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QUESTION 2: Is there a role for the addition of gentamicin to perioperative prophylactic antibiotics in spine surgery?

RECOMMENDATION: No, we recommend AGAINST the inclusion of gentamicin for perioperative prophylaxis in spine surgery. There is no data suggesting that the addition of gentamicin to systemic perioperative prophylactic antibiotic regimens decreases the rate of postoperative infections, and strong evidence showed that it is associated with harm (namely nephrotoxicity). The question of the use of local/topical gentamicin is unresolved.

LEVEL OF EVIDENCE: Strong

DELEGATE VOTE: Agree: 62%, Disagree: 15%, Abstain: 23% (Super Majority, Weak Consensus)

RATIONALE

The use of gentamicin to expand the gram-negative activity for perioperative antimicrobial prophylaxis in spine surgery has been considered for decades, yet positive outcomes data for this practice are lacking. Pons et al. reported on a randomized, blinded study of 826 patients undergoing neurosurgical procedures, including spine surgery, and found similar surgical site infection (SSI) rates for those assigned to ceftizoxime or vancomycin and gentamicin [1]. Ramo et al. reported on a multivariate analysis of 428 posterior spinal fusion patients and found that the addition of an aminoglycoside did not lower the SSI rate [2]. In a mixed population of more than 11,000 orthopaedic surgery patients treated over 5 years in the United Kingdom, Walker et al. noted no difference in SSI rates during a period when a combination of flucloxacillin and gentamicin was given for prophylaxis compared to one where co-amoxiclav was the prophylactic regimen of choice [3].

The association of aminoglycoside prophylaxis (even single-dose) for orthopaedic surgery and acute kidney injury (AKI) has now been well-documented. Dubrovskaya et al. reviewed more than 4,000 patients undergoing orthopaedic surgery, comparing those receiving a single dose of gentamicin combined with another antibiotic to those receiving non-aminoglycoside prophylaxis alone. Although for all patients the addition of gentamicin was not associated with AKI, gentamicin was associated with a statistically significantly higher rate of AKI for those undergoing spine surgery [4]. Bell et al. reported on a Scottish initiative where routine surgical prophylaxis was changed from cefuroxime to flucloxacillin and gentamicin (single-dose) between 2006 and 2010. Among 7,666 patients undergoing orthopaedic surgery, the gentamicin-containing regimen was associated with a 94% higher incidence of AKI [5]. Finally, in the previously-cited study by Walker et al., a change from routine prophylaxis with flucloxacillin and gentamicin to co-amoxiclav alone was associated with a 63% reduction in postoperative AKI [3].

Two meta-analyses on the association of gentamicin prophylaxis with nephrotoxicity have been published. Luo et al. compared the use of gentamicin and flucloxacillin to cefuroxime alone in studies of diverse surgery types. The risk of postoperative renal impairment was higher in the gentamicin group, especially for those undergoing orthopaedic surgery [6]. Srisung et al. analyzed 11 studies containing 18,354 patients comparing gentamicin versus non-gentamicin surgical prophylaxis regimens. Using random effects modeling, gentamicin prophylaxis in orthopaedic surgery was associated with a significantly higher risk of AKI (risk rate (RR) 2.99; 95% confidence interval (CI): 1.84, 4.88) [7].

Data regarding the use of topical or local wound gentamicin are limited. In a single-center study, van Herwijnen et al. reported a higher SSI rate for patients undergoing scoliosis surgery who received wound irrigation with gentamicin versus povidone-iodine [8]. On the other hand, Borkhuu et al. reported on 220 children undergoing spinal fusion and found a four-fold reduction in SSI for those treated with gentamicin-impregnated bone allograft [9]. Han et al. retrospectively analyzed data from 399 patients undergoing spine surgery. Among patients who had a gentamicin-impregnated collagen sponge applied to their wound, the SSI rate was 0.8%, versus 5% for those treated without the sponge [10]. At this time, however, given the variability in reported application methods for local gentamicin and the small number of patients studied, the routine use of topical gentamicin cannot be recommended.

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QUESTION 3: Should prophylactic antibiotic prophylaxis be repeated during spine surgery? If so, when?

RECOMMENDATION: In most uncomplicated spinal procedures, a single preoperative dose of prophylactic antibiotics is sufficient. Prophylactic antibiotics should be redosed intraoperatively for procedures lasting longer than twice the half-life of the antibiotic, or if there is excessive blood loss (blood loss > 1,500 mL) in order to ensure therapeutic levels.

LEVEL OF EVIDENCE: Limited

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

RATIONALE

There are no randomized spine studies that compare the effectiveness of redosing prophylactic antibiotics during surgery to preoperative antibiotics alone. Therefore, this review was expanded to include other surgical subspecialties. Several major guidelines including those from the North American Spine Society (NASS), Infectious Disease Society of America (IDSA) and Surgical Infection Society (SIS) have made similar recommendations supported by pharmacokinetic data and retrospective studies [1,2]. Furthermore, the Centers for Disease Control and Prevention (CDC) recently noted that there is insufficient-quality evidence to make a recommendation regarding whether or not antibiotics should be redosed intraoperatively [3].

In a prospective study of 57 subjects undergoing elective surgery, an analysis of intraoperative serum cefazolin concentrations at approximately 3.5 hours after receiving a preoperative dose showed that antibiotic concentrations dropped below the minimum inhibitory concentration (MIC) for methicillin-susceptible *Staphylococcus aureus* (MSSA) and *Escherichia Coli* (*E. Coli*) [4]. Ohge and colleagues found that cefazolin concentrations had dropped below 80% of the MIC in the adipose tissue and peritoneum for multiple bacteria three hours after the preoperative dose was administered [5]. In a prospective study of 11 elective instrumented spinal procedures with a large expected blood loss, estimated blood loss (EBL) was found to have a strong negative correlation with cefazolin tissue concentrations ($r = -0.66$, $p = 0.5$). Based on the pharmacokinetic values, the authors recommended that procedures with an EBL greater than 1,500 mL should receive an additional dose of cefazolin [6].

In a retrospective study of 1,548 patients undergoing cardiac surgery, intraoperative redosing for procedures lasting greater than 400 minutes was shown to reduce the risk of surgical site infections (SSIs) (adjusted OR 0.44, 95% CI 0.23-0.86) [7]. Similarly, Scher et al. demonstrated that for surgeries longer than three hours, patients who were redosed with cefazolin intraoperatively had a lower SSI rate than those who only received preoperative cefazolin (6.1% vs. 1.3%, $p < 0.01$) [8]. In another retrospective review of 4,078 patients undergoing various general surgery procedures, cases with an EBL of greater than 500 mL or those that were not re-dosed intraoperatively during longer cases were associated with a higher rate of SSI [9].

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