2. Variety of antibiotics used.
3. Small sample sizes, in general.

Thus, it is difficult to determine the effectiveness of SAT, although some evidence can be obtained by indirect means. In a cohort of 112 cases with PJI (52 hip, 51 knee, 4 elbow, 3 ankle, 2 shoulder—most of them diagnosed with early PJI, but also including late infections) managed with debridement, prosthesis retention and prolonged antimicrobial therapy for more than a year, the rate of failure among patients that discontinued antibiotic treatment was 4-fold higher than those who continued [7]. Although 82% of the patients who stopped antibiotics did not fail (probably the infection was actually eradicated), the occurrence of failure in some of them indicates that a proportion of those who were not cured by this strategy benefitted from SAT. Failures mainly occurred within the first four months of antibiotic withdrawal.

Another more recent study is the only one that included controls [9]. Ninety-two patients receiving SAT (71 hip PJI and 51 knee PJI) were compared by a propensity score (based on age, sex, type of prosthesis, type of surgery, Charlson index, number of previous revisions and microorganisms) with 276 controls in which clinicians did not administer SAT. The decision to use SAT was individualized, but it is presumed that it was due to "high risk of failure." In fact, 67% of the patients had undergone prior revision surgery. Thirty-six of the cases were "early" PJI and 56 were "late" PJI (no definition of "early" was provided). Cases were managed either by a two-stage revision (38) or by debridement and exchange of polyethylene (54) followed by intravenous antibiotics before SAT was started. A significantly better result was observed in SAT treated patients than in controls (68.5% vs. 41.1%; $p = 0.08$) at 5 years. When analyzed by type of surgery the differences were clear among those managed by prosthesis retention (64.7% vs. 30.4%; $p < 0.001$) but they were not observed in those managed by two-stage exchange ($p = 0.13$). The proportion of success among patients with "late" infections was 64.3%. One of the drawbacks of the study was the fact that the authors included as failures any death during the first year, and the occurrence of severe pain during the follow-up, making it difficult to assess the proportion of true failures because of a lack of infection control.

Interestingly, most series show reassuring data about the safety of long-term antibiotic administration [4,6,10,11,13]. Those who did not tolerate the first selected agent usually tolerated an alternative [12].

In summary, there seems to be some evidence that SAT benefits patients at high risk of failure of prosthesis retention. The main problem is to select in which patients the risk is high enough to compensate for the inconvenience of long-term antibiotic use.

The following conditions also need to be met when considering SAT:

1. Identification of the microorganism that is causing the infection.
2. Availability of oral antibiotics that are not toxic when administered over long periods of time.
3. Practicality of a close follow-up of the patient.

Bearing all these considerations in mind and also the antibiotic stewardship and resistance implications of long-term antimicrobial therapy, the SAT is only indicated after a careful risk-benefit analysis. The temptation to use this strategy to avoid the need for complex but potentially eradicative surgery should be resisted.

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QUESTION 5: Is there a role for oral suppressive antimicrobial therapy in acute periprosthetic joint infection (PJI) in the setting of retained prostheses after initial intravenous (IV) therapy? Same duration as for lower extremity arthroplasty? Should it differ by pathogen (e.g., methicillin-sensitive *Staphylococcus aureus* (MSSA) vs. methicillin-resistant *S. aureus* (MRSA))?

RECOMMENDATION: While the role of debridement, antibiotics and implant retention (DAIR) in the treatment of acute prosthetic shoulder infection has not been well-studied, there is likely a role for oral suppressive antimicrobial therapy in the setting of retained infected shoulder prostheses after DAIR. There is no evidence to guide the optimal duration of treatment or if treatment should vary by organism.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

A comprehensive systematic review was performed using MeSH terms: "(Arthroplasty, Replacement, Shoulder OR Shoulder joint) AND (Infection OR Debridement OR Anti-Bacterial Agents OR keyword "acute," OR "infection," OR "antibiotics") using Ovid-Medline. The inclusion criteria for this systematic review were English language, shoulder arthroplasty studies that included patients who underwent treatment for periprosthetic shoulder joint infection using irrigation and debridement with component. Exclusion criteria were non-English language articles, technique papers, non-human studies, studies that only presented data on one-stage or two-stage revision, hip or knee arthroplasty articles. Our initial search produced 288 abstracts; 260 were excluded, because they did not fit inclusion criteria, and the remaining 18 manuscripts were obtained and reviewed to assure inclusion criteria. Additionally, the references of these manuscripts were reviewed to ensure no additional relevant material would be missed.

The treatment of an acute hip or knee PJI following irrigation and debridement with implant retention includes a course of oral antibiotics that follows the IV antibiotic therapy [1–3]. Although the efficacy of this approach is debated, with reported success rates ranging from 0% to 89% [4], the use of oral antibiotics (for varying durations) in patients with retained hardware has been reported to be nearly universal, especially in the United States [5]. An analogous algorithm of treatment has been advocated in the setting of acute shoulder PJI when treated with irrigation and debridement with implant retention [6–8], although specific recommendations regarding route and duration of antibiotic therapy are not clear [9,10].

There is very little published literature evaluating the efficacy of this course of treatment in shoulder PJI. Most studies addressing the treatment of acute shoulder PJIs are retrospective case series without control cohorts [11–28]. As many of these studies were comprised of patients undergoing heterogeneous treatment protocols, the subset of patients undergoing DAIR is often only a small subset further limiting the ability of these studies to provide useful data. The overall number of patients presented in these articles is also very small; no study exceeded 50 shoulders and the majority reported on the outcomes of less than 10 patients with acute shoulder PJIs treated with irrigation and debridement and implant retention followed by IV and then oral antibiotics. Details regarding antibiotic use and duration are not always presented or correlated with clinical outcomes. Given the small number of overall cases to draw from, it is difficult to make any inferences regarding the efficacy of this treatment as stratified by organism, including MRSA versus MSSA. Complicating any synthesis of the data further is that patients reported in these studies also varied as to the type of infected arthroplasty (anatomic total shoulder, reverse total shoulder or hemiarthroplasty). Extrapolating these results to assess the actual utility of oral suppressive antimicrobial therapy in acute PJI in the setting of retained prosthesis after initial IV therapy is not feasible nor is it possible to establish a recommended optimal duration of therapy.

Whether DAIR is even a viable treatment approach for shoulder PJIs in any setting has been challenged [10]. A systematic review of the literature published in 2016 found that the failure rate of implant retention in the setting of prosthetic shoulder infection was 31.4% versus a 6.3% failure rate following a two-stage exchange, a 9.7% failure rate following explantation with placement of permanent spacer, and 9.9% following a one-stage exchange [29].

However, despite the lack of supporting medical literature, the use of oral antibiotics, based on the more extensive experience with the treatment of hip and knee infections following debridement as well as the current understanding of the role biofilm plays in treatment failure [25,30–32], is likely a reasonable approach for the treatment of acute prosthetic shoulder infections when treating with implant retention, at least until more rigorous outcomes data that supports the contrary is available.

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QUESTION 6: Should the duration of oral suppressive antimicrobial therapy differ by pathogen (e.g., methicillin-sensitive *Staphylococcus aureus* (MSSA) vs. methicillin-resistant *S. aureus* (MRSA)) in the treatment of subacute or chronic shoulder periprosthetic joint infection (PJI)?

RECOMMENDATION: There is insufficient evidence to determine whether the duration of oral suppressive antimicrobial therapy should differ by pathogen in the treatment of subacute/chronic shoulder PJI.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

There is currently no widely shared and commonly used definition of the term "suppressive antimicrobial therapy" (SAT) in reference to antimicrobial therapy for shoulder PJI. A thorough search of PubMed, Embase and Google Scholar databases was undertaken in February, 2018 to identify articles related to the use of suppressive antibiotic therapy for the treatment of shoulder PJI using search terms: "prosthetic joint infection," "suppressive therapy," "antibiotic suppressive therapy," "suppression."

From the results of this search, it is clear that the term SAT is used in various ways. It is often used to mean prolonged antibiotic therapy following surgery (irrigation and debridement and implant revision) with the intention of effecting a cure and discontinuation of antibiotics. In other cases, SAT is described for the treatment of active PJI in patients unable to undergo additional surgical intervention. Treatment in this scenario is palliative; it is based on the principle that organisms within a biofilm cannot be fully eradicated and that the antimicrobial inhibits the organisms in the biofilm from spreading. This may halt dissemination of the infection and prevent sepsis but is highly unlikely to eradicate the underlying infection. Suppressive antibiotic therapy is also used to define indefinite or life-long use of antibiotic therapy in patients without clinical evidence of active infection but thought to be at high-risk for relapse.

Using an inclusive definition of "suppressive antimicrobial therapy," twelve relevant studies were identified [1–8]. From these studies, 34 patients were noted to have had shoulder PJI and received SAT. Failure was defined as a relapse of infection based on the criteria described in each manuscript. These criteria were not consistent. Collectively, patients prescribed SAT had a PJI relapse rate of 29% (10/34 cases). There was not sufficient level of detail to comment on treatment duration, dose of antibiotics or type of antibiotics.

There is some support for success after discontinuation of SAT. Antimicrobial-free periods are not reported in any of the reported series. Reports of hip and knee PJI demonstrate that there is a relapse rate of around 30% within 4 months when suppressive antibiotic treatment is discontinued, even after a long period of suppressive therapy [7]. A study 24 patients with PJI (2 shoulder patients) did observe that treatment succeeded in almost all patients with a PJI caused by a *S. epidermidis* [1]. This finding may not be surprising since *S. epidermidis* has low virulence and the natural course of infection is often dormant and low-grade in nature.

Safety issues in the setting of SAT are an important consideration. Although information is very scarce, the safety data in the published case series indicate a low rate of antibiotic withdrawal due to adverse events [4,7,9].

Moving forward, it may be useful for clinicians and researchers to more precisely define "suppressive antibiotic therapy." The authors would suggest that SAT refer to "the chronic use of low-dose antibiotic therapy in patients with persistent PJI in which the aim is no longer to cure, but to prevent acute exacerbation or recurrence of local symptoms and/or greater systemic involvement." The key to this definition is the recognition that antibiotic therapy is not curative anymore in its intent. Suppressive antibiotic therapy is thereby differentiated from longer-than-standard "prolonged" administration of antibiotics meant to eradicate infection and cease after the infection is deemed to be cleared. Differentiation of these terms may allow future investigators to make more concrete recommendations regarding the use of SAT in shoulder PJI.

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