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QUESTION 3: Is there a role for nonoperative suppressive treatment in the management of subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: Although there is a role for suppressive antibiotic treatment of selected cases of periprosthetic infection of the shoulder, there are only a few shoulders included in the published literature. The vast majority of published cases describe initial irrigation and debridement, and these are not well separated in the literature from the small number of cases of patients treated with antibiotics alone. No patient treated with antibiotics alone for shoulder PJI has had antibiotics stopped and remained infection-free, thus concerns related to efficacy, long-term toxicity and development of resistant strains are paramount with this strategy. No recommendations can be given on indication, type and duration of suppressive antibiotic treatment.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 96%, Disagree: 0%, Abstain: 4% (Unanimous, Strongest Consensus)

RATIONALE

A literature search (Medline, PubMed) was performed including terms "periprosthetic infection," "PJI," "shoulder arthroplasty," "suppressive treatment," "chronic antibiotic treatment," "ICOAS" to identify studies on suppressive treatment of periprosthetic joint infection of the shoulder. The vast majority of published studies are retrospective, and in total eight shoulder cases were identified (five successful, three failures). Most studies reported on suppressive antibiotic treatment after initial surgical procedure like debridement or emptying abscesses.

Five studies, evaluating suppressive antibiotic treatment included cases of infected shoulder arthroplasty (eight shoulders). Prendki et al. [1] reported on 38 patients with a minimum suppressive treatment of 6 months for a periprosthetic infection (24 hips, 13 knees, **1 shoulder**). Sixty percent of the patients were on antibiotics and without relapse of infection (including the shoulder) at 24 months. There were six failures and nine deaths. Some of these patients had a surgical procedure before initiating suppressive treatment. It is unclear how many patients that were treated without initial surgery.

Wouthuyzen-Bakker et al. reported on a retrospective study of 21 patients (**2 shoulders**) with median follow up of 21 months [2]. They reported 90% success if the patients had a standard prosthesis but only 50% success in patients with a tumor prosthesis. One shoulder case was successful and one was a failure. Only six patients were treated without initial debridement and four had a successful outcome.

Pradier et al. [3] reported on 78 patients (**2 shoulders**) treated with oral tetracyclines as suppressive treatment with a minimum follow up of 2 years. All patients had surgical debridement. Twenty-two patients failed to respond to treatment. Both shoulders were failures. Three cases had acquisition of tetracycline resistance of the initial pathogen.

Prendki et al. [4] reported on a larger series of joint infections, 136 patients. Seventy-nine (58%) had some type of initial surgical procedure. There were **2 shoulders** and both were successfully treated with suppressive antibiotic treatment. It is unclear whether these 2 patients had initial surgery. Prendki et al. also reported on 21 patients (2017) in another study including **1 shoulder** (successful). Of these 21 patients, 5 had fistulas before starting chronic suppressive antibiotic treatment. Forty percent of the patients were free of clinical signs of infection after 2 years [4].

Multiple other studies have included PJI of other joints, primarily hip and knee arthroplasty.

Segreti et al. [5] reported on prolonged suppressive treatment in 18 patients (12 knees and 6 total hip arthroplasties). Eight had acute infection and 10 had chronic infection. All had surgical debridement before antibiotic treatment. Duration of oral antibiotic suppressive treatment varied from 4-103 months. Overall 14 patients remained asymptomatic. Twenty-two percent of the patients had complications related to antibiotic treatment. The authors concluded that suppressive treatment can be an alternative for patients who cannot or will not undergo major surgical revision.

Rao et al. [6] reported on 36 patients (15 hips, 19 knees and 2 elbows). Fouty-seven percent had acute onset (less than 4 weeks) and 53% were chronic infection. All patients had open debridement. Mean duration of treatment was 52.6 months (range 6-128 months). They reported favorable results (retention of a functioning prosthesis) in 86% with a mean follow up of 5 years. Eight percent had complications related to antibiotic treatment.

In 2004, Pavoni et al. reported on 34 patients (again, no shoulders included) with infection. Fourteen had surgical debridement [7]. Seventeen patients had no relapse of infection during the time of this study (11 of these patients had no initial surgical debridement).

Siqueira et al. [8] reported on 92 patients (no shoulders). They compared patients undergoing surgical debridement followed by a short period of antibiotics to prolonged suppressive antibiotic treatment. The five-year infection-free prosthetic survival rate was 68.5% for the antibiotic suppression group compared to 41.1% in the non-suppression group. Hip infections had lower rate of failures, and the suppression group results were better, if there was a *Staphylococcus aureus* infection.

Shelton et al. [9] reported a case of curing of a draining sinus tract in a hip infection. After suppressive treatment the patient discontinued antibiotic treatment and had no relapse of infection or fistula for a period of 8 years.

In summary, a review of the literature demonstrates that there is role for suppressive treatment in periprosthetic joint infection in the hip and knee in patients with stable implants and that cannot,

or do not want, major revision surgery. However, the studies include heterogeneous cohorts of patients with acute, subacute and chronic infections, and the duration and type of treatment varies. Most of the published case series include patients that had long term suppressive antibiotic treatment after an initial surgical irrigation and debridement. It is difficult to identify and evaluate outcome for the patients that only had chronic suppressive treatment. Furthermore, only a few shoulders are included, and, therefore, no recommendations can be given regarding type and duration of suppressive antibiotic treatment for periprosthetic infection in the shoulder. It is difficult to extrapolate from hip and knee infection data, since the clinical manifestation and type of pathogen are different in the shoulder compared to hip and knee. Lastly, profound concerns regarding antibiotic stewardship and antibiotic-related complications must be carefully weighed against any perceived potential modest success of this strategy.

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QUESTION 4: Is there a role for oral suppressive antimicrobial therapy in the setting of retained prostheses after intravenous therapy in subacute or chronic periprosthetic joint infection (PJI)?

RECOMMENDATION: The administration of oral suppressive antimicrobial therapy may have a role in management of patients with chronic or subacute PJI who cannot undergo further surgical intervention.

LEVEL OF EVIDENCE: Limited

DELEGATE VOTE: Agree: 100%, Disagree: 0%, Abstain: 0% (Unanimous, Strongest Consensus)

RATIONALE

Many cases of PJI can be managed by means of an adequate medical-surgical strategy with antibiotic treatment administered for a finite period of time. For patients with a PJI, where the medical-surgical treatment is suboptimal or clearly insufficient to achieve control (because of surgical contraindications, technical difficulties, severe medical comorbidities or multi-drug resistant bacteria), chronic oral SAT is considered an alternative strategy.

SAT refers to the use of antibiotics administered indefinitely with a "non-curative" intention and the objective of avoiding or reducing the symptoms and delaying or preventing the progression that may lead to patient dysfunction and the loss of the implant.

A search of Medline and Embase from 1980 to January 2018 was conducted. The terms used were: prosthetic joint infection or infected arthroplasty and suppressive therapy or suppressive antibiotics. Case reports, reviews and guidelines were excluded. Thirteen articles were finally reviewed. When the search was performed including the term "shoulder arthroplasty" or "prosthetic shoulder" and "suppressive antibiotic therapy" or "suppressive antibiotics" no articles specifically on this topic were found. However, a search in medical literature (Medline and Embase) about prosthetic joint infection or arthroplasty and suppressive therapy or suppressive antibiotics yielded 13 references [1–13]. Twelve are retrospective descriptive series, and one is a propensity score controlled cohort study [9]. The vast majority of the cases contained in these series were hip and knee infections, and only 9 of the 680 were prosthetic infections. Therefore, the present review is based on the results obtained with prosthetic hip and knee infections for shoulder prostheses.

Efficacy of SAT varied from 23% at 3.5 years [2] to 86.2% at 5 years [4]. Nonetheless, these wide discrepancies are explained by the use of different criteria in selecting patients for SAT and in defining the response to treatment. The case mix of patients in whom SAT has been prescribed includes a wide spectrum of situations: from acute PJI cases that could probably be cured by debridement and several weeks of antibiotic therapy, to patients with evident chronic infections showing active fistula and no surgery performed.

In summary, the analysis of the literature on SAT faces the following major problems:

1. Different classifications of the PJIs and the terms that are used to describe them (early, acute, delayed, chronic, subacute and so on).
2. Differences in the used medical-surgical strategies as standard of care of the PJI according to the types of infection.
3. Differences in the criteria used to select patients for SAT.
4. Differences in the criteria used to evaluate the efficacy of SAT.
5. Absence of control groups to compare the efficacy of SAT.

As well as other "minor" problems:

1. Insufficient follow up.