TRATAMIENTO SUPRESIVO

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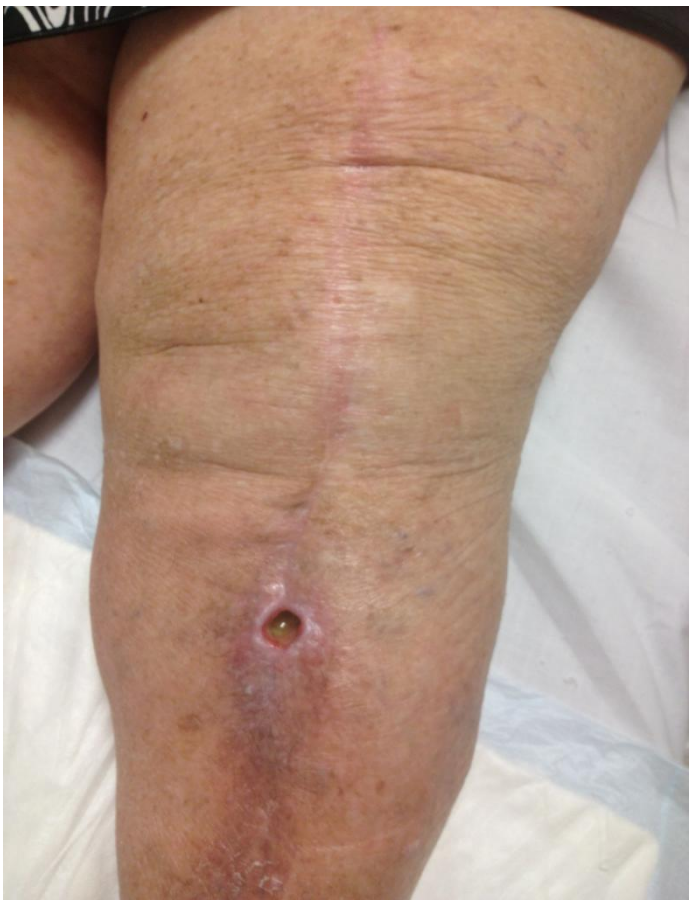

principles as for PJI managed with a 1-step exchange procedure. The outcome after an antimicrobial therapy is satisfactory in most cases[22,264].

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 surgery[93]. 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).

What are the most appropriate antibiotics for SAT? Are combinations of antimicrobials convenient or necessary? What is the role for rifampin?

In published case series, the most frequently reported antibiotics are the combination of minocycline plus rifampin or β-lactams alone[91-93,99]. Other less frequently antibiotics used are co-trimoxazole, clindamycin, and fluoroquinolones. It is difficult to draw recommendations from the literature regarding the usefulness of these antibiotics for SAT.

RECOMMENDATIONS

1. For the choice of the specific antibiotic for SAT, the antimicrobial susceptibility of the microorganism causing the infection, the safety of the drug and the observance of the treatment must be considered. Except for the initial stages of SAT, these aspects must prevail over the optimization of the antimicrobial treatment (C-III).
2. Except for some particular cases, the use of combinations (and therefore the use of rifampin) is not recommended (D-III).

Is it necessary to administer intravenous antibiotics at the beginning of SAT?

In most published series, patients were initially treated with intravenous antibiotics for several weeks. This was very likely done in the setting of the standard protocol of PJI management at each center, and not necessarily as a consequence of choosing a SAT strategy. In addition to the surgical debridement, an initial intravenous antimicrobial treatment may contribute to reducing the bacterial inoculum, thus favouring good evolution. Nevertheless, it seems unlikely that prolonged intravenous treatment is really relevant for the success or failure of SAT, since its efficacy is based on its indefinite administration.

RECOMMENDATION

1. In cases undergoing surgical debridement, an initial intravenous treatment for at least 7 days is recommended. Nevertheless, prolonged intravenous treatment is not necessary when deciding on SAT management (C-III).

Is it possible to have defined periods with no antimicrobial treatment?

Antibiotic-free periods are not reported in any of the series undergoing with SAT. Some of these studies report the occurrence of failure after antibiotic withdrawal, usually within the first 4 months after discontinuation[20].

RECOMMENDATIONS

1. If it is necessary to stop or change the antibiotics due to the occurrence of adverse events, long periods without antibiotics are not recommended (D-III).

Is SAT safe? What about its effect on the microbiota?

Safety issues in the setting of antimicrobial therapy scheduled for long periods (like SAT) are of paramount importance. Although information is very scarce, the safety data published for case series of SAT indicate a low rate of antibiotic withdrawal due to adverse events[31,92,99]. However, caution is required when interpreting these results: the rate of antibiotic withdrawal within the first weeks or months of treatment may have been underestimated, since patients who discontinued treatment early were probably removed from the series.

Nevertheless, information on the safety of prolonged antimicrobial therapies can be obtained not only from SAT in the setting of PJI or other bone and joint infections, but from other clinical scenarios as well, such as antibiotic prophylaxis in immunosuppressed hosts, infections requiring long treatments (multi-drug resistant tuberculosis, actinomycosis, endocarditis caused by *Coxiella*…), or diseases that also need long antibiotic therapies due to a natural history in which bacterial infection and colonization have a significant role (chronic obstructive pulmonary disease, cystic fibrosis, acne, and so on).

The analysis of the diversity of protocols, patients, and antibiotics is overwhelmingly complex. Table 7 summarizes the most interesting information for the management of PJI for each antibiotic separately.

RECOMMENDATIONS

1. The prescription and control of a SAT must be performed by an expert in antimicrobial therapy, who will periodically follow up the clinical evolution of the infection and assess the possible occurrence of adverse events (B-III).
2. The use of linezolid is discouraged in SAT due to high risk of toxicity, which limits its prolonged administration (E-I).
3. The use of β-lactams, or low doses of co-trimoxazole, is recommended. Alternatively, other antimicrobials such as minocycline or clindamycin may be administered (C-III). 

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Conflict of interests

JA has served as speaker for and has received fees for advisory boards from Pfizer and Novartis.

JC has served as speaker for Astellas, AstraZeneca, MSD, Novartis and Angellini, and has received fees for advisory boards from Astellas, Pfizer, AstraZeneca and MSD.

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Apendix 1. Abbreviations

ALS: acrylic cement spacer loaded with antibiotics.
CNS: Coagulase-negative staphylococci.
CRP: C-reactive protein.
DAIR: debridement, antibiotics, implant retention.
ESBL: extended-spectrum β-lactamase.
ESR: erythrocyte sedimentation rate.
GNB: Gram-negative bacilli.
IDSA: Infectious Diseases Society of America.
MSSA: methicillin-susceptible *S. aureus.*
MRSA: methicillin-resistant *S. aureus.*
PIOC: Positive intraoperative cultures.
PJI: prosthetic joint infection(s).
SEIMC: Spanish Society of Clinical Microbiology and Infectious Diseases.
SAT: suppressive antimicrobial therapy.