Evaluation of the Effect of Vancomycin Powder on Bone Healing in a Rat Spinal Arthrodesis Model

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Introduction: Surgical site infections (SSI) after spinal surgery occur in .7% to 11.9% of patients. Such complications are both devastating to patients and are very costly to the healthcare system. Data from the 2005 Healthcare Cost and Utilization Project National Inpatient Sample (HCUPNIS) demonstrated that SSIs extended length of stay by 9.7 days and increased costs by $20,842 per admission. Staphylococcus aureus, including the methicillin-susceptible (MSSA) and methicillin-resistant (MRSA) species, is the most common organism responsible for SSI. As such, an efficacious antibiotic has the potential to serve as a simple, cost-effective solution to the problem. Numerous clinical studies have demonstrated the superior efficacy of local vancomycin powder application compared to the use of intravenous antibiotics alone in the reduction of postoperative infection rates. While recent evidence suggests that vancomycin does not compromise healing in a rat femoral defect, in vitro studies suggest that vancomycin is cytotoxic to differentiating osteoblasts at high doses. As yet, the effect of the antibiotic on spinal arthrodesis rates when utilized in fusion procedures has not been properly evaluated. This study aims to quantify the impact of vancomycin powder application on new bone formation and spine fusion rates in a rat posterolateral arthrodesis model.

Methods: Thirty-six female Sprague-Dawley rats underwent a posterolateral lumbar spinal fusion (PLF) at the L4 and L5 vertebrae. Fusion was elicited via implantation of an absorbable collagen sponge (ACS) containing 3 µg rhBMP-2. Rats were divided into three groups: no vancomycin (control), standard dose vancomycin, and high dose vancomycin. Clinical studies typically describe the application of 1g vancomycin into the surgical wound. Presuming an average individual weight of 70 kg, a weight-based equivalent dose of vancomycin powder was applied subfascially in the PLF model constituting a “standard-dose” treatment group (14.3 mg/kg; n=12). To determine whether there is a critical threshold beyond which vancomycin increases the risk of pseudoarthrosis, a ten-fold higher dose was administered to a “high dose” treatment group (143 mg/kg; n=12). No vancomycin powder was applied to the surgical site in the control group (n=12). Spines were harvested and evaluated at 8 weeks postoperatively using radiographs, fusion scoring, microCT, and histologic analysis. Fusion scores were determined via manual palpation by 3 blinded observers with an established scoring system whereby 0 = no bridging bone, 1 = unilateral bridging, 2 = bilateral bridging and 3 = bilateral bridging with abundant bone formation. Spines with an average score of ≥1.0 were considered successfully fused.
**Results:** Qualitative radiographs demonstrated equivalent bridging bone formation in all groups (Figure 1). No significant differences in fusion scores were seen in the standard-dose or high-dose treatment groups (2.25 and 2.13, respectively) relative to untreated control animals (1.78; Figure 2A). Similarly, fusion rates were not significantly different between vancomycin-treated animals (100% for both groups) and control animals (92%; Figure 2B). Quantification of new bone formation via microCT imaging revealed no significant differences in the volume of newly regenerated bone among groups (Figure 2C).

**Discussion:** This study evaluated the impact of topically-applied vancomycin powder on bone healing in a rat arthrodesis model. Although in vitro studies suggest that vancomycin is cytotoxic to differentiating osteoblasts, our study demonstrates that its application does not inhibit fusion rates at an equivalent wt% dose to what is routinely used by surgeons in such procedures. Moreover, bone formation and fusion rates were not reduced even after administration of vancomycin at a dose ten-fold higher that which is typically administered clinically. Our findings suggests that if there exists a critical threshold above which vancomycin inhibits bone healing, such a dose is out of the range which might be considered reasonable for clinical use.

**Significance:** This is the first in vivo study to specifically address the potential complication of pseudarthrosis (surgical non-union) with topically-applied vancomycin.

**Figure 1:**

![Figure 1](image1.jpg)

Figure 1. (A) No vancomycin (B) Standard dose vancomycin (C) High dose vancomycin

**Figure 2.**

A.  

![Figure 2A](image2A.jpg)

B.  

![Figure 2B](image2B.jpg)

C.  

![Figure 2C](image2C.jpg)

Figure 2. (A) Fusion scores (B) Fusion Rate (C) New Bone Volume
ORS 2015 Annual Meeting

Poster No: 0555