

HK97: What is the optimal duration of antimicrobial treatment for patients undergoing single stage exchange for implant associated infections?

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Response/Recommendation:

Based on the limited available evidence, after single stage exchange an antibiotic course for a total duration of at least 6 weeks is recommended.

Level Of Evidence: Limited

Delegate Vote: Agree: %, Disagree: %, Abstain: %

Rationale:

Antibacterial therapy is a mandatory part in the treatment algorithm following one stage exchange revision arthroplasty in patients with periprosthetic joint infection (PJI). After a structured search in Pubmed, Embase and MEDLINE resources, 30 studies were found, comprising of five prospective studies, 16 retrospective studies, 9 reviews and one systematic review [1-30]. Also 3 studies were added manually [31,32, 33].

The vast majority of studies evaluated the effectiveness of one-stage exchange in hip [7,9,12,13,15,16,20,21,27-32] or knee [1,5,6,10,11,18,19,23-25] PJI, while four studies compared one- and two-stage surgical treatment algorithms [14,17,26,31]. In these studies authors discussed the duration of antimicrobial therapy, referring to other studies, sometimes with a similar design. It is also noteworthy that in 12 studies the analysis was performed on small cohorts consisting less than 40 patients [1,3,4,7,9,16,17,20,21,26,27,32].

Regarding the optimal duration of intravenous antibiotic therapy, in most studies antibiotics were administered intravenously for 7-14 days [2-6,8,9,15,18,19,20,22,23,24,27-29,31,32], even though some studies prolonged this phase up to 42 days [4,7,26,30]. However, the randomized clinical trial OVIVA showed no significant differences in failure after one-stage exchange (n=76) in the subgroups of oral and intravenous antibiotics for 6 weeks (OR 2.16 (95%CI 0.58 to 8.00)) [33]. In the majority of studies the course of oral antibiotics varied from 5 to 10 weeks, with an average infection eradication efficacy 90.2% in these studies [1,2,9,11,13,14,16,17-20,23,25-27,30-32]. Prolonged duration of oral antibiotics does not increase treatment effectiveness, according to a number of studies with infection eradication from 70% to 100% [7,21,22]. According to several studies the decision to discontinue antibacterial therapy could be based on laboratory findings, focusing on the ESR, C-reactive protein or albumin levels [3,6,14,20,26].

Mean total duration of antimicrobial treatment among the studies, that presented full data ranged from 6 to 14 weeks, with an average level of infection eradication from 70% to 93.8% [1-4,7-9,11-15,17-21,23-27,30-32]. Additional prolonged (16 days) intraarticular infusion of antibiotics combined with intravenous therapy led to a comparable outcome [14].

The efficacy of single stage exchange in the setting of a standardized course of antimicrobial treatment was evaluated in 3 of 33 identified publications[2,3,4]. In the study by Dubée et al., the total course of antimicrobial therapy after 1-stage replacement in patients with chronic PJI caused by methicillin-resistant *Staphylococcus aureus* (MRSA) was 12 weeks. The first 6 weeks, patients received combined therapy with continuous infusion of vancomycin followed by 6 weeks of oral antibiotics. Only 2 relapses occurred in 32 PJIs treated with one-stage exchange at 18 months follow-up, however 32% experienced nephrotoxicity during therapy[4]. Another study, which only included 4 cases of single stage exchange arthroplasty, had patients received 12-20 days of intravenous administration with

further 6-26 weeks of oral antibiotics, which resulted in 100% effectiveness at the 2-year follow-up. It is impossible to draw any significant conclusions from the obtained data due to the small cohort size and wide range of antimicrobial therapy duration [3]. A recent retrospective cohort study investigated the outcomes of one-stage revision of hip and knee PJI followed by 6-week antimicrobial therapy in 50 patients. Antibiotics were administered intravenously for an average of 11 days, after which 92% of patients were transferred to oral therapy. The cohort consisted of patients infected with several different pathogens, including polymicrobial infections. Culture-negative infections were excluded. Infection was eradicated in 90% of patients with an average follow-up period of 32 months, lending support to the concept of a short (6-week) course of antimicrobial therapy after one stage exchange for PJI [2].

Antibiotic therapy for 6 weeks was not shown to be noninferior to antibiotic therapy for 12 weeks (all surgical strategies) in the randomized controlled DATIPO trial, the subgroup analysis showed no significant risk difference (1,2 (95% CI 4,8 to 7,1)) for the primary outcome (persistent infection) between 6 and 12 weeks for the 146 patients undergoing one-stage exchange [31]. However, the authors conclude that this observation should be confirmed in a specific RCT.

A systematic review made by Sandiford et al. included 21 publications, and assessed the impact of intravenous treatment duration on the outcome in single stage exchange in 643 patients with hip PJI. The treatment efficacy in short (less than 4 weeks) and long (4-6 weeks) courses of intravenous antibiotics were found to be comparable; PJI eradication rate was 92.6% and 89.3%, respectively ($p = 0.7434$) [22].

In conclusion, currently there is no high-level evidence supporting a significant advantage of one or another antimicrobial treatment duration for patients undergoing single stage exchange for PJIs. Most studies report successful outcome in >90% regardless of postoperative treatment duration. Two recent studies [2,31] lend further support to a strategy consisting of short course of intravenous antibiotics for 10-14 days followed by a course of oral antibiotics for a total duration of 6 weeks after one-stage exchange in PJI. Randomized prospective studies are needed to determine the optimal duration of the overall course of antimicrobial therapy. Furthermore, the role of local administration of antibiotics following one stage exchange needs to be further investigated.

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