

The Use of Antibiotics in Infected Nonunion: A Systematic Review

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ADMINISTRATIVE INFORMATION**Support** - Hospital Beneficente Unimar.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202670112

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 July 2026 and was last updated on 29 July 2026.

INTRODUCTION

Review question / Objective The review was guided by the following focused research question: which antibiotic therapy approach has the best effect in patients undergoing follow-up for infected nonunion?

Condition being studied Nonunion represents a complication of fractures characterized by failure of bone healing and may have a multifactorial origin, being associated with different conditions that interfere with the repair process. Among the factors related to the absence of consolidation, mechanical, biological, and infectious aspects stand out, which may act independently or in combination. When the failure of bone healing is related to the presence of infection, treatment becomes particularly complex, as the infectious process may compromise bone tissue and the local conditions required for consolidation, requiring an individualized and multidisciplinary therapeutic approach.**

Infected nonunions may present different microbiological patterns, including infections caused by a single microorganism or by multiple agents simultaneously. The occurrence of polymicrobial infections highlights the complexity of these cases and reinforces the importance of microbiological investigation for the characterization of the involved pathogens. Identification of the microorganisms present may assist in defining antimicrobial therapy and contribute to treatment planning, especially in situations requiring surgical management combined with antibiotic use.**

In addition to clinically evident infections, the presence of occult infectious processes also represents a relevant aspect in the context of nonunions. Studies conducted in patients undergoing revision surgery have demonstrated that previously unrecognized infections may be identified through microbiological investigation during the procedure, even in the absence of clinical signs suggestive of infection. Therefore, the collection and analysis of microbiological samples during revision surgeries may contribute to the

detection of infections that would otherwise remain undiagnosed and may influence the therapeutic management of these patients.**

The treatment of infected nonunions involves different strategies aimed at controlling the infectious process, removing compromised tissues, restoring stability of the affected segment, and achieving bone union. The therapeutic approach may include surgical procedures associated with debridement, adequate stabilization of the nonunion site, and the use of antimicrobial agents. The choice of strategy should consider the characteristics of the infection, the extent of bone and surrounding soft tissue involvement, the location of the nonunion, and the patient's clinical condition.**

Reconstruction of the bone segment constitutes another fundamental component in the treatment of these patients, particularly in cases involving bone loss or extensive structural alterations. Different stabilization and reconstruction methods may be employed according to the characteristics of each case. Among these alternatives, the Ilizarov method has been applied in the treatment of infected tibial nonunions and may be associated with local wound care strategies. Likewise, in specific situations involving bone compromise, reconstruction techniques using vascularized grafts and autologous bone grafts may be employed to restore bone structure and promote consolidation.

Alongside strategies aimed at treating established infections, measures focused on preventing and controlling infections related to orthopedic procedures have also been investigated. In this context, the use of implants with antimicrobial properties, such as iodine-supported devices, represents an alternative studied particularly in patients considered at higher risk for surgical site infection. These strategies may contribute both to infection prevention and to the treatment of selected patients, constituting a complementary approach within the management of complex cases.**

Given the complexity of infected nonunions, treatment requires the integration of different strategies aimed at infection control and restoration of bone healing. The management of these patients may involve microbiological investigation, surgical treatment, adequate stabilization of the nonunion site, bone reconstruction, and antimicrobial therapy. In this context, antibiotic therapy represents one of the fundamental components of treatment and may be

administered through different routes and strategies according to the clinical and microbiological characteristics of each case. Therefore, the aim of this study is to conduct a systematic review.

METHODS

Search strategy For this review, the PUBMED, COCHRANE, and EMBASE databases were consulted. The guiding principles were based on the PRISMA model (Preferred Reporting Items for Systematic Reviews and Meta-Analyses).

Randomized controlled clinical trials, whether placebo-controlled or not and whether double-blinded or not, retrospective case-control studies, and prospective studies published within the last 10 years were included. The following combination of terms was used: Infected pseudoarthrosis AND fracture AND antibiotic AND treatment.

Participant or population Patients with infected nonunion under follow-up.

Intervention Antibiotic therapy.

Comparator Treatment techniques for nonunion.

Study designs to be included The search included quantitative studies that evaluated the use of systemic and local antibiotics in patients undergoing follow-up for infected nonunion. All articles that combined the descriptors mentioned above were included, except experimental models, reviews, communication letters, case reports, and articles not published in English.

Eligibility criteria The search included quantitative studies that evaluated the use of systemic and local antibiotics in patients undergoing follow-up for infected nonunion. All articles that combined the descriptors mentioned above were included, except experimental models, reviews, communication letters, case reports, and articles not published in English.

Information sources Data extraction, based on the inclusion and exclusion criteria, was independently performed by two reviewers, with the opinion of a third reviewer being consulted in cases of disagreement. The data extracted from eligible articles were analyzed according to the PICO framework (Population, Intervention, Comparison, and Outcomes) and included characteristics of the evaluated population, intervention performed, group comparisons, and

assessed outcomes, as well as publication date, authorship, study design, and sample size. The risk of bias assessment of the clinical trials included in the systematic review was performed according to the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions.

Main outcome(s) After applying the eligibility criteria, six studies were included that investigated different approaches for the treatment of infected nonunion, including strategies involving systemic antibiotic therapy, antimicrobial therapies associated with implants, and complementary reconstructive procedures. Overall, the studies demonstrated that therapeutic success depends on the combination of adequate surgical debridement, mechanical stabilization of the fracture, and antibiotic therapy guided by microbiological results.

In general, the evidence showed high rates of infection control and bone union when treatment was conducted through a multidisciplinary approach. In the included clinical studies, the success rate ranged from approximately 80% to excellent bone outcomes in more than 70% of patients, accompanied by significant functional improvement and a low incidence of infectious recurrence. However, factors such as infection with methicillin-resistant *Staphylococcus aureus* (MRSA), elevated body mass index, and changes in microbiological profiles throughout treatment were associated with a higher risk of therapeutic failure, reinforcing the need for continuous clinical and microbiological monitoring.

Microbiological analysis demonstrated a predominance of *Staphylococcus* species, particularly *Staphylococcus aureus*, as well as the occurrence of polymicrobial infections and changes in etiological agents during revision surgeries. These findings support the importance of obtaining serial intraoperative cultures to optimize antibiotic therapy and maintain infection control throughout treatment.

Additional outcome(s) After the application of the eligibility criteria, six studies were included that investigated different approaches for the treatment of infected nonunion, including systemic antibiotic therapy, antimicrobial strategies associated with implants, and complementary reconstructive procedures. Overall, the studies demonstrated that therapeutic success depends on the combination of adequate surgical debridement, mechanical stabilization of the fracture, and antibiotic therapy guided by microbiological findings.

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Microbiological analyses demonstrated a predominance of *Staphylococcus* species, particularly *Staphylococcus aureus*, as well as the occurrence of polymicrobial infections and changes in etiological agents during revision surgeries. These findings reinforce the importance of obtaining serial intraoperative cultures to guide antibiotic therapy optimization and ensure infection control throughout treatment.

Quality assessment / Risk of bias analysis The risk of bias assessment of the clinical trials included in the systematic review was performed according to the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions.

Strategy of data synthesis After the application of the eligibility criteria, six studies were included that investigated different approaches for the treatment of infected nonunion, including strategies involving systemic antibiotic therapy, antimicrobial therapies associated with implants, and complementary reconstructive procedures. Overall, the studies demonstrated that therapeutic success depends on the combination of adequate surgical debridement, mechanical stabilization of the fracture, and antibiotic therapy guided by microbiological results.

Subgroup analysis After the application of the eligibility criteria, six studies were included that investigated different approaches for the treatment of infected nonunion, including strategies involving systemic antibiotic therapy, antimicrobial therapies associated with implants, and complementary reconstructive procedures. Overall, the studies demonstrated that therapeutic success depends on the combination of adequate surgical debridement, mechanical stabilization of the fracture, and antibiotic therapy guided by microbiological results.

Sensitivity analysis After the application of the eligibility criteria, six studies were included that investigated different approaches for the treatment of infected nonunion, including strategies involving systemic antibiotic therapy, antimicrobial therapies associated with implants, and complementary reconstructive procedures. Overall, the studies demonstrated that therapeutic success depends on the combination of adequate surgical debridement, mechanical stabilization of the fracture, and antibiotic therapy guided by microbiological results.

Country(ies) involved United States.

Keywords Pseudoarthrosis; infected tibial nonunion; infected nonunion; lizarov technique; post traumatic osteomyelitis; tibial nonunion.

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