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Editorial

Antibiotic prophylaxis in orthopaedic surgery: Clinical practice guidelines or individualized prophylaxis?

Profilaxis antibiótica en cirugía ortopédica: ¿guías de práctica clínica o profilaxis individualizada?

Dolors Rodríguez-Pardo[a,b]

[a] Infectious Diseases Department, Hospital Universitari Vall d'Hebron, Universitat Autònoma de Barcelona, Barcelona, Spain
[b] Spanish Network for Research in Infectious Diseases (REIPI RD16/0016/0003), Instituto de Salud Carlos III, Madrid, Spain

Prosthetic joint infection (PJI) is one of the most challenging complications after joint arthroplasty and is associated with substantial patient morbidity.[1] The rising incidence of this condition has led physicians to try to improve preventive measures, with the use of pre-operative antibiotics being one of the most effective steps.[2,3] Peri-operative antibiotic prophylaxis is a key measure in preventing surgical site infections (SSIs) following orthopaedic surgery, achieving a reduction of up to 81% in the relative risk of infection and 8% in the absolute risk.[2] Conversely, inappropriate antibiotic prophylaxis has been associated with acute post-operative infections.[2]

Traditionally, the most widely recommended antimicrobial prophylaxis in orthopaedic surgery, including total joint arthroplasty, has been cefazolin.[2] However, standard prophylaxis may be unsuitable for some subgroups of patients, such as chronic patients in long-term institutional care, due to changes in their normal skin flora.[2] For this reason, some authors consider it more logical to provide prophylaxis with an agent active against methicillin-resistant *Staphylococcus aureus* (MRSA) for patients at risk or known to be colonized with this pathogen, as recommended in clinical practice guidelines for antimicrobial prophylaxis in arthroplasty surgery.[4] To achieve this goal, vancomycin is regarded as an adequate alternative to cefazolin for MRSA-colonized patients or patients in institutions with a high prevalence of MRSA infection.[2] Surprisingly, and contrary to what was expected, the use of glycopeptides as prophylaxis instead of a cephalosporin has not proven to be as effective because the benefit of achieving a decrease in Gram-positive infections, particularly infections due to MRSA, is diluted by a higher rate of Gram-negative infections.[5] In view of this situation, some authors choose to use a combination of vancomycin and a cephalosporin as prophylaxis in othopaedic surgery, even though a clear advantage in reducing SSIs other than MRSA infections has not been proven and exists only if vancomycin administration is started at least 45 min before incision.[6,7] This dual antibiotic prophylaxis has been proven to be effective if the MRSA infection rate is ≥0.25% and the rate of other infections with cephalosporin prophylaxis is ≥0.2%.[8] However, there are concerns about problems associated with the use of vancomycin, including adverse reactions, the need for slow infusion, nephrotoxicity, and bacterial resistance.[9] For these reasons, some authors have proposed that the antibiotic prophylaxis offered by cephalosporins should be extended by adding teicoplanin. Should it be?

Teicoplanin has a more favourable adverse effect profile than vancomycin. It is less nephrotoxic and can be administered in less time because red man syndrome is significantly less common than with vancomycin, an important logistic aspect for operating theatre activity.[10] Evidence of good outcomes obtained with the simultaneous prophylactic use of teicoplanin and cefuroxime among patients undergoing surgery for femoral neck fracture has already been published by Soriano et al.[11] and also recently among patients undergoing primary hip or knee arthroplasty by Tornero et al.[12] These authors compare the PJI rate after total joint arthroplasty in two consecutive periods of treatment with different antibiotic prophylaxes: cefuroxime *versus* cefuroxime plus teicoplanin, concluding that the addition of teicoplanin to cefuroxime was associated with a significant reduction in overall PJI rate due to a decrease in infections caused by Gram-positive bacteria. In addition, the authors go a step further in the discussion and, considering that dual prophylaxis was particularly effective against *S. aureus* in a population with BMI ≥ 30 kg/m^2, they suggest that the addition of teicoplanin could be restricted to *S. aureus* carriers.

In this issue, Barbero-Allende et al.[13] also address this question by carrying out a before-after intervention study to compare the results of combining teicoplanin and cefazolin before primary hip and knee arthroplasty surgery *versus* cefazolin alone in a previous control group. The authors confirmed that the addition of a single pre-operative 800-mg dose of teicoplanin to the usual 2-g cefazolin dose is associated with a 60% reduction in the PJI rate, due to a

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E-mail address: dolorodriguez@vhebron.net

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decrease in Gram-positive infections, particularly *Staphylococcus* spp., without affecting the number of infections caused by Gram-negative or increasing the number of adverse effects.

Although the results seem conclusive, I believe there are several limitations that advise against widespread use of this dual antibiotic prophylaxis. First, as explained by the authors, in both periods all patients underwent selective decontamination of *S. aureus* before surgery, based on a protocol in use at their hospital since 2011. Therefore, the reduction in the PJI rate observed may be due not only to the new prophylactic antibiotic schedule but also to broad use of this decolonization strategy. Second, the authors do not specify if antibiotic-loaded cement was used. Although not a common practice in primary arthroplasties, the use of antibiotic-loaded cement is becoming more frequent in orthopaedic surgery, and some experts classify it as a critical strategy for PJI prophylaxis in the intra-operative phase.[3,4] Third, the authors do not state the prevalence of MRSA infections among patients undergoing orthopaedic surgery at their hospital, although we could presume it was high, as they themselves implemented a selective decontamination protocol. This is crucial to consider when evaluating the study because their results may not be replicated at hospitals with a lower prevalence of MRSA. Last, certain patient subgroups (allergic to beta-lactams and glycopeptides, prosthetic replacement surgeries, and non-elective surgeries due to hip fracture) were excluded from the study and, therefore, the conclusions cannot be applied to these patients, even though these individuals are those at particularly high risk of PJI due to MRSA, in the case of institutionalized elderly patients with femoral neck fracture, or due to coagulase-negative staphylococci in replacement prostheses due to early loosening. Nonetheless, this study makes a compelling case for the combined use of teicoplanin and cefazolin before primary arthroplasty surgery in a context similar to that described by the authors.

Despite the results of the above studies, the issue of antibiotic prophylaxis in orthopaedic surgery continues to be controversial. Some authors support universal prophylaxis, whereas others advocate personalized, directed prophylaxis appropriate for the specific risk factors of each patient.

No supporting evidence has been published in favour of universal prophylaxis using systemic broad-spectrum antibiotics in primary arthroplasties, but some orthopaedic surgeons support it because candidates for joint replacement, depending on their demographics and comorbid illnesses, are at increased risk of carrying not only MRSA but also multidrug-resistant Gram-negative bacilli, including extended-spectrum beta-lactamase-producing Enterobacteriaceae (ESBL-E) or carbapenem-resistant Enterobacteriaceae and, therefore, the idea that antibiotic resistance threatens the efficacy of prophylaxis has become widespread.[14] The detractors of this strategy say that universal prophylaxis increases the risk of colonization by multidrug-resistant microorganisms, such as glycopeptide-resistant enterococci or carbapenem-resistant Enterobacteriaceae, which could compromise subsequent antibiotic treatments if these patients have an infection. Finally, the risk of complications associated with the use of a broader-spectrum antibiotic treatment (*i.e.*, *Clostridium difficile* infections) and the unwarranted costs cannot be ignored.

As an alternative to universal prophylaxis, strategies based on nasal and skin selective decolonization of known *S. aureus* carriers before surgery have been recommended and proven to be effective,[15] as Barbero-Allende et al. found at their institution.[13] However, targeted strategies based on either rapid molecular techniques or conventional cultures and used only in *S. aureus* carriers are complicated and costly in daily practice. Although patients undergoing elective surgery could be screened in outpatient settings, screening results would need to be communicated on time and appropriately utilized by administering the correct therapy, a process which has its own challenges. Consequently, some authors propose universal decolonization, irrespective of carrier status, which is more feasible and less costly.[16] Although the best alternative to implementation will probably depend on the particular conditions and the prevalence of *S. aureus* SSIs at each hospital, I consider it preferable to avoid routine universal decolonization whenever possible. Rather, as recommended by the latest published guidelines,[4] it might be advisable to perform selective decontamination of patients at high risk or known to be colonized by *S. aureus*, particularly in the case of MRSA.

It is important to note that all these decolonization strategies are designed to reduce Gram-positive infections but have no impact on Gram-negative infections which, particularly in the case of acute infections of hip prostheses, are common.[17] A published experience regarding the efficacy of an oral decolonization regimen for ESBL-E has shown that this effort temporarily suppressed ESBL-E carriage, but the effect had disappeared by day 7 post-treatment; therefore, its use has not become widespread.[18] Another subject of debate has been the possible impact of eradicating asymptomatic bacteriuria (ASB) to reduce early post-surgical infection before hip arthroplasty.[19] Under the hypothesis that the genitourinary tract is a possible source of infection by haematogenous seeding or by surgical wound contamination by continuity, ASB has been considered a possible risk factor for PJI. Unfortunately, current evidence does not support routine screening and antibiotic therapy for ASB prior to primary joint arthroplasty.[20] Thus, it seems that there is no well-defined strategy of prophylaxis directed against Gram-negative bacteria beyond extending systemic antibiotic coverage to bacteria for which a specific patient is known to be colonized. The possible role of bone cement loaded with antibiotic (usually vancomycin and gentamicin) in preventing post-arthroplasty infections caused by both Gram-positive and Gram-negative microorganisms remains to be defined, and current guidelines do not specifically address this issue.[4]

In summary, the balance of evidence provided by Barbero-Allende favours the combined use of teicoplanin and cefazolin before primary hip arthroplasty surgery. Although the authors used this strategy in all their patients during the study period, it is likely that maximum benefit is obtained only in some populations, particularly when MRSA prevalence is high. It will be necessary to define the patient subgroups that can benefit most from selective decolonization and dual prophylaxis as part of a set of measures to prevent PJIs. This would avoid the universal use of dual prophylaxis that could favour the appearance of antibiotic resistances or result in unnecessary increases in health care costs.

Keypoints

The balance of evidence provided by Barbero-Allende et al. favours the combined use of teicoplanin and cefazolin before primary hip and knee arthroplasty instead of standard prophylaxis with cefazolin. It will be necessary to define the utility and safety of routine universal dual antibiotic *versus* individualized prophylaxis in order to target patients who can benefit most from this strategy.

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Conflict of interest

The author certifies that there are no potential conflicts of interest regarding this study.

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