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QUESTION 7: What are the recommendations for the route (intravenous (IV) vs. oral (PO)) and duration of postoperative antibiotic treatment when a one-stage revision arthroplasty is performed for subacute or chronic shoulder periprosthetic joint infection (PJI) of the shoulder caused by an indolent organism (e.g., *C. acnes* or coagulase-negative Staphylococcus)?

RECOMMENDATION: Prior to identification of pathogenic organisms from intraoperative cultures, a course of oral antibiotics may be initiated that covers the potential organism until intraoperative cultures are finalized. If the cultures are positive and periprosthetic infection is diagnosed, then a continued course of antibiotics (up to six weeks) should be pursued. There is no evidence to support a preferred route (PO vs. IV), type and duration of antibiotic treatment.

LEVEL OF EVIDENCE: Consensus

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

RATIONALE

Periprosthetic shoulder infection negatively impacts the outcome of shoulder arthroplasty and is often treated with revision surgery [1]. The overall rate of infection after shoulder replacement is reported as 1.2-3.0% (0.5-3.9% for anatomic and up to 10.0% for reverse shoulder arthroplasty) [2–4]. Prosthetic shoulder infection commonly presents as painful arthroplasty and often lacks typical clinical findings of acute infection. Laboratory workup, such as inflammatory markers, white blood cell count and shoulder aspiration are usually negative, leaving clinicians with limited tools to confirm infection prior to revision surgery. This is mostly due to predominance of indolent organisms, such as *Cutibacterium acnes* (formerly known as *Propionibacterium acnes)* (39-66%) and *Coagulase negative staphylococcus* (24-28%) in periprosthetic shoulder infection [5,6]. Two-stage revision including aggressive debridement, antibiotic spacer placement followed by prolonged IV antibiotics was adopted by shoulder surgeons from treatment of PJI of other joints and showed 63-100% success rate in eradicating infection in short to mid-term follow up [7–9]. This approach has many short-comings, including subjecting patients to two operations and spacer complications, such as fracture, dislocation and loss of rotator cuff and bone stock, leading to poor joint function. Recently, one-stage revision has been advocated for low virulence indolent infections. Nelson et al. [10] and Cuff et al. [11] showed similar rates of eradication after one-stage versus two-stage revision arthroplasty. Beekman et al. reported results of single stage revision for infected reverse shoulder arthroplasty and showed at two year follow-up 90% of patients were infection free with a Constant score of 55.6% [4]. George et al. did a systematic review and found that the average Constant score was 51% after one-stage revision which was better than 41% two-stage revision [12]. These studies make a reasonable case for one-stage revision arthroplasty to eradicate indolent infections while preserving the function of the patient's joint, but they have highly variable protocols for type and duration of postoperative antibiotics. To answer the question above we review and summarize the limited evidence around antibiotic therapy following one-stage revision arthroplasty for periprosthetic shoulder infection with indolent organisms.

A PubMed search was conducted with terms arthroplasty, replacement, shoulder (Mesh) and revision which resulted in 120 papers. Abstracts of the papers were reviewed to identify papers reporting one-stage revision for indolent periprosthetic shoulder infection which resulted in 8 relevant articles that are included in this review.

Most authors retrospectively reporting their experience with treatment of shoulder arthroplasty infection incompletely report the antibiotic therapy following revision surgery. This section will review and summarize the current literature on treatment outcome of infected shoulder arthroplasty with specific focus on antibiotic regimen, as incomplete as it may be, including route (IV vs. PO), type and duration.

Grosso et al. [13] retrospectively reviewed patients with no perioperative sign of infection who underwent single stage revision shoulder arthroplasty and postoperatively had at least 1 positive culture and were not treated with an extended course of antibiotics. The majority of the cultures (56%) were *C. acnes* followed by coagulase negative staphylococci (CoNS) (35%). The rate of recurrence was very low (5.9%). Authors suggested unexpected cultures after a seemingly uninfected one-stage revision did not require extended antibiotic therapy.

Padegimas et al. [14] reviewed 117 one-stage revision shoulder arthroplasty with no preoperative concern for infection who were followed for more than 4 years and found that 28 (23.9%) had an unexpected positive culture postoperatively of which 15 (57.1%) were *C. acnes,* and majority were in male patients. They did not identify any predictor for reoperation, but they observed a higher rate of reoperation in patients without unexpected cultures (20.2% vs. 7.1%) but this did not reach clinical significance. In their cohort, 18 (64.3%) patients were treated with IV antibiotics for 6 weeks, and 10 (35.75) patients only received 2 weeks of PO antibiotics. There was only one reoperation among culture positive patients and that was in a patient who did not receive prolonged antibiotics.

Coste et al. [1] reported on the outcome of treatment in 42 patients with infected shoulder arthroplasty with a mean 34 months follow up. They defined infection based on seven criteria including

presence of a sinus tract, elevated serum white blood cell (WBC) count, elevated erythrocyte sedimentation rate, or C-reactive protein (CRP), positive culture including preoperative aspiration, X-ray evidence of implant loosening and positive bone scan, with no further details on how these criteria were weighted in their definition. There were 20 infections following primary arthroplasty and 22 after revision surgery. Thirty patients (71.4%) had subacute or chronic infection. At final follow up, 22 (73.3%) were infection-free, but there was a wide variation in how patients were treated. They were able to obtain antibiotic information in 30 patients and they judged treatment to be inadequate in 15 patients with regards to duration and type of antibiotics. Five patients were treated with antibiotics only, and only two remained infection-free at final follow up (60% failure rate).

Cuff et al. [11] reported their results of 22 patients with infection following hemiarthroplasty (n = 17) and open cuff repair (n = 5) treated with one versus two-stage revision. In their series, *S. aureus* was the most common organism. CoNS (n = 3) and *C. acnes* (n = 1) were also identified. None of their patients had recurrent infection at mean follow up of 43 months and there was no difference in any of the outcome measures between one versus two-stage revision. The majority of the patients were given six weeks of IV antibiotics, while patients with no clinical signs of infection and with negative intraoperative histology were treated with two weeks of IV antibiotics. It is not clear what type of IV antibiotics were perscribed.

Keller et al. [15] performed a retrospective study of orthopaedic hardware infection that was treated with debridement and retention of hardware, single-stage revision or without surgery to determine if treatment with six weeks of oral antibiotics alters the rate of success at one year. They only included patients who had two separate positive cultures of the same organism from samples taken with a sterile technique from the same site. Of the 89 patients in their study, 42 (47.2%) were infection-free at one year. Patients with methicillin-resistant *S. aureus* (MRSA) or gram-negative organisms, prior infection at the same site, and higher Charlson comorbidity score were less likely to achieve treatment success. They concluded that patients who were on oral suppression for 3-6 months had a significantly lower recurrence rate but continuing antibiotics beyond 6 months did not have the same benefit. Specifically, *C. acnes* infection (n = 32) was associated with a higher likelihood of treatment success at one year (odds ratio: 5.1, 95% confidence interval: 1.32-19.75).

Piggott et al. [16] reported a retrospective study of surgical and nonsurgical management of 24 patients with *C. acnes* PJI from one center with median follow up of 2 years. They defined definite PJI as two positive *C. acnes* cultures or one positive *C. acnes* culture plus sinus tract, clinical purulence or positive histopathology. Probable PJI was defined as one positive *C. acnes* infection and any suspicious clinical sign of infection. There were 11 (46%) definite and 13 (54%) probable PJI cases. The surgery group included 1 incision and debridement with retention, 4 one-stage revisions, 7 two-stage revisions and 3 spacer placements with no re-implantation. The median duration of antibiotic treatment was 6.3 months (range 1.3-50.7). They showed similar success rates with antibiotics only (67%) versus surgery plus antibiotic treatment (71%) (p = 1.0). Fifteen patients (71%) had rifampin as part of their antibiotic treatment but being on rifampin did not significantly change their outcome (73% vs. 60%; p = 0.61) and 40% of patients who received rifampin had to stop it due to side effects.

Hsu et al. [17] reported a retrospective study of 55 failed shoulder arthroplasty cases without clinical evidence of infection who underwent one-stage revision and compared their outcome at average 4 years between patients with ≥ 2 positive cultures (n = 27) and those with 1 or no positive cultures (n = 28). They reported comparable Simple Shoulder Test scores and reoperation rates. All patients received IV vancomycin and ceftriaxone as prophylaxis. If the index of suspicion for infection was high, the IV antibiotics were continued for 3 weeks until the cultures were finalized. If suspicion was low, the patients were started on oral amoxicillin and clavulanic acid for 3 weeks. If cultures were negative or only one culture was positive, antibiotic was stopped at 3 weeks. If ≥ 2 positive cultures became positive at any point, IV ceftriaxone +/- vancomycin was started and/or continued for 6 weeks. They reported 42% antibiotic side effects in this cohort which was higher than the IV antibiotics group.

Klatte et al. [18] retrospectively reviewed their experience with 26 infected shoulder arthroplasty patients treated with one-stage revision at mean follow-up of 4.7 years (range 1.1-13.3 years). The most common organisms were *Staphylococcus epidermis* and *C. acnes*. The majority of patients (94%) were infection-free at final follow up. Antibiotic therapy was tailored to clinical signs, serial CRP levels and serum WBC count. IV antibiotics were given for a mean of 10.6 days (range: 5-29 days). PO antibiotics were given to 4 patients for 5 days, 8 patients for 14 days and 2 patients for 24 days and stopped when CRP normalized and the wound had healed.

The literature on antibiotic treatment following one-stage revision shoulder arthroplasty for subacute and chronic infection is primarily based on heterogeneous case series with inconsistent definitions for infection, and variable treatment protocols. Shoulder PJI with indolent slow growing organisms, such as *C. acnes* and CNS, often have minimal clinical signs of infection. Thus, the diagnosis of infection is frequently made up to two weeks after the revision has been completed. As a practical approach to management, many clinicians recommend using antibiotics for all revision shoulder arthroplasty surgery pending the final cultures results [19].

There is no consensus on duration and type of antibiotics for this period. Antibiotic treatment after cultures are finalized should be dictated by the clinical index of suspicion for infection, culture results, and risk-benefit analysis of antibiotic side effects. There is no high-level evidence currently available to guide this decision.

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QUESTION 8: What are the recommendations regarding the route (intravenous (IV) vs. oral (PO)) and length of postoperative antibiotic treatment when a one-stage revision arthroplasty is performed for subacute/chronic shoulder periprosthetic joint infection (PJI) caused by a virulent organism (e.g., methicillin-sensitive *Staphylococcus aureus* (*S. aureus*), or MSSA, vs. methicillin-resistant *S. aureus* (MRSA), E. coli)?

RECOMMENDATION: Intravenous antibiotics or intravenous followed by oral antibiotics are both reasonable options for one-stage revision shoulder arthroplasty for subacute/chronic shoulder PJI caused by a virulent organism. As there is no consensus on the route or duration, these treatment parameters should be selected in consultation with an infectious disease specialist.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

Single-stage revision shoulder arthroplasty is an option for infected shoulder arthroplasty [1–4]. However, the outcomes depending on the virulence of the organism and the ideal duration and mode of antibiotic (IV or oral) treatment associated with single stage revision for PJI is not known.

For this purpose, a comprehensive search on PubMed and Embase database of all English literature till March 2018 was conducted to query keywords: (shoulder OR 'upper extremity') AND (arthroplasty OR replacement) AND (infection OR infected). A total of 1,434 articles were retrieved by the initial search. After review of the title and abstract of all studies, articles focusing on "management of infection" were extracted for further review (n = 31). After applying final exclusion ("two stage revision," "antibiotic spacer" or "antibiotic suppression") and inclusion criteria ("single stage revision," "antibiotic"), a full text review of the articles was conducted, and 6 articles were selected for final analysis. Articles reporting single stage revision but without any information on antibiotic type and or duration were further excluded (n = 2).

The selected studies for analysis (n = 4) evaluated the role of postoperative antibiotic therapy for single stage revision shoulder arthroplasty for PJI. However, it must be emphasized that these studies did not stratify results by the virulence of the organism. Thus, no firm conclusions regarding treatment according to the virulence of the organism can be made.

Beekman et al. retrospectively reviewed 11 consecutive patients with an infected reverse shoulder arthroplasty who underwent single stage revision arthroplasty [5]. Two of these patients had monobacterial infection with a virulent organism (*Staphylococcus aureus* and *Escherichia coli*). Both of these patients received at least three days of IV antibiotic and were discharged on oral antibiotics, which were continued for at least three months. Ince et al. retrospectively reviewed 16 patients with an infected shoulder arthroplasty (three with identified virulent organisms) that underwent single stage revision shoulder arthroplasty [6]. Three patients (~19%) had undergone revision surgery prior to review. All patients received intravenous antibiotics for mean of 8.6 days (range: 5-14 days) and antibiotics were stopped when the surgical incision had healed and/or infection labs (erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and white blood cell (WBC) count) were down trending. No recurrence of infection was reported in 9 patients that were reviewed. Klatte et al. reported their results of single stage revision shoulder arthroplasty for PJI in 35 patients, of which 26 were available for review [7]. Patients received IV antibiotics for a mean of 10.6 days (range: 5-29 days), and 11 patients received PO antibiotics for a mean duration of 12.8 days (range: 5-24 days). There were two recurrences. Cuff et al. retrospectively reviewed 22 infected shoulder arthroplasties of which 11 were treated with single stage revision to reverse shoulder arthroplasty and intravenous antibiotics [8]. Five of the 10 patients had virulent pathogens. Patients received antibiotics for 2 (1 patient) or 6 (4 patients) weeks depending on cultures and intraoperative histology results. There was one recurrence of infection.

There is little evidence regarding the subsequent antibiotic management of subacute and chronic shoulder PJI due to high viru-