G37: Are there any concerns for the use of topical antibiotics (e.g. vancomycin) in patients undergoing major orthopedic surgery?

Edward Vasarhelyi, Sebastian Braun, Li Bingyun, Daniel Ramierz, Justinas Stucinskas, Gwo Lee, Thananjeyen Srirangarajan

Response/Recommendation: Topical antibiotics (TA) have been associated with rare complications, including aseptic wound complications, delayed wound healing, and systemic absorption risks potentially resulting in nephrotoxicity. There are also theoretical concerns for an increased risk of antibiotic resistance or tissue toxicity leading to delayed bone healing/fusion.

Level of Evidence: Moderate

Delegate Vote:

Rationale:

Surgical site infections (SSI) and periprosthetic joint infections (PJI) remain significant challenges in major orthopedic surgeries. The incidence rates of SSI and PJI range from 0.4% to 2.4% in primary joint arthroplasties and can reach up to 10% in revision surgeries (1–4). These infections impose a significant burden on patients through prolonged recovery times and reduced quality of life, while also placing considerable financial and logistical strain on healthcare systems (5–7). The management of these infections is further complicated by the growing prevalence of antibiotic-resistant organisms, which limit the effectiveness of traditional systemic therapies (8).

Topical antibiotics (TA), including vancomycin powder, antibiotic-loaded polymethylmethacrylate (PMMA), intra-articular infusion and advanced carriers like calcium sulphate (CS), hydrogels and collagen fleece, have emerged as strategies for preventing and treating infection. When treating PJI and complex bone infection, these modalities offer localized, high-dose antimicrobial delivery, targeting pathogens directly at the surgical site while minimizing systemic toxicity (8–12). Additionally, they address the challenge of biofilm-associated infections in poorly vascularized tissues (13).

Despite their potential, the use of TA raises several concerns, including the risk of local wound complications, tissue toxicity, concerns of antibiotic resistance, and variable efficacy due to inconsistent application techniques (14,15). Understanding these factors is crucial for optimizing their use in orthopedic surgeries.

To address the question posed above, we performed a comprehensive systematic review to identify literature that directly addressed the safety of topical antibiotics, exploring diverse delivery methods such as powders, liquids, ceramic beads, PMMA, and biodegradable materials, with a focus on safety and cost-effectiveness.

Hypersensitivity Reactions: Reports of allergic reactions, including hypersensitivity, have been rare in the included studies, with a single case of anaphylaxis reaction attributable to topical

rifampicin. Nonetheless, caution should be exercised, particularly in patients with known sensitivities to antibiotics like vancomycin (16,17). Milder hypersensitivity reactions such as localised pruritic or erythematous skin changes can occur and may warrant close monitoring and consideration for allergic testing (18).

Wound Complications: High concentrations of TA, particularly vancomycin powder and CS beads, are associated with aseptic wound complications. These complications, which may include delayed wound healing, seroma formation, and wound dehiscence, could potentially impact overall surgical outcomes and necessitate further intervention (19,20). The presence of CS beads has been linked to increased wound drainage, possibly due to their rapid dissolution and osmotic effects, which may delay wound closure and healing (21,22). Furthermore, factors such as patient comorbidities and surgical technique of where the TA are applied may influence the incidence and severity of these complications.

Systemic Absorption and Toxicity: Although designed for localized delivery, systemic side effects of glycopeptides have been observed, occasionally leading to complications such as acute kidney injury (23,24). There have been no concerns of clinically significantly raised serum levels or ototoxicity with topical glycopeptides (25). Clinicians should remain vigilant in patients with pre-existing renal impairment or those receiving concurrent nephrotoxic medications. Monitoring renal function postoperatively in high-risk individuals may be advisable (26). Despite the low risk of systemic toxicity, consideration to evaluate the pharmacokinetics of TA in different patient populations can refine safety recommendations.

Tissue Toxicity: There are no significant clinical evidence in orthopedics that attributes the use of TA to cytotoxic effects that contribute to pseudoarthrosis in spinal surgery or delayed/non-union in trauma surgery (27–29). *In vitro* studies have indicated that high concentrations of certain antibiotics may have transient inhibitory effects on osteoprogenitor proliferation, but these effects appear to be dose-dependent and not clinically relevant in orthopaedic applications (30). Additionally, the incorporation of antibiotics into biomaterials such as PMMA or collagen fleece have not been associated with compromised bone healing, supporting the overall biocompatibility of these delivery systems (12,31). An improved understanding of long-term bone healing outcomes with different antibiotic carriers may further strengthen clinical recommendations.

Antibiotic Resistance: The potential correlation between the use of topical antibiotics and emergence of antimicrobial resistance has not been explored in orthopedic surgery. This theoretical association has been the impetus behind the recommendations from various authorities, including the Center for Disease Control, to avoid placing topical antibiotics in the wound. This issue needs to be studied further in the future. However, the unique pharmacokinetic profile of TA potentially allows for high initial peak concentrations that rapidly reduce bacterial loads, decreasing the selective pressure that promotes resistance (32). When combined with systemic antibiotics, this dual approach enhances infection prevention by providing both immediate localized action and sustained systemic coverage (33). Evidence in bone infection management suggests that using antibiotic combinations in local carriers may further mitigate resistance risks while improving bactericidal efficacy (34,35). To maximize

these benefits, appropriate dosing strategies and adherence to evidence-based protocols may improve standardization.

Economic Considerations: Vancomycin powder is relatively inexpensive, but its routine use must be weighed against its potential to prevent costly reoperations due to infection. Multiple studies in spinal surgery have demonstrated cost savings of over $100 000 per 100 spinal fusion operations with the use of prophylactic TA (16,36). Variability in application modalities and indications complicates cost-effectiveness analyses. Newer carriers, such as hydrogels and collagen fleece, may offer improved efficacy but often come at higher costs.

In conclusion, topical antibiotics, like vancomycin, may have a role in reduction of infections in major orthopedic surgeries, particularly for high-risk patients. However, concerns about aseptic wound complications, and systemic toxicity must be considered. The need for standardized protocols and high-quality evidence is paramount to ensure their safe and effective use. Future research should prioritize long-term safety evaluations to guide clinical decision-making.

REFERENCES

1. Edwards JR, Peterson KD, Mu Y, Banerjee S, Allen-Bridson K, Morrell G, et al. National Healthcare Safety Network (NHSN) report: data summary for 2006 through 2008, issued December 2009. Am J Infect Control. 2009 Dec;37(10):783–805.

2. Kamath AF MD, Ong KL PhD, Lau E MS, Chan V MPH, Vail TP MD, Rubash HE MD, et al. Quantifying the Burden of Revision Total Joint Arthroplasty for Periprosthetic Infection. The Journal of arthroplasty. 2015;30(9):1492–7.

3. Bozic KJ, Kurtz SM, Lau E, Ong K, Vail TP, Berry DJ. The epidemiology of revision total hip arthroplasty in the United States. J Bone Joint Surg Am. 2009 Jan;91(1):128–33.

4. Bozic KJ, Kurtz SM, Lau E, Ong K, Chiu V, Vail TP, et al. The epidemiology of revision total knee arthroplasty in the United States. Clin Orthop Relat Res. 2010 Jan;468(1):45–51.

5. Kurtz SM, Lau E, Watson H, Schmier JK, Parvizi J. Economic burden of periprosthetic joint infection in the United States. J Arthroplasty. 2012 Sep;27(8 Suppl):61-65.e1.

6. Vanhegan IS, Malik AK, Jayakumar P, Ul Islam S, Haddad FS. A financial analysis of revision hip arthroplasty: the economic burden in relation to the national tariff. J Bone Joint Surg Br. 2012 May;94(5):619–23.

7. Kapadia BH, McElroy MJ, Issa K, Johnson AJ, Bozic KJ, Mont MA. The Economic Impact of Periprosthetic Infections Following Total Knee Arthroplasty at a Specialized Tertiary-Care Center. The Journal of Arthroplasty. 2014 May 1;29(5):929–32.

8. Chen AF, Fleischman A, Austin MS. Use of Intrawound Antibiotics in Orthopaedic Surgery. J Am Acad Orthop Surg. 2018;26(17):e371–8.

9. Fraval A, Zhou Y, Parvizi J. Antibiotic-loaded cement in total joint arthroplasty: a comprehensive review. Arch Orthop Trauma Surg. 2024;

10. Ge SM, Harvey EJ. Collagen fleece in orthopaedic infections. OTA Int. 2021;4(3 Suppl).

11. Whiteside LA, Roy ME. One-stage Revision With Catheter Infusion of Intraarticular Antibiotics Successfully Treats Infected THA. Clin Orthop Relat Res. 2017 Feb;475(2):419–29.

12. Flores MJ, Brown KE, Morshed S, Shearer DW. Evidence for Local Antibiotics in the Prevention of Infection in Orthopaedic Trauma. J Clin Med. 2022;11(24).

13. Steadman W, Chapman PR, Schuetz M, Schmutz B, Trampuz A, Tetsworth K. Local Antibiotic Delivery Options in Prosthetic Joint Infection. Antibiotics (Basel). 2023;12(4).

14. Saidahmed A, Sarraj M, Ekhtiari S, Mundi R, Tushinski D, Wood TJ, et al. Local antibiotics in primary hip and knee arthroplasty: a systematic review and meta-analysis. Eur J Orthop Surg Traumatol. 2021;31(4):669–81.

15. Jacob CC, Daw JH, Santiago-Torres J. The efficacy of antibiotic-impregnated calcium sulfate (AICS) in the treatment of infected non-union and fracture-related infection: a systematic review. J Bone Jt Infect. 2023;8(2):91–7.

16. Bakhsheshian J, Dahdaleh NS, Lam SK, Savage JW, Smith ZA. The use of vancomycin powder in modern spine surgery: systematic review and meta-analysis of the clinical evidence. World Neurosurg. 2015;83(5):816–23.

17. Cardot E, Tillie-Leblond I, Jeannin P, Facon A, Breuil K, Patte F, et al. Anaphylactic reaction to local administration of rifamycin SV. J Allergy Clin Immunol. 1995;95(1 Pt 1):1–7.

18. Ji B, Li G, Zhang X, Wang Y, Mu W, Cao L. Effective treatment of single-stage revision using intra-articular antibiotic infusion for culture-negative prosthetic joint infection. Bone Joint J. 2020;102-b(3):336–44.

19. Fernando N, Werner S, Elhaddad M, Davies J, Firoozabadi R. Do Antibiotic Beads Need to be Removed? Arch Bone Jt Surg. 2020;8(4):502–5.

20. Hanada M, Nishikino S, Hotta K, Furuhashi H, Hoshino H, Matsuyama Y. Intrawound vancomycin powder increases post-operative wound complications and does not decrease periprosthetic joint infection in primary total and unicompartmental knee arthroplasties. Knee Surg Sports Traumatol Arthrosc. 2019;27(7):2322–7.

21. Kallala R, Harris WE, Ibrahim M, Dipane M, McPherson E. Use of Stimulan absorbable calcium sulphate beads in revision lower limb arthroplasty: Safety profile and complication rates. Bone Joint Res. 2018 Oct;7(10):570–9.

22. McPherson E, Dipane M, Sherif S. Dissolvable antibiotic beads in treatment of periprosthetic joint infection and revision arthroplasty-the use of synthetic pure calcium sulfate (Stimulan®) impregnated with vancomycin & tobramycin. Reconstructive Review. 2013;3(1).

23. Haonga BT, Ngunyale P, von Kaeppler EP, Donnelley CA, Won NY, Eliezer EN, et al. A pilot, masked, randomized controlled trial to evaluate local gentamicin versus saline in open tibial fractures (pGO-Tibia). OTA Int. 2023;6(2):e268.

24. Balabanova A, Chu X, Chambers L, Mauffrey C, Parry JA. Incidence of Surgical Site Infections and Acute Kidney Injuries After Topical Antibiotic Powder Application in Orthopaedic Trauma Surgery. J Orthop Trauma. 2021;35(10):e377–80.

25. Barksfield R, Hamal P, Hamal D, Porteous A, Murray J. The Safety of Glycopeptide-Impregnated Calcium Sulphate Following Debridement, Antibiotics and Implant Retention (DAIR) for Infected Total Knee Replacement. Cureus. 2024;16(4):e57955.

26. van Raaij TM, Visser LE, Vulto AG, Verhaar JA. Acute renal failure after local gentamicin treatment in an infected total knee arthroplasty. J Arthroplasty. 2002;17(7):948–50.

27. Caroom C, Tullar JM, Benton EG Jr, Jones JR, Chaput CD. Intrawound vancomycin powder reduces surgical site infections in posterior cervical fusion. Spine (Phila Pa 1976). 2013;38(14):1183–7.

28. Xie LL, Zhu J, Yang MS, Yang CY, Luo SH, Xie Y, et al. Effect of Intra-wound Vancomycin for Spinal Surgery: A Systematic Review and Meta-analysis. Orthop Surg. 2017;9(4):350–8.

29. Burbank K.M., Schauer S.G., De Lorenzo R.A., Wenke J.C. Early application of topical antibiotic powder in open-fracture wounds: A strategy to prevent biofilm formation and infections. OTA International. 2020;3(4):E091.

30. Yamamoto Y, Fukui T, Sawauchi K, Yoshikawa R, Takase K, Kumabe Y, et al. Effects of high antibiotic concentrations applied to continuous local antibiotic perfusion on human bone tissue-derived cells. Bone Joint Res. 2024;13(3):91–100.

31. Ge SM, Harvey EJ. Collagen fleece in orthopaedic infections. OTA Int. 2021;4(3 Suppl).

32. Hansen EN, Adeli B, Kenyon R, Parvizi J. Routine Use of Antibiotic Laden Bone Cement for Primary Total Knee Arthroplasty: Impact on Infecting Microbial Patterns and Resistance Profiles. The Journal of Arthroplasty. 2014 Jun 1;29(6):1123–7.

33. Berberich C, Sanz-Ruiz P. Risk assessment of antibiotic resistance development by antibiotic-loaded bone cements: is it a clinical concern? EFORT Open Rev. 2019;4(10):576–84.

34. Luo S, Jiang T, Yang Y, Yang X, Zhao J. Combination therapy with vancomycin-loaded calcium sulfate and vancomycin-loaded PMMA in the treatment of chronic osteomyelitis. BMC Musculoskelet Disord. 2016;17(1):502.

35. Mereddy P, Nallamilli SR, Gowda VP, Kasha S, Godey SK, Nallamilli RR, et al. The use of Stimulan in bone and joint infections. Bone Jt Open. 2023;4(7):516–22.

36. Armaghani SJ, Menge TJ, Lovejoy SA, Mencio GA, Martus JE. Safety of topical vancomycin for pediatric spinal deformity: nontoxic serum levels with supratherapeutic drain levels. Spine (Phila Pa 1976). 2014;39(20):1683–7.