SH64: What is the optimal oral or iv antibiotic treatment in cases of culture negative PJI?

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Recommendation: There is insufficient evidence to recommend a specific antibiotic regimen or even whether an oral or intravenous strategy is preferred in this group. Selection of antibiotic type and route should be dictated by infection characteristics in consultation with Infectious Disease specialists when available.

Strength of Recommendation: Limited

Delegate Vote: 53 (100%) agree; 0 disagree; 0 abstain

Rationale: A comprehensive literature review was performed to identify all studies on the optimal oral or iv antibiotic treatment in cases of culture negative shoulder PJI. Searches for the terms "prosthesis-related infections", "prosthetic joint infection", "shoulder", "culture negative", "oral antibiotics", and "intravenous antibiotics" were performed using the search engines Medline, Embase, and Google Scholar with no time restriction. MESH terms were used but key words were also included. An initial strict search identified 0 potential papers therefore the search was adapted to include "antibiotic therapy". This identified 104 papers in Medline, 78 in Embase, and 0 in Google Scholar. Following a title and abstract screen 10 papers were selected for further review.

Inclusion criteria for systematic review were all English language studies (Level I-IV evidence) that reported on oral or intravenous antibiotic treatment in cases of culture negative shoulder PJI. Exclusion criteria were non-English language articles, non-human studies, retracted papers, case reports, review papers, studies with less than <10 patients in the sample size, studies without clinical follow-up/infection rates, and technique papers without patient data. PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) criteria were followed. Zero articles meeting inclusion and exclusion criteria were identified.

Although no papers met the specified inclusion and exclusion criteria a limited amount of potentially relevant information is available from several reviews and a small number of related studies. Most of the reviews focussed on hips and knees and specifically excluded shoulders and other smaller joints due to limited evidence. Additionally, several reviews looking at antibiotic treatment of PJI did not include culture negative cases.

The incidence of culture negative PJI ranged from 7 to 42% with a pooled result of 11% in a systematic review [1]. This incidence may increase following the recent publication of diagnostic criteria from EBJIS which appear to be more sensitive [2]. Several factors potentially contribute to negative cultures in the setting of PJI, including prior antibiotic administration, suboptimal tissue sampling, delayed transport, atypical or difficult to culture organisms, and inadequate incubation time. Many of these reasons may be relevant in shoulder PJI due to the increased proportion of *Cutibacterium acnes* infection. Negative cultures contribute to diagnostic uncertainty around whether there is truly an infection.

Culture negativity poses a significant challenge in selecting appropriate antibiotic treatment due to lack of specific sensitivity data and the optimal antibiotic treatment has not yet been established. In 2013 an Emerging Infections Network surveyed 556 members regarding antibiotic choices for culture-negative PJIs. A two-drug regimen was selected by 68% of providers for knee infections and 69% for hip infections. The most common antibiotic combinations included vancomycin with fluroquinolone, ceftriaxone, or cefepime. A treatment duration of 6–8 weeks was preferred by 77 % of respondents [3].

The 2018 ICM recommendations state, “in patients with true CN-PJIs, antibiotics should be selected to have broad spectrum activity against both Gram positive and Gram negative organisms. In addition, the exact choice should relate to the known modern epidemiology in that country.” This was agreed upon by 87% of expert delegates [4]. Neither of these papers were specific to shoulder PJI.

In 2019 Li et al published a large study of 1054 patients comparing oral vs intravenous antibiotics in orthopaedic infection [5]. Oral antibiotic therapy was noninferior to intravenous antibiotic therapy when used during the first 6 weeks for complex orthopaedic infection, assessed by treatment failure at 1 year. This study included all orthopaedic infection, including DFI, spinal infection, osteomyelitis, and septic arthritis as well as PJI. From the supplementary data there were 102 upper limb patients (9.67%), however, the proportion involving a shoulder PJI was not specified. Across the whole population 15.5% patients had culture negative infection and were evenly split between oral and intravenous arms. Outcomes slightly favoured intravenous treatment, however, these results did not reach statistical significance. Additionally, the study did not specify antibiotic choice, only whether they were oral or intravenous.

Outcomes of culture negative PJI vary with some studies reporting better outcomes, some reporting no difference, and others reporting worse outcomes compared with culture positive PJI. None of these studies are specific to the shoulder joint, all are retrospective, and none compare antibiotic regimens. The most commonly used oral regimens included Rifampicin based combinations, usually with a fluoroquinolone, Clindamycin, or Linezolid [6]. The most common intravenous regimens included cephalosporins, glycopeptides, or daptomycin.

References:

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2. McNally M, Sousa R, Wouthuyzen-Bakker M, et al. The EBJIS definition of periprosthetic joint infection. Bone Joint J. 2021;103-B(1):18–25
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5. Li HK, et al. Oral versus Intravenous Antibiotics for Bone and Joint Infection. NEJM 2019;380:425-36. DOI: 10.1056/NEJMoa1710926
6. van Sloten, et al. Should all patients with a culture-negative periprosthetic joint infection be treated with antibiotics? Bone Joint J 2022;104-B(1):183–188