EDITORIAL

Vancomycin, bone growth, and wound healing**Paul M. Arnold, MD,¹ Zoher Ghogawala, MD,² and Candan Tamerler, PhD³**¹Department of Neurosurgery, The University of Kansas Medical Center; ³Department of Mechanical Engineering, The University of Kansas, Kansas City, Kansas; and ²Department of Neurosurgery, Lahey Clinic, Burlington, Massachusetts

POSTOPERATIVE wound infections, also known as surgical-site infections, are among the most dreaded complications encountered by spine surgeons. They are associated with increased length of hospital stay, decreased patient satisfaction, and increased morbidity and mortality. In more stark terms, the price of a surgical-site infection can add as much as \$100,000 to the cost of care for a single patient event.^{6,8} CMS (Centers for Medicare and Medicaid Services) treats wound infections as “never events,” which means neither the hospital nor the physician will be reimbursed for the cost of treating this problem. With estimated wound infection rates of 5%–10% for all spine cases, the total cost of managing this complication easily tops \$1 billion annually.^{1,5}

Surgeons have several tools to combat this problem, including meticulous surgical technique, minimally invasive procedures, intravenous antibiotics, and early mobilization/rehabilitation. Another potential tool is the intra-wound use of vancomycin, which was developed as one of the first glycopeptide antibiotics. While there have been conflicting reports regarding the efficacy of this treatment, a recent multicenter study of 2000 patients demonstrated a significant reduction in surgical-site infections in patients undergoing posterior spine surgery, even if the patient was at increased risk for infectious complications.² Extensive beta-lactam resistance also brought attention back to the vancomycin usage for gram-positive infections. The low cost of vancomycin powder (estimated at \$40) also makes it a very attractive option.

Some surgeons have been reluctant to use vancomycin, as there have been some concerns that it may be toxic to bone growth and therefore inhibit fusion.^{3,4,8–10} A paper in

this issue of *Journal of Neurosurgery: Spine* may alleviate some of these fears. Mendoza et al.⁷ demonstrated that, in a rat spinal fusion model, vancomycin was not inhibitory to bone growth. Animals in this study, a rhBMP model, received either no vancomycin (the control group), standard-dose vancomycin, or high-dose vancomycin (equivalent to 10 times the standard human dosage) applied to the posterolateral fusion bed. Postoperative radiographs, microCTs, and histological analysis showed no statistically significant differences in fusion rates among the 3 groups (in fact, the vancomycin-treated animals actually had higher fusion rates). This novel study demonstrated that vancomycin was not inhibitory to bone growth or fusion at standard or even supratherapeutic doses.

While this study clearly demonstrates that vancomycin does not lead to increased rates of pseudarthrosis, there are some caveats to consider. The authors used a rodent model well known for its fusion success; they also used rhBMP, enhancing the likelihood that fusion would take place. It is therefore possible that by using even a low dose of rhBMP, the inhibitory effect of vancomycin could have been masked, if it existed. If another treatment arm were employed, consisting of autograft and vancomycin, and similar fusion rates were observed, the results would be more convincing. Also, the rhBMP was placed in the posterolateral gutters, which is not an FDA-approved use. It is not clear whether similar results would be achieved if interbody fusion was performed. The experimental design must therefore be kept in mind when interpreting these results.

Nevertheless, despite the design flaws, the authors have shown that, even at very high doses, vancomycin does not appear to inhibit fusion in this particular rodent model.

The next set of studies should look at fusion rates in a non-rhBMP model. In the meantime, these results, combined with the emerging clinical data, show that vancomycin is a viable and perhaps even potent weapon in the campaign against postoperative wound infection.

<http://thejns.org/doi/abs/10.3171/2015.12.SPINE151351>

References

1. Awad SS: Adherence to surgical care improvement project measures and post-operative surgical site infections. **Surg Infect (Larchmt)** **13**:234–237, 2002
2. Devin CJ, Chotai S, McGirt MJ, Vaccaro AR, Youssef JA, Orndorff DG, et al: Intrawound vancomycin decreases the risk of surgical site infection after posterior spine surgery—a multicenter analysis. **Spine (Phila Pa 1976)** [epub ahead of print], 2015
3. Emohare O, Ledonio CG, Hill BW, Davis RA, Polly DW Jr, Kang MM: Cost savings analysis of intrawound vancomycin powder in posterior spinal surgery. **Spine J** **14**:2710–2715, 2014
4. Ghobrial GM, Cadotte DW, Williams K Jr, Fehlings MG, Harrop JS: Complications from the use of intrawound vancomycin in lumbar spinal surgery: a systematic review. **Neurosurg Focus** **39**(4):11–15, 2015
5. Hedequist D, Haugen A, Hresko T, Emans J: Failure of attempted implant retention in spinal deformity delayed surgical site infections. **Spine (Phila Pa 1976)** **34**:60–64, 2009
6. McGirt MJ, Godil SS: Reduction of surgical site infection in spine surgery: an opportunity for quality improvement and cost reduction. **Spine J** **13**:1030–1031, 2013
7. Mendoza MC, Sonn KA, Kannan AS, Bellary SS, Mitchell SM, Singh G, et al: The effect of vancomycin powder on bone healing in a rat spinal rhBMP-2 model. **J Neurosurg Spine** [epub ahead of print April 1, 2016. DOI: 10.3171/2015.11.SPINE15536]
8. O'Neill KR, Smith JG, Abtahi AM, Archer KR, Spengler DM, McGirt MJ, et al: Reduced surgical site infections in patients undergoing posterior spinal stabilization of traumatic injuries using vancomycin powder. **Spine J** **11**:641–646, 2011
9. Strom RG, Pacione D, Kalhorn SP, Frempong-Boadu AK: Lumbar laminectomy and fusion with routine local application of vancomycin powder: decreased infection rate instrumented and non-instrumented cases. **Clin Neurol Neurosurg** **115**:1766–1769, 2013
10. Theologis AA, Demirkiran G, Callahan M, Pekmezci M, Ames C, Deviren V: Local intrawound vancomycin powder decreases the risk of surgical site infections in complex adult deformity reconstruction: a cost analysis. **Spine (Phila Pa 1976)** **39**:1875–1880, 2014

Disclosures

Dr. Arnold reports direct stock ownership in Evoke Medical and Z-Plasty; a consultant relationship with Medtronic Sofamor Danek, Stryker Spine, and FzioMed; intellectual property rights and interest in Evoke Medical; and sponsorship or reimbursement of travel by Stryker, AOSpine North America, and FzioMed.

Response

Marco C. Mendoza, MD,¹ and Wellington K. Hsu, MD²

¹Department of Orthopaedic Surgery, Northwestern University; and

²Department of Orthopaedic Surgery, Simpson Querrey Institute for Bionanotechnology and Regenerative Nanomedicine, Northwestern University, Chicago, Illinois

We thank Dr. Arnold, Dr. Ghogawala, and Dr. Tamerler for their review and comments regarding our study. As indicated in our *Discussion* section, the rodent posterolateral fusion model has inherent limitations that prevent the wide applicability of our results to humans, particularly with the use of rhBMP-2. The use of an autograft model would certainly remedy this limitation; however, prior investigations demonstrate its inability to reliably fuse, which is also itself different from the human condition.² To this end, based on historical data,^{3,4} the dose of 3.0 µg rhBMP-2 was chosen, specifically, to facilitate fusion rates near 100% but hopefully still capture any potential inhibitory effect of vancomycin. In other words, this was the most appropriate dose chosen to prevent saturation of the effect from a growth factor. We agree that even with these measures taken, there is still a difference in mechanism compared to autograft.

It is true that the experimental design must be kept in mind before applying these results to clinical practice. Although rhBMP-2 is only FDA-approved for anterior lumbar interbody fusions, recent data demonstrates that it is utilized off label in a variety of fusion techniques by spine surgeons, including posterolateral fusions.^{1,5} Therefore, this study still hold value, as it is the only study to date specifically designed to investigate the effect of vancomycin on bone healing.

References

1. Deyo RA, Ching A, Matsen L, Martin BI, Kreuter W, Jarvik JG, et al: Use of bone morphogenetic proteins in spinal fusion surgery for older adults with lumbar stenosis: trends, complications, repeat surgery, and charges. **Spine (Phila Pa 1976)** **37**:222–230, 2012
2. Grauer JN, Bomback DA, Lugo R, Troiano NW, Patel TC, Friedlaender GE: Posterolateral lumbar fusions in athymic rats: characterization of a model. **Spine J** **4**:281–286, 2004
3. Hsu WK, Polavarapu M, Riaz R, Roc GC, Stock SR, Glicksman ZS, et al: Nanocomposite therapy as a more efficacious and less inflammatory alternative to bone morphogenetic protein-2 in a rodent arthrodesis model. **J Orthop Res** **29**:1812–1819, 2011
4. Lee SS, Hsu EL, Mendoza M, Ghodasra J, Nickoli MS, Ashtekar A, et al: Gel scaffolds of BMP-2-binding peptide amphiphile nanofibers for spinal arthrodesis. **Adv Healthc Mater** **4**:131–141, 2015
5. Schroeder GH, Hsu WK: Use of bone morphogenetic protein in the lumbar spine. **Contemporary Spine Surgery** **15**:1–8, 2014