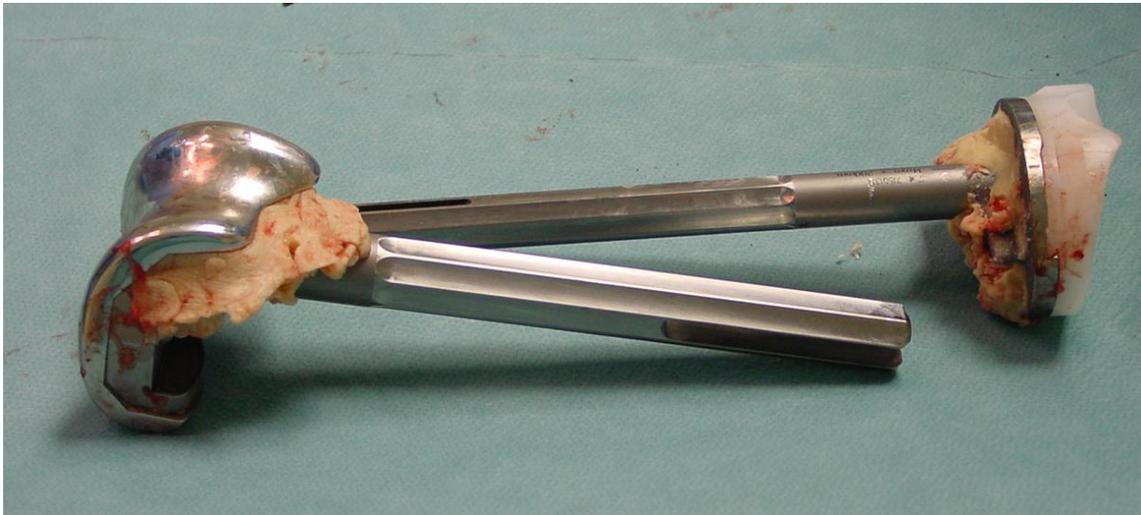


RECAMBIO PROTÉSICO EN UN TIEMPO

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2. “Preemptive treatment” including microorganisms that could be isolated during the second-step surgery (usually multi-drug resistant SNC) is recommended: vancomycin (or another glycopeptide or lipopeptide) during the first 5 days after re-implantation or until confirmation that the samples taken during the second-step surgery yield no microorganisms (C-III).



Attempted eradication with prosthesis removal and a 1-step exchange procedure

What is the antimicrobial treatment for patients undergoing a 1-step exchange procedure?

There is no consensus on the best antimicrobial treatment for patients undergoing a 1-step exchange procedure, since no randomized or comparative studies have been carried out in this setting. Our evaluation of the literature includes 28 studies (Table 4), but few specify the antibiotic therapy or report the use of various treatment regimens; therefore, no recommendations are forthcoming^{62-84,86,255,256}. In spite of this heterogeneity, the cure rates reported were higher than 80%, suggesting that the efficacy of this strategy depends mostly on the surgeon’s ability to perform an exhaustive debridement and removal of all foreign bodies and necrotic tissues.

In the majority of reports, antimicrobial treatment begins at the time of prosthesis removal. However, some authors start antibiotics some time (one week to several months) before the surgical procedure^{81,83,86}, in order to reduce the bacterial load and lower the risk of contamination of the new prosthesis. This seems reasonable, especially in cases with a highly inflammatory clinical presentation or those caused by pathogenic and virulent microorganisms such as *S. aureus* or GNB. In these cases, active antibiotics administered for 3 to 5 days prior to the procedure may be sufficient. It is very important to establish the microbiological diagnosis of the infection before-hand in order to be able to target the antibiotic therapy.

If there is no microbiological diagnosis at the time of the procedure, wide-spectrum antibiotic therapy should be initiated after the sampling and maintained until the results of these cultures are available. This empirical antimicrobial therapy should include a glycopeptide (vancomycin or teicoplanin), daptomycin, or linezolid, in combination with a β -lactam with anti-pseudomonal activity (ceftazidime or cefepime, or else meropenem in patients colonized or with previous infections by ESBL-producing *Enterobacteriaceae*, or in those presenting with risk factors for infection by these microorganisms). Once the etiology is known, a tailored specific antimicrobial treatment may be administered, following the same criteria as in the management of PJI with implant retention (Table 5).

Regardless of the decision regarding the time to start antibiotics, it is crucial to meet the fundamental principles of antimicrobial prophylaxis for the new prosthesis and to include a high antimicrobial concentration at the surgical site throughout the procedure²⁵⁷. Two studies have suggested that the administration of antibiotics prior to intraoperative sampling does not reduce the sensitivity of the cultures^{258,259}, but this is still a matter of controversy. The recommendation is to delay the infusion of antibiotics until the samples have been taken. This issue is less important if the etiological diagnosis

is already available and a targeted antimicrobial therapy has been decided in the days prior to the procedure.

As mentioned above, high antibiotic concentrations must be achieved at the surgical site throughout the procedure. Therefore, the antibiotic dose must be repeated if the operation lasts for more than twice the antibiotic's half-life or if the blood loss is greater than 1.5 L²⁶⁰.

RECOMMENDATIONS

1. Beginning an antimicrobial therapy 3 to 5 days prior to the 1-step exchange procedure is recommended if the etiological diagnosis has already been made, especially in infections caused by *S. aureus* or GNB (C-II).
2. Regardless of the decision regarding when to start antibiotics, an appropriate antimicrobial prophylaxis throughout the procedure must be guaranteed (A-I).
3. If no antimicrobial therapy has been initiated before the procedure, it should be delayed until the intraoperative sampling has been performed (C-III).

How long should antimicrobial treatment last?

A tailored antimicrobial therapy should be administered once the results of the cultures taken during surgery are available, the goal being to complete the treatment of peri-prosthetic osteomyelitis that may still persist after the prosthesis exchange. The authors with the most experience with 1-step exchange procedure²⁶¹ report a cure rate of 80% after following a protocol that only includes 10-14 days of intravenous antibiotics, usually without rifampin. These results may be due to the performance of a thorough debridement and the use of cement loaded with antibiotics during the procedure. In contrast, in the setting of staphylococcal infections the IDSA guidelines recommend intravenous antibiotics for a period of 2 to 6 weeks, then switching to a rifampin-based combination for a total of 3 months of antimicrobial therapy¹².

The overall success of this medical and surgical strategy depends not only on the surgeon's ability to thoroughly eradicate the lifeless tissues and the inert material, but also on the administration of an appropriate antimicrobial therapy that prevents the new prosthesis from being colonized. The total length of therapy (including intravenous and oral antibiotics) reported in the literature varies widely, from 10 days to 6 months (Table 4). These studies do not take into consideration the degree of inflammation that finally leads to the prosthesis exchange or the etiology of the infection. The 1-step exchange procedure strategy is halfway between DAIR (indicated in acute cases of infection, with a high degree of inflammation and usually caused by virulent microorganisms) and the 2-step exchange procedure (chronic or subacute PJI, rarely suppurative, and caused by less virulent microorganisms). Thus, it seems reasonable that the length of therapy in this scenario will vary according to these parameters.

RECOMMENDATION

1. A minimum of 7 days of intravenous antibiotics with activity against the microorganisms causing the infection is recommended (dosage summarized in Table 5), followed by oral antibiotics for a total of 4-8 weeks (B-II).

What is the role of the local antimicrobial treatment (cement)?

There are no comparative studies evaluating the efficacy of mixing antibiotics with cement during 1-step exchange procedure. In our review of the literature (Table 4), we found five studies reporting 237 patients who underwent prosthesis exchange with no local antibiotics, with a cure rate ranging between 83 and 100%, while there were 22 papers including 1,704 cases in which cement with antibiotics was used, with cure rates between 72-100%. The data reported in the literature support the practice of 1-step exchange procedure with non-cemented prosthesis, thus with no possibility of using local antibiotics. Still, in these cases bone allograft or calcium sulfate beads may be used as carriers of local antibiotics⁸². It is the surgeon who decides whether the prosthesis should be cemented or non-cemented. If a cemented prosthesis is selected, the usual antibiotics are gentamicin, tobramycin, and vancomycin. The accumulated experience suggests that these local antibiotics are safe, have minimal toxicity, and do not disrupt the cement's consistency in the long term.

RECOMMENDATION

1. If it has been decided to use a cemented prosthesis, a local antibiotic with activity against the microorganism causing the infection is recommended. If the etiology is unknown at the moment of the exchange procedure, the combination of vancomycin plus gentamicin is recommended (C-III).

What is the treatment for the 'positive intraoperative cultures' (PIOC) category of Tsukayama's classification?

The PIOC category described by Tsukayama (Table 2) includes patients submitted to a 1-step exchange procedure due to the loosening of a prosthesis which was assumed to be non-infectious, but in which the samples taken during surgery finally yielded microorganisms. Actually, these patients are very similar to those with a chronic PJI undergoing a 1-step exchange procedure; however, they have very subtle or non-existent symptoms, and so do not receive antimicrobials except for the standard surgical antibiotic prophylaxis.

The interpretation of these cultures and the management of this scenario are quite controversial, and reconsideration of the whole clinical picture and complementary data is needed: pre-surgical CRP and ESR, patient's age and condition, data on synovial fluid, histological information, and so on. In some cases these cultures are just read as contaminants, especially if there is one single positive culture²⁶², and in other cases the surgical debridement and irrigation are considered to be sufficient treatment. Nevertheless, some patients have later developed an infection of the new prosthesis, caused by the microorganisms isolated during the previous prosthesis exchange (PIOC)²⁶³.

In spite of the absence of contrasted evidence in this setting, when the cultures are considered to be significant most authors support the use of antibiotics during 4-6 weeks and see no need for additional surgery. Broadly speaking, they follow the same

principles as for PJI managed with a 1-step exchange procedure. The outcome after an antimicrobial therapy is satisfactory in most cases^{22,264}.

RECOMMENDATION

1. In the case of PIOC (Tsukayama's classification) an antimicrobial treatment of 4 to 6 weeks is recommended. There is no need for further surgery. The same protocol is followed as in cases of PJI managed with a 1-step exchange procedure (B-III).

What is the treatment for cases in which no new prosthesis is to be inserted after the removal of the infected one?

The difficulty of treatment is significantly reduced when the infected prosthesis is not to be replaced. The same antibiotics and dosages used in DAIR (Table 5) may help the choice of the antimicrobial treatment, but the length of treatment may be shortened to 4-6 weeks, depending on the clinical follow-up.

RECOMMENDATION

1. For cases in which the infected prosthesis is not to be replaced after its removal, the same antibiotics as those used for DAIR may be administered (Table 5) (B-II).
2. In these cases, the length of therapy may be shortened to 4 to 6 weeks (C-III). 

Implant retention and long-term suppressive antibiotics (SAT) without attempted eradication

Is it necessary to perform a surgical debridement before initiating SAT?

It is reasonable to think that reducing the bacterial inoculum and debriding the infected tissues may favour the success of SAT. Indeed, in most series of PJI managed with SAT, patients underwent surgical debridement. However, in many of these cases the decision to initiate SAT may well have been taken after performing the debridement. The difficult decision to starting SAT is considered in clinically stable patients, with few symptoms, and especially if the surgical risk is high. Indeed, in a case series of elderly patients with PJI managed with SAT, only 24% underwent surgery⁹³. Another important advantage of performing surgical debridement is the possibility of obtaining valuable samples for culture. Access to reliable cultures in this setting is particularly important, since the samples taken from sinus tracts are not really representative. If the patient cannot undergo surgical debridement, obtaining a valid sample via joint aspirate or synovial biopsy should be considered.

RECOMMENDATIONS

1. A surgical debridement before beginning SAT is recommended, if feasible (C-III).
2. Obtaining a valid sample for culture before starting SAT is particularly important (C-III).