frequent and serious complications. Bacterial contamination has been reported in approximately 70% of open-fracture wounds.[3] For this reason, prophylactic antibiotic therapy has become a cornerstone of management to reduce the risk of infection and osteomyelitis.[4]

The Gustilo-Anderson classification remains the most widely accepted system for categorizing open fractures and guiding their management. This classification is based on the degree of energy transfer, the extent of soft-tissue injury, and the level of contamination, all of which are closely associated with the risk of complications.[3] Grade I injuries are characterized by a clean wound measuring less than 1 cm in length, whereas Grade II injuries involve a laceration greater than 1 cm without extensive soft-tissue damage, flaps, or avulsions. Grade III injuries include open segmental fractures, fractures with extensive soft-tissue damage, or traumatic amputations.[5] Grade II open fractures are commonly associated with high-energy mechanisms, including motor vehicle trauma and gunshot injuries, and patients may present with concomitant injuries involving other anatomical regions.[2]

The severity of injury is a well-established predictor of infection in open fractures.[3] In a study of 422 open fractures, the overall infection rate was 4.3%, with a deep infection rate of 4% among patients with Grade II injuries.[4] In the original study by Gustilo and Anderson, the infection rate for Type II fractures was reported as 2.4%.[6] Although these rates are lower than those observed in more severe injuries, Grade II open fractures remain clinically important because they occupy an intermediate position between low- and high-grade trauma, and optimal prophylactic antibiotic strategies for this group remain a subject of ongoing discussion.

Prompt antibiotic administration, meticulous wound debridement, early identification of causative microorganisms, antimicrobial susceptibility testing, and appropriate surgical management are all essential components of treatment. Nevertheless, despite appropriate management, some degree of bacterial contamination is almost always present in open fractures. [6,7] Moreover, variation in the choice, timing, and duration of prophylactic antibiotic regimens continues to raise questions regarding the most effective strategy for preventing infection in Grade II open fractures. Therefore, this study aimed to review antibiotic prophylaxis regimens and summarize current evidence on more effective prophylactic algorithms for Grade II open fractures.

METHODS

Study Design

This study was conducted as a literature-based review to evaluate antibiotic prophylaxis strategies in Grade II open fractures. The review aimed to identify and summarize published evidence regarding the type, timing, and duration of antibiotic administration, as well as infection-related outcomes.

Search Strategy and Study Selection

A literature search was conducted in PubMed to identify relevant studies published through December 2025. The search strategy was constructed according to the PICO framework. The population comprised patients with open fractures, with particular emphasis on Grade II open fractures. The intervention was prophylactic antibiotic administration. The comparison included different antibiotic regimens, timing of administration, and prophylaxis duration. The outcomes of interest were wound infection, deep infection, osteomyelitis, and other infection-related complications.

Based on the PICO framework, the search was performed using the following keywords and Boolean operators: ("open fracture" OR "Grade II open fracture" OR "Gustilo type II fracture") AND ("antibiotic prophylaxis" OR "prophylactic antibiotic" OR "cefazolin" OR "clindamycin" OR "gentamicin") AND ("infection" OR "wound infection" OR "osteomyelitis"). The initial search identified 253 records. After title and abstract screening, potentially relevant studies underwent full-text assessment according to the predefined inclusion and exclusion criteria. Studies were included if they evaluated prophylactic antibiotic use in open fractures and were relevant to Grade II injuries. Studies were excluded if they were published in a language other than English, were unavailable in full text, or could not be accessed through open-access sources or institutional subscriptions. After the screening and eligibility assessment process, 8 articles were included in the final review.

RESULT

Study selection followed the PRISMA Guidelines. A detailed summary of the literature search and study selection process is presented in Figure 1.

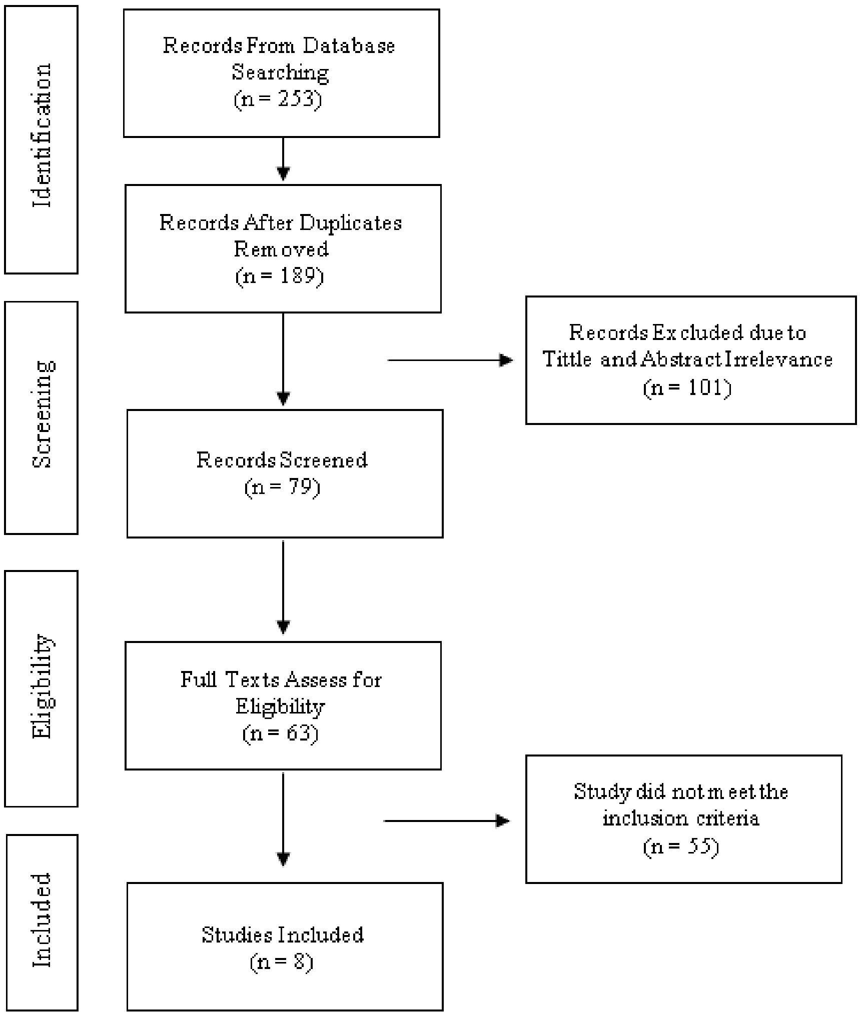

Figure 1. Flow diagram showing stages of the database search and study selection following PRISMA Guidelines

Characteristics of Included Studies

The 8 included articles evaluated antibiotic prophylaxis in open fractures, with particular relevance to Grade II injuries. The included studies examined several antibiotic classes, including beta-lactams, aminoglycosides, and fluoroquinolones, and reported outcomes related to infection prevention, wound complications, and osteomyelitis.

Antibiotic Prophylaxis in Grade II Open Fractures

Among the included studies, first-generation cephalosporins were the most frequently recommended prophylactic antibiotics for

Grade II open fractures. Cefazolin was consistently identified as the preferred first-line agent due to its effectiveness against common Gram-positive organisms associated with open fracture infections. In patients with penicillin allergy, clindamycin was the most commonly recommended alternative.

Evidence regarding aminoglycosides was mixed. Some studies suggested that gentamicin may reduce infection rates when administered appropriately, whereas others did not recommend its routine use in Grade II open fractures because of limited additional benefit and the risk of toxicity. Findings related to cefuroxime were also inconsistent, with some reports indicating inadequate protection against infection, particularly in cases involving multidrug-resistant organisms. Fluoroquinolones were not recommended for pediatric patients with open fractures due to safety concerns. The antibiotic prophylaxis recommendations identified from the 8 included studies are summarized in Table 1.

Table 1. The recommended antibiotic prophylaxis algorithm for open fracture grade II

Antibiotic Class	Recommendation for prophylaxis	Study Sources
Beta-lactams	First-generation cephalosporins have been the most common and most effective prophylactic agents after open fractures.	Hoff et al., 2011[8]; Isaac et al., 2016[9]; Chang et al., 2015[10]
	Grade II fractures should be treated with intravenous cefazolin 2 g immediately, followed by dosing every 8 hours for a total of 3 doses. In patients with penicillin allergy, intravenous clindamycin 900 mg every 8 hours for 24 hours is recommended.	Garner et al., 2020[11]
	The combination of Cephalosporin and Aminoglycoside for grade II open fracture showed 6,0% inhibition of infection. The admission of intravenous (IV) cefuroxime 750	Patzakis et al., 2000[12]
	The admission of intravenous (IV) cefuroxime 750 mg as antibiotic prophylaxis in a grade II open fracture did not prevent the infection. It was supported by elevated infection and inflammation markers in the rare, tropical, multi-drug-resistant (MDR) organisms isolated.	Er et al., 2021[13]
	Admission for 1.5 mg cefuroxime parenterally thrice daily for 5 days did not prevent wound infection, as osteomyelitis was present.	Tremp et al., 2020[14]
Aminoglycosides	Full-dose gentamicin admission for type II open fractures had a lower infection rate than divided dosing with the equivalent of 5 mg/kg/day given over three doses.	Sorger et al., 1999[15]
	Aminoglycosides are not recommended to be used for prophylactic management of open fractures	Garner et al., 2020[11]
Fluoroquinolones	The use of fluoroquinolones is contraindicated in pediatric patients with open fractures.	Garner et al., 2020[11]

DISCUSSION

Wound infection remains one of the most serious complications associated with open fractures and may result in delayed union, non-union, chronic osteomyelitis, prolonged hospitalization, and permanent loss of function.[16] The clinical burden of open fractures is substantial; for example, more than 12,000 cases of open wounds or lower-limb fractures were reported in the United Kingdom in 2007–2008.[10] Surgical debridement continues to be the cornerstone of treatment for open fractures, but antibiotic therapy is an equally important component of standard management. When administered promptly and combined with adequate debridement, prophylactic antibiotics play a critical role in reducing the risk of infection.[9]

The findings of this review indicate that first-generation cephalosporins remain the preferred prophylactic agents for Grade II open fractures. This is consistent with a study recommendation: administer 2 g of intravenous cefazolin for Type I and II fractures, then repeat every 8 hours for a total of 3 doses. In patients with penicillin allergy, clindamycin was recommended as an alternative at a dose of 900 mg intravenously every 8 hours for 24 hours. Additional penicillin may be considered in cases of fecal or farm-related contamination at the discretion of the treating surgeon. Antibiotics are generally discontinued 24 hours after definitive wound closure, unless clinical signs of infection are present.[11]

Beta-lactam antibiotics

Beta-lactam antibiotics, including penicillins and cephalosporins, act as bactericidal agents by inhibiting bacterial cell wall synthesis.[7] Historically, these agents have formed the basis of prophylactic therapy for open fractures. In an early study of wound cultures obtained from 352 consecutive open long-bone fractures, approximately 60% of isolates were gram-positive cocci susceptible to cephalosporins.[11] Since then, first-generation cephalosporins have become the most commonly recommended prophylactic antibiotics in this setting. Their widespread use is supported by evidence showing lower infection rates with cefazolin prophylaxis compared with penicillin- or streptomycin-based regimens.[7] This observation is consistent with several studies which supported the early administration of first-generation cephalosporins in patients with open fractures.[9,10]

Broader-spectrum beta-lactam regimens have also been explored. Piperacillin-tazobactam provides gram-positive, gram-negative, and anaerobic coverage and may simplify treatment by avoiding aminoglycoside-related toxicity.[11] However, evidence supporting its routine use in open fractures remains limited. A study found no statistically significant difference in infection rates at 30 days or 1 year between patients treated with cefazolin plus gentamicin and those treated with piperacillin-tazobactam alone.[17] Therefore, although piperacillin-tazobactam may be a reasonable alternative in selected patients, current evidence does not clearly demonstrate superiority over standard cefazolin-based prophylaxis.

Aztreonam has also been proposed as an alternative, particularly for patients at risk of nephrotoxicity. This monobactam is active against aerobic Gram-negative organisms, including Pseudomonas aeruginosa, but lacks coverage against Gram-positive and anaerobic organisms.[14] Because it is not nephrotoxic, aztreonam may be considered in patients at increased risk of kidney injury, especially when aminoglycosides are undesirable.[10] Nevertheless, its role in routine prophylaxis for Grade II open fractures remains insufficiently defined.

The evidence supporting amoxicillin/clavulanic acid in open fracture prophylaxis is similarly limited. A case report of a Gustilo Grade II open-dislocated trimalleolar fracture treated with amoxicillin/clavulanic acid before immediate reduction and internal fixation described an unsatisfactory clinical course, with subsequent wound infection despite low C-reactive protein levels and identification of Clostridium species.[14] As this evidence is limited to isolated reports, no firm recommendation can be made regarding its routine use in Grade II open fractures.

Cefuroxime has also shown inconsistent results. In one report, intravenous cefuroxime 750 mg, administered before debridement and continued three times daily, did not prevent infection in a Grade II open fracture of the radius and ulna, despite elevated inflammatory markers and isolation of rare multidrug-resistant tropical organisms.[13] Similarly, another case involving a bimalleolar fracture with Type II soft-tissue injury developed osteomyelitis despite cefuroxime 1.5 g administered parenterally three times daily for 5 days.[14] These findings suggest that cefuroxime may be less effective in certain contaminated wounds or in the presence of unusual or resistant pathogens.

There is also no clear evidence that multiple-dose regimens are superior to shorter perioperative prophylaxis in uncomplicated cases. Although some studies have suggested that three or four perioperative doses may be associated with lower long-term reoperation rates, routine continuation of prophylaxis beyond 48 hours is not recommended because prolonged antibiotic exposure may promote bacterial resistance and endospore formation.[6,18]

Lincosamides

Clindamycin is the most commonly recommended lincosamide for patients with penicillin allergy.[11] It acts by binding to the 50S ribosomal subunit and inhibiting bacterial protein synthesis.[19] Because it provides reliable coverage against Gram-positive organisms, clindamycin is widely accepted as an alternative prophylactic agent for Grade I and II open fractures.[11,20] A study demonstrated that clindamycin monotherapy achieved infection rates comparable to those of dual-agent therapy with cefamandole and gentamicin in Type II open fractures.[12] In another report, infection rates in clindamycin-treated fractures were 3.3% for Type I fractures and 1.8% for Type II fractures, compared with 20% and 3.8%, respectively, in the cloxacillin group.[20] These findings support the role of clindamycin as an effective alternative in patients who cannot receive beta-lactams.

Aminoglycosides

Aminoglycosides exert bactericidal activity by binding to the 30S ribosomal subunit, thereby causing misreading of bacterial mRNA and inhibiting protein synthesis.[20] These agents are active against many aerobic gram-negative organisms and were historically used in combination regimens for open fractures. However, their role has become increasingly controversial because of dose-dependent nephrotoxicity and irreversible ototoxicity.[6]

A study reported no significant difference in infection rates between cefazolin plus gentamicin and piperacillin-tazobactam monotherapy following open injury.[17] Similarly, in a study of 219 patients with Type II open fractures, once-daily gentamicin dosing was associated with a lower infection rate than divided dosing, although the difference did not reach statistical significance.[6] Overall, current evidence does not support routine coverage for all open fractures with gram-negative organisms.[12] Given the limited incremental benefit of aminoglycosides and their potential toxicity, their routine prophylactic use in Grade II open fractures appears difficult to justify.[11]

Fluoroquinolones

Fluoroquinolones act by inhibiting bacterial DNA gyrase and topoisomerases, thereby preventing DNA replication. Although they provide broad-spectrum coverage and are less nephrotoxic than aminoglycosides, concerns remain regarding their potential adverse effects on fracture healing.[21] In a clinical series of 171 open fractures, fluoroquinolone monotherapy was associated with a high infection rate in Type III fractures, although infection rates in Type I and II fractures were similar to those observed with cephalosporin-plus-aminoglycoside therapy.[17] Experimental evidence is more concerning: ciprofloxacin-treated rat femur fractures demonstrated less bridging bone, reduced torsional strength, and incomplete endochondral ossification compared with cefazolin-treated fractures.[19,22] For this reason, fluoroquinolones are contraindicated in pediatric open-fracture patients, whereas their role in adults remains uncertain and should be considered cautiously.[22]

Glycopeptides

Vancomycin is a glycopeptide antibiotic with activity against gram-positive organisms and is sometimes considered in penicillin-allergic patients.[7] It inhibits bacterial cell wall synthesis by interfering with peptidoglycan polymerization and exhibits time-dependent killing. However, current guidelines indicate that there is insufficient evidence to support vancomycin as a sole prophylactic agent in open fractures.[12] Accordingly, its use should generally be limited to selected circumstances, such as suspected resistant gram-positive infection or specific microbiological considerations.

Timing of antibiotic therapy

The timing of initial antibiotic administration is one of the most important factors in infection prevention. Delayed administration of the first antibiotic dose has been associated with a marked increase in the risk of infection.[23] In contrast, the timing of surgical debridement appears less critical, provided it is performed within 24 hours of injury, and no gross contamination is present.[23,24] These findings support the concept that prompt antibiotic administration should be prioritized immediately after diagnosis of an open fracture.

Duration of therapy

Another important issue is the optimal duration of antibiotic prophylaxis. Prolonged antibiotic administration beyond 24 hours has not been shown to provide additional benefit in reducing the risk of infection.[25] A series of 77 Type II tibial fractures found no difference in infection rates between 24 hours and 5 days of antibiotic treatment.[26] Likewise, a prospective cohortl involving 736 subjects demonstrated that 24 hours of antibiotic therapy was non-inferior to 5 days of treatment with a second-generation cephalosporin, regardless of fracture severity.[27] These findings were supported by systematic reviews published in 2015 and 2017, both of which found no benefit for extended antibiotic courses.[8,28]

Several guidelines therefore recommend discontinuing prophylactic antibiotics within 24 hours after wound closure in Grade I and II open fractures.[28,29] Several studies concluded that a short course of first-generation cephalosporins, combined with prompt wound management, reduces the risk of infection, whereas prolonged or repeated short courses provide no additional benefit.[30,31] Longer courses may instead contribute to antibiotic resistance and increase the risk of Clostridioides difficile-associated diarrhea.[2] Taken together, these findings support short-duration prophylaxis for Grade II open fractures in the absence of established infection.

Systemic versus local therapy

The role of local antibiotic therapy remains an evolving area of interest. At present, there are no robust aggregate human data supporting the use of topical antibiotic therapy without adjunct systemic prophylaxis.[32] Nevertheless, animal studies have produced promising results. In a rat model of open femoral fractures, topical vancomycin powder achieved high local tissue concentrations while maintaining low systemic exposure.[19] Fracture-site concentrations remained above typical intravenous levels for up to 48 hours and became undetectable by 96 hours.[19,33] Another experimental study suggested that topical vancomycin reduced surgical-site infection rates when applied within 24 hours of injury.[29]

Clinical studies have also suggested potential benefit. In pelvic and acetabular fractures, intraoperative topical vancomycin powder applied at wound closure was associated with fewer surgical-site infections and no increase in renal failure.[34,35] The infection risk was 14.5% in the control group and 4.2% in the treatment group.[34] Additional preliminary data have suggested reduced infection rates in other high-risk fractures, including calcaneal, pilon, and bicondylar tibial plateau fractures, when topical vancomycin was used at the time of definitive fixation and soft-tissue coverage.[8] Despite these encouraging findings, the indications, dosage, and optimal integration of local antibiotic therapy into standard prophylactic protocols remain poorly defined.[11] Therefore, topical vancomycin should currently be considered an adjunct to systemic antibiotic prophylaxis rather than a replacement for it.

Clinical implications

Overall, the available evidence supports early administration of a first-generation cephalosporin as the preferred prophylactic regimen for Grade II open fractures. Clindamycin remains the most appropriate alternative in patients with penicillin allergy. Routine use of aminoglycosides does not appear to be justified for most Grade II injuries because of limited evidence of benefit and the risk of toxicity. Similarly, prolonged prophylaxis beyond 24 hours is not supported by current evidence. Although local antibiotic strategies, particularly topical vancomycin, appear promising, further high-quality clinical studies are needed before they can be routinely recommended.

Discuss findings of your study with relevant reasoning along with proper citations/references.

CONCLUSION

This review showed that prophylactic antibiotics remain essential for preventing infection in Grade II open fractures when combined with prompt surgical debridement and appropriate wound management. First-generation cephalosporins, particularly intravenous cefazolin, remain the preferred first-line regimen, while clindamycin is an appropriate alternative for patients with penicillin allergy. Current evidence supports early antibiotic administration and short-course therapy, with no clear benefit from extending prophylaxis beyond 24 hours after definitive wound closure. Overall, the most appropriate prophylactic strategy for Grade II open fractures is early intravenous cefazolin for 24 hours, together with meticulous surgical management.

Declaration by Authors

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