1.4. PREVENTION: ANTIMICROBIALS (LOCAL)

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QUESTION 1: Is there sufficient evidence to support the use of antibiotic-loaded cement in primary total knee arthroplasty (TKA) or total hip arthroplasty (THA) to reduce the risk of surgical site infections/periprosthetic joint infections (SSIs/PJIs)?

RECOMMENDATION: There is no conclusive evidence to demonstrate that routine use of antibiotic-loaded cement in primary TKA or THA reduces the risk of subsequent SSIs/PJIs. Recent high level evidence and registry data has not demonstrated a reduction in SSI/PJIs. Furthermore, the added cost, the potential for the emergence of resistant organisms and the potential adverse effect of antibiotics on the host provide adequate reasons to refrain from routine use of antibiotic loaded cement during primary total joint arthroplasty.

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 38%, Disagree: 58%, Abstain: 4% (NO Consensus)

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QUESTION 2: Is there a role for the use of antibiotic-impregnated cement in primary total joint arthroplasty (TJA)?

RECOMMENDATION: Antibiotic-impregnated cement may be used during primary TJA to reduce the risk of surgical site infections/periprosthetic joint infections (SSIs/PJIs). The benefits of antibiotic-impregnated cement versus its cost and other potential adverse effects, may be most justified in patients at high risk of infection

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 93%, Disagree: 7%, Abstain: 0% (Super Majority, Strong Consensus)

RATIONALE

The concept of using bone cement as a depot for antibiotics makes sense, as it allows for delivery of antibiotics directly to the site of potential infection. However, its role in the prevention of infection remains controversial [1–3].

The elution profile of cemented antibiotics has been evaluated, which demonstrates the elution kinetics of vancomycin, tobramycin, gentamicin, moxifloxacin and clindamycin are better than cefazolin, daptomycin, meropenem, ertapenem, cefotaxime, ampicillin, amoxicillin-clavulanate and cefepime [4–6]. Thus, the two most common antibiotics mixed with bone cement are vancomycin and aminoglycosides such as tobramycin and gentamicin.

Recent annual arthroplasty registries have shown that 96.3% of total knee arthroplasties (TKAs) and 93.7% of total hip arthroplasties (THAs) using cement, used antibiotic-loaded cement [7]. Plain cement has a slightly higher rate of revision than antibiotic-loaded cement when used in TKA [7]. Likewise, in THA, a lower rate of revision is observed for antibiotic-loaded cement in the first five years from surgery [7]. However, the rates of revision in THA were no different between antibiotic-loaded and plain cement beyond five years [7].

Commercially available antibiotic-loaded cements include Palacos® R+G (Zimmer Biomet), Simplex™ P with Tobramycin (Stryker), Smartset™ GHV (DePuy) or Refobacin® (BioMet), but several concerns remain about having readily available antibiotic-loaded cements. Studies have raised concerns regarding the following: (a) increasing microbial resistant; (b) insufficient dose of antibiotic in commercial preparations; (c) additional unnecessary cost; and (d) reduced mechanical properties of antibiotic-loaded cement [7–10].

While most primary THAs in the United States are done with cementless fixation [11], cemented THA is still commonly used in other geographic regions of the world. In the case of cemented arthroplasty, a retrospective comparison study on the use of antibiotic-loaded cement demonstrated an approximately 50% lower infection rate and lower rate of wound infection [11,12]. In addition to lower rates of infection, there is evidence that the addition of antibiotics to the cement leads to a reduction of all time failures of THA [13,14]. Results of a recent systematic review and meta-analysis on 12 clinical trials showed that conventional ventilation together with systemic antibiotics and antibiotic-loaded cement was most likely to provide the best protection against THA-related SSIs [15].

Previous evidence has shown that antibiotic-loaded cement together with systemic antibiotic prophylaxis was effective in reducing PJI in TKA compared with plain cement and systemic antibiotic prophylaxis [16–18]; however, new evidence does not support these results. Two recent prospective studies showed that antibiotic-loaded cement did not reduce the rate of deep infection following primary TKA compared with plain cement [19,20]. More recently, a systematic review on the use of antibiotic-loaded cement in total joint arthroplasty evaluated six articles encompassing 6,318 arthroplasties. Among the study population, 3,217 of these arthroplasties received antibiotic-loaded cement and 3,101 arthroplasties served as the control. Only two studies showed a significant effect of antibiotic-loaded cement in preventing deep infection in primary TKA. Contra-

dictory results were reported in the remaining four prospective and randomized clinical trial studies that showed no statistical difference between the two groups in terms of the incidence of deep or superficial SSIs [21]. In another meta-analysis, Kleppel et al. reported on 4,092 patients following TKA (3,903 primary TKA and 189 revision TKA). At the average follow-up time of 47.2 months for primary TKA, the use of antibiotic-loaded cement did not have a significant reduction in PJI/SSI [22]. Additionally, an analysis of 64,566 joints from the New Zealand Joint Registry demonstrated that the use of antibiotic-laden cement was actually associated with an increase in revision for PJI after a multivariate analysis (odds ratio (OR) 1.93, 95% confidence intervals (CI) 1.19 to 3.13) [23].

We must also consider the cost associated with the use of the antibiotic-loaded cement. Industrially manufactured antibiotic-loaded bone cement may be preferred, due to the ease of access [24]. However, biomechanical and elution testing has demonstrated 1-gram of vancomycin in handmade antibiotic-loaded cement can reduce the cost without compromising the mechanical strength or elution of the drug [25]. Additionally, vancomycin potentially has a higher antimicrobial activity when compared with gentamicin for methicillin-resistant *Staphylococcus aureus* (MRSA) while remaining heat-stable with adequate elution [26–28].

Overall, the literature still lacks an appropriately sized randomized clinical trial to better support the use of antibiotic-loaded cement.

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QUESTION 3: What is the optimal antibiotic(s) dosage to be used in cement during reimplantation that does not significantly interfere with the mechanical strength of cement used for fixation?

RECOMMENDATION: The mechanical strength of most cement is maintained if ≤5% (w/w) of antibiotics is added (equating to 2 grams in a 40 gram packet).

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 92%, Disagree: 3%, Abstain: 5% (Super Majority, Strong Consensus)