Role of Systemic and Local Antibiotics in the Treatment of Open Fractures

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KEYWORDS

• Open fractures • Systemic antibiotics • Infection • Local antibiotics • PMMA • Chitosan sponge
• Calcium sulfate

KEY POINTS

- Systemic antibiotics have been shown to decrease infection rates after open fracture.
- Controversy continues to exist over the ideal systemic antibiotic prophylaxis, particularly for type III open fractures.
- Local antibiotic delivery, although not new, is an area of renewed interest.
- Local antibiotics allow delivery of high concentrations of antibiotic without systemic toxicity.
- Many modes of local antibiotic delivery currently exist.

INTRODUCTION

Open fractures can be problematic for the patient, orthopedic surgeon, and society in general. An open fracture occurs when communication exists between fracture or fracture hematoma and the outside environment. This communication potentially allows bacteria from the environment to colonize the fracture site. Colonization of the fracture site with pathogenic bacteria may result in infection, which is known to be one of the more common causes of fracture nonunion.[1] Infection and nonunion result in significant cost to the patient and society.[2,3]

Antibiotics work in many different ways to disrupt the life cycle of bacteria. Antibiotics can be administered systemically or locally to a fracture site. Both methods of administration have been used in attempts to reduce infection after open fracture. This article reviews the data supporting both systemic and local antibiotics.

SYSTEMIC ANTIBIOTICS

History, Incidence of Infection, and Infecting Organisms

Patzakis and colleagues[4] in 1974 were the first to demonstrate in a prospective randomized trial the efficacy of systemic antibiotics in decreasing infection rates after open fractures. Patients (310 open fractures) were randomized to 3 groups: no antibiotics, penicillin/streptomycin, or cephalothin. Patients receiving cephalothin had a lower incidence of infection (2.4%) than those receiving penicillin/streptomycin (9.8%) and patients not receiving antibiotics at all (13.9%).

Gustilo and Anderson[5] in 1976 reported antibiotic sensitivity data as part of analysis of more than 1000 open fractures; 50.7% of open fractures were colonized on admission and an additional 20.0% of patients had a positive culture at wound closure. Sensitivity analysis of cultured organisms led to the investigators' recommendation that a first-generation cephalosporin was the antibiotic of choice for open fractures. All *Staphylococcus* species, both coagulation

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positive and negative, were sensitive to cephalothin. Fifty-seven of 143 isolates reported were gram negative. Of these 57 gram-negative isolates, 23 were either *Pseudomonas* or *Enterobacter* and were not sensitive to cephalothin. Interestingly, the investigators cautioned about the nephrotoxic effects of adding aminoglycosides and advocated doing so only when "the anticipated beneficial effects are deemed essential after careful weighing of the potential benefits and dangers."[5]

Gustilo and colleagues[6] in 1984 further classified type III open fractures (Table 1).[6] Subclassifications of type III open fractures were found to be predictive of infection and need for amputation. The infection rate was found to be 4%, 52%, and 42% for type IIIA, type IIIB (Fig. 1), and type IIIC open fractures, respectively. Of the infections reported after type III open fractures, 77% (24/31) were caused by gram-negative bacteria. Ten of 24 gram-negative infections were secondary to *Enterobacter* or *Pseudomonas* species, 2 organisms previously shown not to be sensitive to cephalothin.[5] The investigators did recommend a change in antibiotic prophylaxis for type III open fractures. They recommended adding an aminoglycoside to a first-generation cephalosporin or using a third-generation cephalosporin with the goal of "avoiding potential aminoglycoside toxicity."[6]

Table 1
Gustilo and Anderson[5] classification of open fractures

Type	Description
I	Wound <1 cm; clean; simple fracture pattern; minimal comminution; minimal soft tissue injury.
II	Wound 1–10 cm; simple fracture pattern; moderate soft tissue injury.
IIIA	Extensive soft tissue injury but with adequate soft tissue coverage over bone; high-energy, comminuted, or segmental injuries.
IIIB	Extensive soft tissue injury with soft tissue loss and periosteal stripping; inadequate soft tissue coverage over bone.
IIIC	Open fracture with associated vascular injury requiring repair.

From Gustilo RB, Anderson JT. Prevention of infection in the treatment of one thousand and twenty-five open fractures of long bones: retrospective and prospective analyses. J Bone Joint Surg Am 1976;58A:453–8; and Gustilo RB, Mendoza RM, Williams DN. Problems in the management of type III (severe) open fractures: a new classification of type III open fractures. J Trauma 1984;24:742–6.

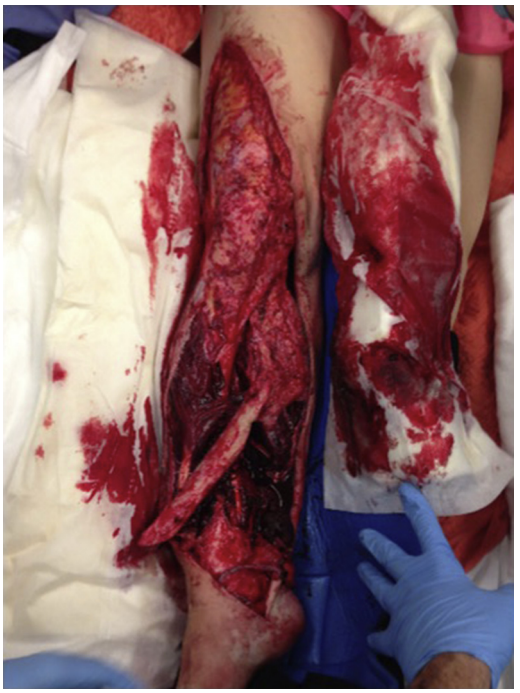

Fig. 1. Clinical photo of patient with type IIIB open tibia fracture.

Templeman and colleagues[7] retrospectively evaluated infection rate based on the Gustilo and Anderson[5] classification; 11.3% of open tibia shaft fractures were complicated by infection with infection rates of 0%, 3%, and 21% for type I, II, and III open tibial shaft fractures, respectively. Patzakis and Wilkins[8] reported similar infection rates based on the Gustilo and Anderson[5] classification. They reported infections rates of 1.4%, 3.6%, and 22.7% for type I, II, and III open fractures, respectively, with an overall incidence of 10.5%. They also reported that the rate of infection is dependent on anatomic site, with the tibia having a 10% infection rate versus a 5.3% infection rate for other sites combined.

In a more contemporary study, Chen and colleagues[9] reported the most common infecting organisms after open fracture. Overall, the investigators reported a 10% infection rate after 202 open fractures. *Staphylococcus* was the most common organism cultured (55% of infections), with coagulase-negative *Staphylococcus* and methicillin-resistant *Staphylococcus aureus* (MRSA) representing 30% and 25% of infections, respectively. Interestingly, 67% (4/6) of coagulase-negative *Staphylococcus* infections