

### QUESTION 3: What is the optimal antibiotic for perioperative prophylaxis in methicillin-resistant *Staphylococcus aureus* (MRSA) carriers who are undergoing orthopaedic procedures?

RECOMMENDATION: Vancomycin or teicoplanin is recommended as a perioperative prophylactic antibiotic agent for the current MRSA colonizer undergoing total joint arthroplasty (TJA).

LEVEL OF EVIDENCE: Moderate

DELEGATE VOTE: Agree: 94%, Disagree: 4%, Abstain: 2% (Super Majority, Strong Consensus)

#### RATIONALE

MRSA surgical site infections (SSIs) are an increasing concern after orthopaedic surgical procedures [1]. It is well-known that MRSA colonization is an independent major risk factor of MRSA SSIs [2–4]. Efforts have been made to screen for MRSA carriers and decolonize preoperatively using nasal mupirocin ointment or povidone iodine [5–7]. However, after the decolonization protocol [8,9], questions still exist as to which glycopeptide (such as vancomycin or teicoplanin) is recommended as the preferred prophylactic preoperative antibiotic for MRSA carriers [10].

Despite the vast body of literature investigating the effect of different antibiotic treatments in various kinds of surgical procedures, to the best of our knowledge, only a few studies have compared SSI rates after orthopaedic surgery among different antibiotic prophylactic regimens in MRSA carriers [11,12]. Iqbal et al. reported in a retrospective study of orthopaedic trauma patients that, among 27 MRSA carriers, none of the 5 patients who received teicoplanin developed SSIs, whereas 5 out of 22 patients who received cefuroxime developed MRSA SSI [11]. However, Gupta et al. demonstrated different results in their retrospective cohort study of veterans undergoing surgical procedures including orthopaedic surgery. They showed that vancomycin prophylaxis was not associated with a significant risk reduction of SSIs compared to other antibiotics in MRSA carriers with a relative risk (RR) of 0.61 (95% confidence interval (CI) 0.06 to 5.75) [12]. Nevertheless, both studies were retrospective observational studies with flaws that could be classify them as very low-quality.

Although little has been studied in MRSA carriers undergoing orthopaedic surgery, there are several studies that compared MRSA SSI rate between different prophylactic antibiotics in patients undergoing orthopaedic surgery regardless of preoperative MRSA colonization [13–22]. Two moderate-quality randomized controlled trials [16,17] and six low to very low-quality observational studies [14,15,18–21] compared MRSA SSI rate between glycopeptides and first or second-generation cephalosporins. Although two randomized controlled trials (RCTs) [16,17] have shown no significant difference in MRSA SSI development between glycopeptides and cephalosporins, a random effects model meta-analysis of a total of eight studies [14–21] has shown a significantly lower risk in the glycopeptide group (pooled RR: 0.29, 95% CI 0.14 to 0.62,  $p = 0.001$ ,  $I^2 = 10\%$ ). Subgroup analysis has also revealed that, compared to cephalosporins, both vancomycin and teicoplanin demonstrate lower risks of MRSA SSI after orthopaedic surgery (RR: 0.36, 95% CI 0.15 to 0.90; RR: 0.16, 95% CI 0.04 to 0.65, respectively). Among the eight studies, three [15,18,20] compared dual prophylactic antibiotics (glycopeptide + cephalosporin) with cephalosporin alone. When a selective analysis was performed excluding these three studies, pooled RR was 0.47 with 95% CI of 0.21 to 1.05  $I^2 = 0\%$ .

As a result, we recommend vancomycin or teicoplanin as a preoperative antibiotic prophylaxis for MRSA carriers, however, with a moderate level of strength due to the lack of high-quality studies performed on MRSA carriers.

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