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Antibiotic Prophylaxis in Adults With Open Tibial Fractures: What Is the Evidence for Duration of Administration? A Systematic Review

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ABSTRACT

Open tibial fractures are common injuries after high-energy trauma such as road traffic accidents. Infection is one of the main complications of open fractures. Broad-spectrum antibiotics have been used for prophylaxis and treatment of infection in these fractures. The duration of antibiotic prophylaxis remains controversial, especially for the different types and grades of open fractures. No complete review, to date, has been performed of published studies to demonstrate the wide variety of duration of antibiotic use in practice to prevent infection, especially in open tibial fractures. The purpose of the present study was to review the evidence in the current data regarding the duration of prophylactic antibiotic administration in open tibial fractures and to identify the optimum duration of administration of antibiotics to minimize the risk of infection in these fractures. We reviewed and evaluated all published clinical trials claiming or cited elsewhere as being authoritative regarding the duration of prophylactic antibiotic use in open tibial fracture management. A large number of studies reported antibiotic prophylaxis in open fractures; however, only 8 met the inclusion criteria set out for our review. Only 1 randomized, double-blind, prospective study examined the duration of prophylactic antibiotic administration in open tibial fractures. That study suggested a short course of antibiotics is as effective as a long course in infection prophylaxis. The results of the present review highlight the need for a rigorous randomized, double-blind, multicenter trial to establish an agreed protocol for the optimal length of prophylactic antibiotic administration in open tibial fractures.

Open fractures are fractures that communicate with the outside environment through a breach in the skin and the underlying soft tissues. This usually results from high-energy trauma, commonly a road traffic accident. These fractures are severe injuries with the potential for serious complications such as infection and nonunion and, therefore, constitute a challenging problem for the treating orthopedic surgeon.

The tibia is the most commonly fractured long bone, and many of these fractures are open (1). The goals of treatment are to prevent infection at the fracture site, achieve fracture healing, and restore function to the extremity. By definition, open fractures are contaminated, and contamination has usually occurred at the time of injury. Bacterial contamination has been shown to occur in ≤70% of wounds in open fractures (2–4).

The Gustilo and Anderson classification is the most widely used classification for open fractures (2). The incidence of wound infection correlates directly with the grade of fracture (2,5–11). The rate of infection in grade I fractures is 0% to 2%, in grade II fractures is from 2% to 7%, in grade IIIA is 7%, in grade IIIB is from 10% to 50% and in grade IIIC is from 25% to 50%.

The use of antibiotics has been a standard management to either prevent or treat infection in open tibial fractures, but the optimal duration of antibiotic therapy is still not clear. We aimed to review the published data to identify the optimum duration of antibiotic prophylaxis in open fractures of the tibia.

Materials and Methods

Eligibility

The Table lists the inclusion and exclusion criteria used for assessing eligibility.

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Table
Inclusion and exclusion criteria used to assess eligibility

Criteria	Description
Inclusion	
Target population	Adult patients with open fractures of the tibia
Intervention	Hospital admission, operative and/or nonoperative management of fractures and administration of prophylactic antibiotics
Comparison	Short- versus long-term prophylactic antibiotics
Study design	Published clinical trials, randomized or quasi-randomized
Exclusion	
Eligibility criteria	Studies that did not meet the criteria
Language	Studies reported in a language other than English
Study size	Small studies of ≤20 patients

Study Identification

Studies were identified from a computerized search of MEDLINE (1950 to date), EMBASE (1974 to date), and COCHRANE database and by a review of the references cited in the studies thus recovered. The MEDLINE and EMBASE search was done on OvidSP (available at: http://ovidsp.tx.ovid.com/spa/ovidweb.cgi). The search terms were open fractures, open tibial fractures, and antibiotics. These terms were searched for in isolation and combined (MeSH search in PubMed and OvidSP).

Data Extraction

We extracted all the relevant information regarding the population, intervention, antibiotic administration, rate of infection, both deep and superficial, and fracture healing from each report.

Outcome Measures

The primary outcome measure was infection in the wound of an open fracture, either deep or superficial. The secondary outcome measure was bony union.

Results

Despite the enormous body of data on the subject of antibiotic use in open fractures, very few well-designed studies were identified. The computerized database search resulted in 14 citations (1,4,7,8,12–21). Ten additional studies were identified by a manual search through the references of the recovered studies (2,22–30). A total of 24 reports was reviewed and examined against the eligibility criteria. Eight studies met the inclusion criteria and were included in the present review (2,7,8,14,22–24,29). The remaining 15 studies were excluded from our review, because they did not meet the inclusion criteria.

Studies Excluded From the Present Study

Of the 15 excluded studies, 1 had reviewed a small number of patients (<20) (1). In a study by Patzakis et al (4) in 1974, 310 patients were included in a review of the infection rate as a specific function of antibiotic use in open fractures within 2 years. Their prospective, randomized placebo-controlled study examined, for the first time, the role of antibiotics in the management of open fractures but did not specifically review the effects of the duration of antibiotic administration on the infection rate or fracture healing.

Two studies described evidence-based guidelines for the use of antibiotics as prophylaxis in open fractures (12,16). Another study compared the use of soap to antibiotic solution for irrigation in open fractures of the lower limb (13). The patients were randomly allocated into 2 groups to receive either an antibiotic solution or a nonsterile soap solution for irrigation of the open wound. The duration of antibiotic administration was different in the 2 groups. Nevertheless, the investigators believed that the infection rate did not depend on the duration of antibiotic administration; therefore, in 1 group, antibiotics were applied locally as well as systemically (13).

Another report compared intravenous and oral antibiotic therapy in fractures caused only by gunshots. That prospective randomized trial was excluded, because it tested the mode of application of antibiotics, rather than the duration, which was identical in the 2 groups (17). In addition, 4 studies were not clinical trials and described either a review or concepts for the use of antibiotics in open fractures (15,18,19,27). Another report described different methods of management of open fractures in adult patients used by academic orthopedic residency programs in the United States and was excluded, because no direct study was performed of the effects of antibiotic use or the length of administration (20).

Clancey and Hansen (21) in 1978 retrospectively reviewed 102 patients with open tibial fractures. The grade of fracture and soft tissue injury determined the management (21). A standard protocol was used for all the patients and included surgical debridement of wounds, 3 days of intravenous antibiotics, and delayed primary closure. If infection developed, the antibiotics were continued until the systemic and local inflammatory reactions had resolved. The infection rate was 15%, and the nonunion rate was 13%. No comparisons of antibiotic use or duration of administration were performed. The investigators concluded that the severity of the fracture and soft tissue injury is the most important prognostic indicator of infection and fracture healing.

In 1975, Patzakis (25) published a prospective, randomized study that reviewed the use of antibiotics in the management of open fractures from 1970 to 1972. Excluding those injuries caused by missiles, 501 patients with open fractures were blindly randomized into 3 groups to receive no antibiotics, penicillin and streptomycin, or cephalexin. Group 1 was discontinued during the second year because of the high infection rate (13.9%). In groups 2 and 3, intravenous antibiotics were given for 10 days during the first year; however, during the second year, the regimen was changed to intravenous antibiotics for 5 days, followed by oral antibiotics for another 5 days. All wounds were closed primarily. The infection rate in group 2 was 9.7% during the first year and 10.1% during the second year. In group 3, the infection rate increased from 2.3% during the first year to 5.4% in the second year. The investigator claimed that the increase in infection rate in group 3 resulted from a greater incidence of severe degloving injuries and the development of antibiotic-resistant organisms during the second year rather than the change in the duration of systemic antibiotics. This concept was not included in the investigator's conclusion that cephalexin should not be used in degloving injuries (25). In summary, Patzakis (25) concluded that cephalexin is effective. However, because the randomization method was not clear, the fractures were not graded according to severity, and no records were provided on the fracture union rate or fracture site, the review was not considered suitable despite being randomized and prospective.

Velmahos et al (28) in 2002 reviewed 250 trauma victims admitted with critical injuries but not necessarily open fractures of the tibia. They examined the hypothesis of a long course of >1 antibiotic versus a short course of 1 antibiotic (28). Their study was prospective but nonrandomized and included patients without open tibia fractures. The study showed a statistically significant high rate of resistant infection among the patients who had received >1 antibiotic for a longer period, but it was still excluded from our review, because it did not fit the inclusion criteria.

The final study excluded from the present review was published by Craig et al (26) in 2014. They performed a systematic review and meta-analysis of published data pertaining to the additional benefit of providing local prophylactic antibiotics alongside systemic antibiotics on infection rates in open tibial fractures, specifically those treated by intramedullary nailing (26). They performed 2 separate data searches and applied the findings to a meta-analysis. The first search found 14 reports and included studies reporting on infection rates in patients