

Antibiotic Prophylaxis in Periprosthetic Joint Infection (PJI): Literature Review and World Consensus (Part Six)

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Abstract

Context: There is a need to find the recommended perioperative antibiotic prophylaxis for current MRSA carriers and to determine if patients with prior history of MRSA should be re-screened and what should the choice of perioperative prophylactic antibiotics be in these patients. There is also a need to determine the recommended prophylaxis in patients undergoing major orthopaedic reconstructions for either tumor or non-neoplastic conditions using megaprosthesis or allograft.

Evidence Acquisition: Delegates in workgroup 3 of the consensus meeting on PJI reviewed English literature for relevant articles. 30 of 221 articles were relevant to the 4 following questions regarding perioperative antibiotic prophylaxis to prevent PJI.

Results: For current MRSA carriers, vancomycin or teicoplanin is the recommended perioperative antibiotic prophylaxis. Patients with prior history of MRSA should be re-screened preoperatively. If patients are found to be negative for MRSA, we recommend routine perioperative antibiotic prophylaxis. Until the emergence of further evidence, we recommend the use of routine antibiotic prophylaxis for patients undergoing major reconstructions such as allograft or megaprotheses.

Conclusions: Based on evidences in the literature and consensus of expert delegates from consensus meeting recommendations for type of antibiotic prophylaxis in patients who are current MRSA carriers, the protocol for screening and type of prophylactic antibiotics for patients with prior history of MRSA and antibiotic prophylaxis for patients undergoing major reconstructions such as megaprosthesis and allograft were provided.

Keywords: Infection, Joint, Periprosthetic

1. Context

Decision making in choosing the appropriate antibiotic prophylaxis for current carriers, need for screening of patients with history of MRSA and type of antibiotic prophylaxis and type of antibiotic prophylaxis for patients undergoing major reconstructions such as megaprosthesis or allograft need to be defined.

2. Evidence Acquisition

From November 2012 till August 2013, 400 delegates from all over the world formed 15 workgroups to review the current literature and find high level evidence for all issues related to PJI. Workgroup No.3 (authors) was assigned to review current literature on perioperative antibiotics. The goal was to find answers and recommendations for more than 264 questions based on the high level evidence

if present or reach to a consensus when there is a lack of high level evidence.

After 10 months of hard work by delegates from 58 countries and 100 societies, relevant publications reviewed, communications exchanged and finally a draft was prepared to be presented for vote at the final meeting on 1st of August 2013. The draft included recommendations for management on the basis of high level of evidence if present. Otherwise the cumulative wisdom of 400 delegates from 58 countries and over 100 societies used to reach consensus about practices lacking higher level of evidence.

3. Results

3.1. Question 17A

What type of perioperative antibiotic prophylaxis is recommended for current MRSA carriers?

3.2. Consensus

For current MRSA carriers, vancomycin or teicoplanin is the recommended perioperative antibiotic prophylaxis.

3.3. Delegate Vote

Agree: 86%, disagree: 12%, abstain: 2% (strong consensus).

3.4. Question 17B

Should patients with prior history of MRSA be re-screened? What should the choice of perioperative prophylactic antibiotics be in these patients?

3.5. Consensus

Patients with prior history of MRSA should be re-screened preoperatively. If patients are found to be negative for MRSA, we recommend routine perioperative antibiotic prophylaxis.

3.6. Delegate Vote

Agree: 76%, disagree: 23%, abstain: 1% (strong consensus)

3.7. Justification

Implementation of a MRSA prevention program may significantly reduce MRSA SSIs. However, it is unlikely that any single MRSA-specific intervention (such as adding or switching to vancomycin) can optimally prevent SSIs. Several studies provide convincing data on the clinical effectiveness of vancomycin in preventing SSIs when MRSA prevalence is high (1-3). Further research is needed to determine which components of a MRSA prevention program are essential in successfully preventing MRSA SSIs (4). It is uncertain whether decontamination should alter the type of antibiotic prophylaxis, as few studies have retested patients for MRSA status immediately prior to surgery.

The AAOS recommendations for the use of IV antibiotic prophylaxis in primary TJA, recommendation (5), states that vancomycin may be used in patients with known colonization with MRSA or in facilities with recent MRSA outbreaks. Additionally, the Society for Healthcare Epidemiology of America recently recommended routine surveillance cultures at the time of admission to the hospital for patients at high risk of MRSA (6). Walsh *et al.* implemented a comprehensive MRSA program in which vancomycin was added to the routine cefazolin prophylaxis regimen for patients who tested positive for nasal MRSA carriage. Other components of the program included decolonization of all cardiothoracic staff who screened positive for nasal MRSA carriage, application of nasal mupirocin ointment for 5

days in all patients starting one day before surgery, application of topical mupirocin to exit sites after removal of chest and mediastinal tubes, and rescreening of patients for MRSA colonization at the time of hospital discharge. This program resulted in a significant reduction in the SSI rate (2.1% vs. 0.8%, $P < 0.001$) as well as a 93% reduction in postoperative MRSA wound infections (from 32 infections/2,767 procedures during the 3 year pre-intervention period to 2 infections/2,496 procedures during the 3 year postintervention period). The data suggest that a bundled approach to preventing MRSA SSIs may be more critical than a single intervention (3).

Pofahl *et al.* published on the impact of introducing MRSA screening programs and treatment of subsequent MRSA SSIs. After a MRSA surveillance program was instituted, the rate of MRSA SSI decreased from 0.23% to 0.09%, with the most pronounced reduction seen in TJA procedures (0.30% to 0%, $P = 0.04$). However, the authors note that changes in perioperative antibiotics in MRSA-positive patients was at the discretion of the attending surgeon (7).

3.8. Question 18

What is the recommended prophylaxis in patients undergoing major orthopaedic reconstructions for either tumor or non-neoplastic conditions using megaprosthesis?

3.9. Consensus

Until the emergence of further evidence, we recommend the use of routine antibiotic prophylaxis for patients undergoing major reconstruction.

3.10. Delegate Vote

Agree: 93%, disagree: 6%, abstain: 1% (strong consensus)

3.11. Justification

Deep infection has been reported as being one of the most common complications following endoprosthetic replacement of large bone defects, ranging between 5% - 35% in some series. Despite this there is insufficient (8-12). Reinfection rates after revision surgery for endoprosthetic infection have been reported as high as 43% (11). Despite this there is insufficient evidence to suggest that a different perioperative antibiotic regimen is warranted. Recently a multicenter, blinded, randomized, controlled trial, using a parallel two-arm design has been set up that will evaluate 920 patients from Canada and the USA who are undergoing surgical excision and endoprosthetic reconstruction of a primary bone tumor. The patients will receive either short (24 hours) or long (5 days) duration postoperative antibiotics. The primary outcome will be rates of deep postoperative infections in each arm. Secondary outcomes

will include type and frequency of antibiotic-related adverse events, patient functional outcomes and quality-of-life scores, reoperation and mortality (13).

Another area of development involves silver coating of foreign materials, such as heart valves, cardiac catheters, and urinary catheters, that has shown the ability to reduce the infection rate of medical devices; therefore, a logical extension of this work was to translate this concept to the field of endoprosthetics (14, 15). Both basic science and clinical research suggests a decreased incidence of SSI and PJI in endoprostheses coated with silver. Recently iodine-supported titanium implants have been also effective for preventing and treating infections after major orthopaedic surgery (16, 17).

In a rabbit study, the infection rate of silver-coated versus noncoated prostheses after inoculation with *Staphylococcus aureus* was determined and the silver concentrations in blood, urine, and organs with possible toxic side effects were documented. The authors convincingly demonstrated that megaprotheses coated with silver showed a significantly lower infection rate (7% vs. 47%, $P < 0.05$) in comparison with a titanium group (18). Furthermore, measurements of C reactive protein, neutrophilic leukocytes, rectal temperature, and body weight showed significantly lower ($P < 0.05$) signs of inflammation in the silver group. In a second study, authors analyzed the potential toxicological side effects of these implants and found that the silver concentration in blood (median 1.883 parts per billion (PPB)) and in organs (0.798 - 86.002 PPB) showed elevated silver concentrations, without pathologic changes in laboratory parameters and without histologic changes of organs (19).

In a prospective observational study, Hardes et al. (18) compared the infection rate in 51 patients with sarcoma (proximal femur, $n = 22$; proximal tibia, $n = 29$) who underwent placement of a silver-coated megaprosthesis to 74 patients (proximal femur, $n = 33$; proximal tibia, $n = 41$) in whom an uncoated titanium megaprosthesis was used. The authors reported a substantial reduction in the infection rate from 17.6% in the titanium group compared to 5.9% in the silver group ($P = 0.06$). Furthermore, while 38.5% of patients ultimately underwent amputation when PJI developed, this was not necessary in any case in the study group. However, the authors note that the operating time required for the proximal tibia replacement was significantly shorter in the silver-coated prosthesis group ($P = 0.034$) and that prolonged operating time was associated with a higher rate of PJI ($P = 0.025$).

The same group reported a lack of toxicological side effects of silver-coated megaprotheses in 20 patients with bone metastases (18). They reported that silver levels in the blood did not exceed 56.4 PPB and can be considered

non-toxic. They further excluded significant changes in liver and kidney function based on laboratory values; and histopathologic examination of the periprosthetic environment in two patients showed no signs of foreign body granulomas or chronic inflammation, despite effective silver concentrations up to 1,626 PPB directly related to the prosthetic surface (18).

Tsuchiya et al. reported that iodine-supported implants were used to prevent infection in 257 patients with compromised status. Acute infection developed only in 3 tumor cases and one diabetic foot among the 257 patients. Abnormalities of thyroid gland function were not detected. None of the patients experienced loosening of the implant. Excellent bone ingrowth was found around all hip and tumor prostheses. The results indicate that iodine-supported titanium has favorable antibacterial activity, biocompatibility, and no cytotoxicity (16).

Gosheger reviewed 197 patients with megaprotheses and discovered that those with cobalt chrome implants had more infections than those with titanium implants (20). Reviewing 197 patients (77 patients with a cobalt chrome alloy system and 120 patients with a titanium alloy system) who underwent lower extremity reconstruction with a megaprosthesis, the authors reported a 31.2% infection rate in the cobalt chrome group compared to 14.2% in the titanium group ($P < 0.01$). When they performed a secondary analysis matching two identical subgroups, the cobalt chrome group was still associated with a significantly higher infection rate, with 5 infections of 26 megaprotheses vs one infection of 36 titanium megaprotheses ($P < 0.05$) (21).

3.12. Question 19

Should antibiotic prophylaxis be different in patients who have reconstruction by bulk allograft?

3.13. Consensus

We recommend the use of routine antibiotic prophylaxis in patients who have reconstruction by bulk allograft.

3.14. Delegate Vote

Agree: 93%, disagree: 5%, abstain: 2% (strong consensus)

3.15. Justification

The periprosthetic area is inherently a locus minoris resistance. Bulk allograft is in essence is a large foreign body and therefore represents a nidus for deep infection following surgery, apart from the prosthetic components.

Additionally, bulk allografts are used most often in the setting of revision arthroplasty when there is frequently additional local soft tissue and vascular compromise, which compounds the risk for infection. Therefore, it would seem reasonable to want to modify the perioperative antibiotic protocol to protect these reconstructions. Unfortunately, there is insufficient literature to support altering antibiotic regimens, as most studies on the use of bulk allograft do not indicate or detail the antibiotic regimens utilized. Even if this data were available, it would not be accurate to properly compare the infection rates of different clinical series based on their perioperative antibiotic protocols because of the heterogeneity of patient populations. However, there is a growing body of literature to support the use of antibiotic-impregnated allograft in the revision setting as a means of decreasing infection rates. In addition, there are several reports of using antibiotic impregnated graft substitute or grafts as a way to fill bony defects and promote bony ingrowth while delivering supra-therapeutic doses of antibiotics to the local environment in cases of osteomyelitis. While there is no current literature applying this technology to the use of bone defects in infected revision arthroplasty, it may be a promising technique.

Witso *et al.* used netilmicin-impregnated allografts for reconstruction in revision hip and knee surgery and found no adverse effects (22). Buttaro *et al.* (23) favorably used vancomycin supplemented cancellous grafts for reconstruction after infected THA (20, 23). Michalak *et al.* and Khoo *et al.* impregnated segmental allografts with gentamicin and flucloxacillin respectively (24, 25). However, all these groups used antibiotic impregnated grafts only in the second stage of a two-stage revision, after resolution of clinical and laboratory evidence of infection.

Winkler *et al.* performed 37 one-stage uncemented revision THAs using cancellous allograft bone impregnated with antibiotics and noted a 92% success rate, defined as recurrent infection at a mean follow-up of 4.4 years (range 2 - 8 years). In addition, no adverse effects were seen and the incorporation of bone graft was comparable to unimpregnated grafts (26).

In a similar series, Buttaro analyzed the incidence of infection after one-stage aseptic revision hip reconstruction using acetabular and/or femoral vancomycin-impregnated impacted bone allograft and a THA fixed with cement containing no antibiotic. In 75 consecutive patients (80 hips), followed for a mean of 36 months (range 24 - 59 months), deep infection occurred in one patient for an incidence of infection of 1.25%, which occurred 2 years after the index procedure and was thought to be hematogenous in origin (27).

Cancellous bone allograft can store and release high

initial local amounts of vancomycin without compromising incorporation of the graft, and some favorable results have been published following two-stage revision of infected THA with this technique (20, 23, 28-30)

4. Conclusions

4.1. Question 17A

What type of perioperative antibiotic prophylaxis is recommended for current MRSA carriers?

4.2. Consensus

For current MRSA carriers, vancomycin or teicoplanin is the recommended perioperative antibiotic prophylaxis.

4.3. Consensus

Delegate Vote: Agree: 86%, disagree: 12%, abstain: 2% (strong consensus)

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Should patients with prior history of MRSA be re-screened? What should the choice of perioperative prophylactic antibiotics be in these patients?

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What is the recommended prophylaxis in patients undergoing major orthopaedic reconstructions for either tumor or non-neoplastic conditions using megaprosthesis?

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4.9. Delegate Vote

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Should antibiotic prophylaxis be different in patients who have reconstruction by bulk allograft?

4.11. Consensus

We recommend the use of routine antibiotic prophylaxis in patients who have reconstruction by bulk allograft.

4.12. Delegate Vote

Agree: 93%, disagree: 5%, abstain: 2% (strong consensus)

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