The Use of Vancomycin Powder In Modern Spine Surgery: Systematic Review and Meta-Analysis of the Clinical Evidence

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Key words
- Methicillin-resistant *Staphylococcus aureus*
- Spine surgery
- Surgical-site infection
- Systematic review

Abbreviations and Acronyms
POD: Postoperative day
RCT: Randomized controlled trial
SSI: Surgical-site infection

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BACKGROUND: **Surgical-site infections (SSIs) can lead to greater postoperative morbidity, mortality, and health care costs. Despite current prophylactic measures, rates of SSIs have been reported in up to 15% of patients undergoing spine surgery. The adjunctive local application of vancomycin powder in spine surgery is a low-cost strategy to help reduce SSIs. Vancomycin is active against skin pathogens that can potentially contaminate the wound during spinal surgery. The local application of vancomycin in its powder form ensures adequate surgical-site concentrations while minimizing adverse effects caused by undetectable systemic distribution. However, clinical studies have produced conflicting results, and the clinical evidence behind the use of vancomycin powder in modern spinal surgery practices is not clear.**

PURPOSE: **To examine the current clinical evidence on the use of vancomycin powder in spine surgery.**

STUDY DESIGN: **Systematic review and meta-analysis of literature.**

METHODS: **A comprehensive search of the English literature was conducted with PubMed (MEDLINE). The inclusion criteria consisted of intrawound vancomycin powder use in spine surgery as a prophylactic agent for SSIs. Studies that investigated nonspine surgeries, selected patients on the basis of clinical suspicion, or included patients with infections were excluded. Studies that compared intrawound vancomycin in spine surgery against their standard practice were pooled in the meta-analysis using a random-effects model.**

RESULTS: **A total of 671 abstracts were reviewed, and 18 papers met inclusion/exclusion criteria and were included in this review. These included 1 randomized controlled trial, 13 comparative studies, and 4 case series. The level of evidence in hierarchical order was as follows: 1 level II, 13 level III, and 4 level IV. Fourteen of the studies, 1 randomized controlled trial and 13 comparative studies, were eligible for the meta-analysis. The odds of developing a deep infection with intrawound vancomycin powder were 0.23 times the odds of experiencing an infection without intrawound vancomycin (95% confidence interval 0.11–0.50, $P = 0.0002$, $I^2 = 47\%$). For combined superficial and deep infections the odds ratio was 0.43 (95% confidence interval 0.22–0.82, $P = 0.01$, $I^2 = 36\%$).**

CONCLUSIONS: **Numerous clinical studies have confirmed the safety of using vancomycin powder in the surgical site. The pooled clinical data supports the use of vancomycin to prevent SSIs in adult spine surgeries. The majority of the supporting literature is class III evidence. Existing studies use different definitions for surgical site infections and different pre-, peri-, and postoperative antibiotic regimens. Further high-quality investigations should use standardized protocols to confirm these findings.**

INTRODUCTION

Surgical-Site Infections (SSIs)

SSIs can lead to greater postoperative morbidity, mortality, and health care costs. In the United States, *Staphylococcus aureus* (*S. aureus*) is the leading cause of SSIs (1, 22). It is estimated that 15%–25% of the healthy population are chronic carriers of *S. aureus* and carry a greater risk for SSIs (29, 44). Screening and decolonization programs have significantly lowered rate of SSIs. Despite current prophylactic measures, SSIs have been reported in up to 15% of patients undergoing spine surgery (5, 13, 39, 47). These rates vary as the result of the indications for surgery, type of surgery, and use of instrumentation. Infections in the spine region can necessitate reoperations that may result in further increased medical morbidity, neurologic deficit, soft-tissue damage, spinal deformity, and resource use. SSIs can carry an additional cost of $33,705 in postoperative patients undergoing spinal fusion for trauma (18). In addition, insurance carriers are taking actions to reduce the reimbursement for SSIs after spine procedures (7). Currently, the superiority of an antimicrobial agent or protocol for spine surgery is not defined (4, 53).

Vancomycin

Vancomycin is a glycopeptide antibiotic used widely to treat gram-positive infections involving methicillin-resistant *Staphylococcus aureus*. It is not as effective against methicillin-sensitive *Staphylococcus aureus* and other gram-negative pathogens. To date, the intravenous administration of vancomycin has not been shown to be more effective than cephalosporins in the prevention of SSIs (30, 49). In an effort to control resistance, the Centers for Disease Control and Prevention recommends against the routine use of intravenous vancomycin for any surgical procedure and is reserved for patients with an allergy to β-lactam antibiotics. The prophylactic use of systemic vancomycin has been shown to increase SSIs in select populations (19). The clinical evidence, however, for nonparenteral administration of vancomycin in spine surgery is unclear.

Parenteral Administration of Vancomycin

Vancomycin levels need to reach a critical value to exert antimicrobial activity; increasing its concentration greater than this threshold does not alter its effectiveness. When vancomycin is used for surgical antimicrobial prophylaxis, an infusion period of 1 hour is recommended for adults and pediatric patients (30, 34). Achieving optimal systemic levels before an incision is made with the parenteral administration of antibiotics is difficult and may cause delays in surgery. Furthermore, the pharmacokinetics of vancomycin can be altered by several factors. The distribution of intravenous antimicrobial agents in surgical wounds can be limited by avascular zones, hematomas, and wound infections. These inaccessible areas are assumed to be even more extensive in the surgical site. The systemic delivery of vancomycin can be further reduced by comorbidities, such as diabetes and obesity. Pharmacokinetic studies of intravenous vancomycin have demonstrated difficulties in delivering targeted concentrations even when a continuous intravenous infusion was used after the loading dose (38, 46). Increasing the loading dosage of vancomycin runs the risks of adverse events such as hypotension, flushing, rashes, colitis, and Stevens-Johnson syndrome (45).

Local Administration of Vancomycin

To overcome the systemic complications and difficulties in delivering antimicrobial agents to the surgical site, perioperative application of vancomycin and the resulting drug levels have been investigated. This method of drug delivery can achieve high local antimicrobial concentrations with limited systemic absorptions (50). Preclinical studies have confirmed that intrawound vancomycin powder can eliminate *S. aureus* inoculation in models of spine SSI (55). Vancomycin powder is increasingly used off-label as an adjunctive nonparenteral antimicrobial prophylactic agent in spine surgeries (54). It is unclear whether intrawound vancomycin powder has an impact on SSIs (50, 52, 56). In previous reviews on the use of vancomycin powder, investigators did not include current studies on spine surgery in their systematic analyses, extract superficial and deep SSIs data, and did not report the level of evidence (8, 12, 27, 44). By assessing the level of evidence through standardized validated methodologies, clinicians can assess the availability of critically appraised literature (20, 24-26). In this report, it is our goal to summarize the current clinical evidence on the use of vancomycin powder in reducing SSIs in spine surgeries.

METHODS

An extensive search of the electronic PubMed database (MEDLINE) from January 1, 1970, to August 21, 2014, was performed to identify studies with the following search terms: vancomycin powder or vancomycin surgical-site infection. Clinical papers in which authors investigated the intraoperative vancomycin powder application in spine surgery were included. The exclusion criteria consisted of vancomycin powder use based on clinical suspicion, in vitro studies, nonspine surgery, and studies that included patients with infections. When inclusion or exclusion was unclear on the basis of title and abstract, full text articles were retrieved. Further data extracted from each article included the following: publication year, number of patients, study population and etiologies, average follow-up period, assessment or outcome measures (rates of superficial and/or deep SSIs), and study conclusions.

Levels of evidence were assigned to the studies according to the criteria set forth from the *Journal of Clinical Orthopaedics and Related Research*, which is adapted from the Oxford Centre of Evidence-Based Medicine levels of evidence (20, 24-26). The level of evidence scale has 5 levels, with 1 being the highest and 5 the lowest.

The meta-analysis was conducted with studies in which authors compared intrawound vancomycin in spine surgery against their standard practice with the primary outcome of infection. Odds ratios were computed from the SSIs rate data for each study, weighted by sample size, pooled using the Mantel—Haenszel method and a random-effects model, and displayed with forest plots. Data on combined superficial and deep or deep only SSIs were pooled separately. The forest plots were created with Review Manager (RevMan Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2012). Publication bias was assessed by summarizing treatment methods, selection of patients for vancomycin intervention, and how SSIs was defined. Ambiguity or any disagreements between reviewers was resolved through discussion and the addition of a third reviewer as needed.

RESULTS

Summary of Literature Search

The search criteria yielded 671 abstracts, and 18 clinical studies involving vancomycin powder in spine surgery met the inclusion and exclusion criteria (**Figure 1**) (2, 5, 11, 14, 15, 18, 21, 23, 28, 32, 35-37, 48-52). These included 1 randomized controlled trial (RCT), 13 comparative, and 4 case series. Two were prospective and 16 were retrospective. The level of evidence in hierarchical order was: level II (n = 1, 5.6%), level III (n = 13, 72.2%), and level IV (n = 4, 22.2%). The studies are summarized herein with an emphasis an emphasis on higher-level (II and III) studies (**Table 1**).

Summary of Meta-Analysis

Fourteen of the studies, 1 RCT and 13 comparative cohort studies, were eligible for the meta-analysis. Of these, 1 RCT and 7 comparative studies reported both superficial and deep SSIs. Pooling the results from these studies, we found that the odds of a superficial or deep infection with intrawound vancomycin was 0.43 times the odds of experiencing an infection without