SH73: During protracted revision arthroplasty surgery, should a second dose of prophylactic antibiotics be given during the course of surgery and if so, when? If applicable, should the administration of a second dose be based on the duration of the surgery, blood loss, magnitude of revision (size of implant) or other factors?

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Recommendation: Even though the avaliable literature lacks evidence specific to the shoulder; decision for a second dose of prophylactic antibiotics may be given based on duration of the surgery, especially if the surgery duration exceeds two half-life times of the administered antibiotics. Other factors such as blood loss, patient weight, or magnitude of revision do not seem to have significant impact on this concern.

Strength of recommendation: Limited

Rationale: A comprehensive literature review was performed on January 2025 to identify all the available data regarding association between second dose intraoperative prophlyactic antibiotics and shoulder revision arthoplasty surgery. Selected terms included "shoulder arthoplasty", "revision arthroplasty", "prophylactic antibiotics", "antibiotics prophylaxis", "second dose", "redose" and "readministration" which were searched through PubMed, Scopus and Cochrane databases. Exclusion criteria were articles on non-English languages, non-human studies, case reports, editorial comments and opinion pieces. Following title and abstract assessment, retracted results specifically for "shoulder arthroplasty" were highly scarce; thus, 7 previous studies and other related studies which had been cited in these reports were included into this review.

No previous reports confined to "shoulder arthroplasty" was found; however, most of the studies had general population consisting various surgical interventions (inluding orthopedic and arthroplasty procedures). Pharmacokinetic properties of the administered antibiotics are strongly recommended to be considered by the NICE guidelines (1); and also by some other previous studies (2,3). Antibiotic selection and dose must consider probable microorganisms, local pathogen susceptibility, and, crucially, the penetration of the target tissue for the desired duration. Nonetheless, the most neglected and inadequately comprehended aspects of antibiotic selection are pharmacokinetic concerns. The justification for administering antibiotic prophylaxis before surgery to prevent potential infection is founded on the principle of establishing a protective antibiotic concentration at the surgical site prior to incision. The preventive antimicrobial agent must be administered at a dosage sufficient to achieve an antibacterial action, namely exceeding the minimum inhibitory concentration (MIC) of the possible pathogen for the length of the procedure (4). Cefazolin, which is the mainstay of surgical infection prophylaxis, exhibits timedependent pharmacokinetics rather than concentration-dependent pharmacokinetics, with no dosedependent enhancement of antibacterial efficacy at elevated doses. Cefazolin is a hydrophilic antibiotic that fails to penetrate adipose tissue, irrespective of the intravenous dosage administered. Increased dosages lead to correspondingly elevated blood and non-adipose tissue concentrations, whereas adipose tissue concentrations remain unchanged. Thus; an increased dosage or redosage of antibiotic prophylaxis may not be effective in obese patients (2).

In 2017, the CDC did not find adequate high-quality evidence to assess the benefits of intraoperative redosing of antibiotics for infection prophylaxis; however, from a pharmacokinetic perspective, supplementary intraoperative doses should be administered for procedures lasting longer than two antibiotic half-lives or for those involving substantial blood loss (exceeding 1.5 L). This ensures an antibiotic concentration exceeding the minimal inhibitory concentration at the surgical site for the entire procedure (5). A recently published meta-analysis validated the significance of antibiotic redosing. Despite the variability in the antibiotics used, intraoperative redosing of prophylactic antibiotics lowered infection rates compared to a single preoperative dose across all surgical procedures. In a cefazolin case with a half-life of roughly 2 hours, an extra intraoperative dose should be administered after approximately 4 hours (6). Another study has demonstrated that inadequate re-dosing of preventive antibiotics during prolonged surgeries may elevate the risk of infections (7). A comprehensive multicenter collaborative investigation demonstrated a correlation between the timing of antibiotics and infection risk, confirming that intraoperative re-dosing seems to diminish infection risk in procedures beyond 4 hours, contingent upon the accurate administration of the preoperative dose (8).

The intraoperative re-administration of prophylactic antibiotics may serve as an independent preventive factor against infection in diabetic patients. A targeted perioperative antibiotic administration protocol should be advocated for diabetic patients undergoing extended procedures to reduce the risk of infection (9).

Available data in the literature concerning the influence of blood loss during surgery on serum antibiotics concentration is is highly confined. For orthopedic procedures, a previous study examining vancomycin showed modest negative correlation between amount of blood loss and intraoperative serum vancomycin levels, without significance (10). Consequently, blood loss during orthopedic surgeries is likely to have negligible effects on the intraoperative kinetics of vancomycin. Redosing is rarely warranted.

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