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POLICY STATEMENT

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Prehospital Antibiotic Administration for Suspected Open Fractures

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Joint Position Statement of the American College of Surgeons Committee on Trauma (COT), Orthopaedic Trauma Association (OTA), American College of Emergency Physicians (ACEP), National Association of EMS Physicians (NAEMSP), and the National Association of Emergency Medical Technicians (NAEMT)

Introduction

Open fractures involve any broken bone with an associated open wound that allows for communication with the external environment. These injuries are often the result of high-energy trauma (eg, motor vehicle crashes, falls from height, pedestrians struck, etc.) but can also be seen in lower-energy environments, such as falls from standing in the elderly population. They can be suspected in the field when a fractured bone is visible, a large wound over an obvious deformity, or with a partial or complete amputation. Gustilo and Anderson originally described open fractures based on the size of the open wound and the degree of soft tissue disruption in tibia fractures.[1] Type one fractures have a wound one centimeter or less, the wound in type two fractures is slightly larger but less than ten centimeters, and type III wounds are ten centimeters or greater and sometimes necessitate vascular repair or flap coverage.[1]

One of the primary concerns associated with these injuries is the development of a fracture-related infection (FRI).[2] Open fractures are at high risk for FRI given their direct communication with the environment, the associated soft tissue injuries, and contamination at the time of injury.[1] Additionally, FRI are often the cause of significant orthopedic complications, such as osteomyelitis (infection of the bone) and non-unions, both of which represent a substantial cost to both society and the patient. To minimize the risk of developing an FRI and subsequent morbidity, prophylactic antibiotics should be administered to patients with open fractures as soon as possible.[1,3,4] Significant research has been performed to determine the appropriate pharmacologic interventions for these injuries, as well as to delineate the importance of timing associated with antibiotic prophylaxis.[1,4,5] The need for rapid administration of antibiotics in these injuries makes early administration a key intervention that can be provided in the prehospital setting to improve patient outcomes. The American

College of Surgeons Committee on Trauma (COT), the Orthopedic Trauma Association (OTA), the American College of Emergency Medicine (ACEP), the National Association of EMS Physicians (NAEMSP), and the National Association of Emergency Medical Technicians (NAEMT) drafted the recommendations below after review of the evidence and expert consensus.

Importance of Time to Antibiotics

Multiple studies have examined the role of the timing of delivery of antibiotics to infectious outcomes associated with open fractures. A study by Lack et al. demonstrated a significant increase in infectious complications when antibiotic prophylaxis was delayed 66+ minutes past the time of injury.[6] Several clinical studies have demonstrated that quality improvement processes can decrease the time of hospital delivery of antibiotics to closer to this 66-minute threshold.[7-10] While these studies are retrospective in nature and thus have associated limitations, they represent the best data available on the impact of early antibiotic prophylaxis on open fractures. Additionally, the 2006 Surgical Infection Society and the Eastern Association for the Surgery of Trauma (EAST) Practice Management Guidelines recommend that antibiotic prophylaxis be delivered to open fracture patients as soon as possible, further reiterating the importance of timeliness to prevent infectious complications associated with open fractures.[11,12] Even with this knowledge, timely administration of antibiotics for open fractures remains challenging, and many centers report delays in antibiotic administration.[13,14] One study performed in 2019 queried the National Trauma Data Bank and demonstrated that in all trauma centers, only 47.6% of patients received antibiotic administration within 1 hour of arrival.[13]

Prolonged extrication and transportation times can delay the administration of antibiotics since they are typically given upon reaching the hospital. This is key for patients injured in rural settings, where multiple studies have demonstrated that EMS response and transport times are often much longer than their urban counterparts.[15,16] Given the greater geographical distances covered in the rural areas, it is likely that there is a corresponding increase in time to antibiotics administration for these patients due to prolonged travel times. In many cases, these transport times exceed an hour from the time of injury, already putting patients outside of the ideal administration window.[6,16]

Role of EMS

Several studies have evaluated the efficacy and safety of antibiotic administration to patients with open fractures by EMS providers.[17-20] These studies demonstrate a low inappropriate administration rate and a strong safety profile for antibiotic administration.[17-19] Additionally, these studies also show a decreased time to antibiotic administration than if they waited until arriving at the emergency department.[17,18] In the study by Hendrickson et al., they were able to decrease time to administration by 20 minutes (from 180 minutes to 160 minutes on average), but likely because this was still substantially longer than the previously described window of opportunity, they could not find a decrease in complications. Collopy et al. reported zero allergic reactions when a cephalosporin was administered prior to arrival at a hospital in their cohort of 278 patients.[19] In this manner, EMS can play a critical role in the care of open fracture patients and reduce the risks of negative sequelae associated with open fractures.[19] EMS providers can help improve patient outcomes and decrease the societal burden of infections in open fracture patients.[21]

While the administration of prehospital antibiotics does represent an expansion of EMS responsibilities, there have been several other treatment expansions in the prehospital setting, such as the administration of tranexamic acid and the application of pelvic binders.[22-25] The administration of antibiotics, specifically cefazolin, is inexpensive, technically simple, and does not require special storage. The greatest technical challenge for this is the establishment of IV access. These examples support the feasibility of expanding the prehospital phase of care, which can be done in a safe and productive manner.

Antibiotic administration in the field should never be done prior to management of immediate life threats of the patient and should not delay transport. Prehospital antibiotic administration in most systems would be best done during the transport phase after stabilization of the patient.

History of Antibiotics in Open Fracture Prophylaxis
Historically, it was thought that time to operative debridement was the key predictor of outcomes in open fractures; however, multiple studies have subsequently demonstrated that this is not the driving factor in reducing infectious complications.[26,27] More importantly, the use of antibiotics in open fractures has been common orthopedic practice for over four decades and has been shown to decrease the rate of FRI.[1,4] These studies demonstrate that antibiotic prophylaxis is one of the most important interventions in preventing infectious complications associated with open fractures.

Antibiotic Selection
The use of a cephalosporin in prophylactic treatment of open fractures is well supported in the literature and by several surgical societies. In 2006, the Surgical Infection Society published guidelines supporting the use of a short course of a first-generation cephalosporin as prophylactic treatment for open fractures.[11] This recommendation was reiterated in the 2022 update to the Surgical Infection Society guidelines.[28] Both the 2006 and 2022 guidelines stated that further data is needed to recommend for or against the use of gram-negative prophylaxis.[11,28] The EAST Practice Management Guidelines similarly recommend gram-positive coverage of all open fractures.[12] In various unique clinical scenarios, different antibiotic recommendations have been made. In barnyard injuries, adding Penicillin G has been recommended as further prophylaxis against clostridium species.[12] In fractures occurring in bodies of water or in combat theatres, fluoroquinolones have been recommended as adjunct therapy.[29]

In much of the orthopedic literature, certain antibiotics are recommended to cover gram-negative bacteria in high-grade open fractures. However, strong evidence to support this prophylaxis is lacking.[3,5] The EAST Practice Management Guidelines do endorse (at a lower evidence-based recommendation) the use of aminoglycosides for grade II and grade III open fractures, though evidence for this is limited.[12] However, many of the antibiotics recommended for gram-negative coverage can have serious systemic side effects (eg, nephrotoxicity and ototoxicity), and thus, the risk-benefit ratio should be considered.[30] While the antibiotic recommendations for severe open fractures are somewhat debatable, ***the use of a cephalosporin still remains a mainstay of prophylactic treatment.***[13]

The choice of a prophylactic antibiotic (cefazolin, 2g) in the prehospital setting is designed to be safe and rapid and cover potential gram-positive bacteria in suspected open fractures. Additionally, a one-time dose of cefazolin for suspected open fractures would be in line with most, if not all, antimicrobial stewardship guidelines. Given the limitation of requiring IV access in the field, ideally, there would be an IM or oral option. However, currently, there is no data to support this alternative. Antibiotic decisions to expand coverage can be made based on hospital protocols once the patient arrives in the emergency department.

Cefazolin Safety and Cross-Reactivity
Cefazolin allergy is rare, and the few reported side effects are generally mild. Anaphylactic reactions, while serious events are fortunately very uncommon with cefazolin. This safety profile has led to it becoming one of the most widely used antibiotics in orthopedic procedural settings.[31] In most centers, the first dose of cephalosporin is given as 2 grams, even in patients with renal impairment. Historically, the rate of penicillin allergy having cross-reactivity with a cephalosporin was reported to be as high as 10%. However, these claims have not been validated and have, in fact, been refuted by newer studies.[32,33] Additionally, it was also discovered that in many of these initial reports, there was a high rate of contamination of the cephalosporins with penicillin; this likely caused the rate of reported cross-reactivity to be falsely high.[31] Newer level one data, in adult and pediatric populations, has demonstrated that this rate of cross-reactivity of cefazolin with

penicillin is lower than 1%, and administering cefazolin to penicillin- allergic patients is very safe.[34,35] We therefore recommend that in the obtunded patient where allergies are unknown, cephalosporins are safe with appropriate monitoring.

Pediatric Treatment

While there has been some debate regarding the need for surgical debridement of pediatric open fractures, there is a consensus that antibiotic prophylaxis should be provided to these patients.[36,37] While these recommendations are based largely on adult studies, the recommendation for rapid gram-positive coverage for pediatric populations is still consistent across the orthopedic literature.[36,37]

COT/OTA/ACEP/NAEMSP/NAEMT Recommendations

The above organizations support the following recommendations for patients with suspected open fractures for EMS clinicians whose scope of practice allows for the administration of antibiotics and whose agencies have the resources to administer prehospital antibiotics.

1. In a responsive patient with no history of penicillin allergy, the administration by EMS of a 1st generation cephalosporin should be performed after the management of life threats. This intervention should not delay transport.
2. In an obtunded patient with a protected airway, the administration by EMS of a 1st generation cephalosporin should be performed after the management of life-threats. This intervention should not delay transport.
3. In a responsive patient with a documented penicillin allergy, the administration by EMS of a 1st generation cephalosporin should be performed with close monitoring after the management of life-threats. This intervention should not delay transport.

Conclusion

Open fractures represent a common injury with the potential for serious infectious-related sequelae along with significant patient and societal costs. Early antibiotic prophylaxis plays a critical role in the prevention of infection. The early administration of a 1st generation cephalosporin has been shown to decrease the rate of infections in open fractures. Additionally, this medicine has an excellent safety profile in patients with and without a penicillin allergy. Through early antibiotic administration in the prehospital setting, EMS providers can play a crucial role in the treatment of these patients in preventing serious long-term infectious sequelae. As with all prehospital interventions, this implementation should be part of the system approach, and coordination with the receiving facility is essential. We recommend early, pre-hospital administration of prophylactic antibiotics for open fractures while not delaying transport to the receiving hospital or superseding any normal life or limb-saving care provided in the field.

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