A meta-analysis of spinal surgical site infection and vancomycin powder

A review

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Object. Surgical site infection (SSI) is a serious and costly complication of spinal surgery. There have been several conflicting reports on the use of intrawound vancomycin powder in decreasing SSI in spine surgery. The purpose of this study is to answer the question: “Does intrawound vancomycin powder reduce the rate of SSIs in spine surgery?”

Methods. A comprehensive search of multiple electronic databases and bibliographies was conducted to identify clinical studies that evaluated the rates of SSI with and without the use of intrawound vancomycin powder in spine surgery. Independent reviewers extracted data and graded the quality of each paper that met inclusion criteria. A random effects meta-analysis was then performed.

Results. The search identified 9 retrospective cohort studies (Level III evidence) and 1 randomized controlled trial (Level II evidence). There were 2574 cases and 106 infections in the control group (4.1%) and 2518 cases and 33 infections (1.3%) in the treatment group, yielding a pooled absolute risk reduction and relative risk reduction of 2.8% and 68%, respectively. The meta-analysis revealed the use of vancomycin powder to be protective in preventing SSI (relative risk = 0.34, 95% confidence interval 0.17–0.66, p = 0.021). The number needed to treat to prevent 1 SSI was 36. A subgroup analysis found that patients who had implants had a reduced risk of SSI with vancomycin powder (p = 0.023), compared with those who had noninstrumented spinal operations (p = 0.226).

Conclusions. This meta-analysis suggests that the use of vancomycin powder may be protective against SSI in open spinal surgery; however, the exact population in which it should be used is not clear. This benefit may be most appreciated in higher-risk populations or in facilities with a high baseline rate of infection.

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Key Words • vancomycin powder • spine surgery • surgical site infection • meta-analysis

Surgical site infection (SSI) remains one of the most common nosocomial infections. According to a study of 100,449 surgeries presented at an infectious disease symposium in October 2013, SSIs are now the most frequent hospital-acquired infection, surpassing urinary catheter infections, ventilator acquired pneumonias, central line–related infections, and Clostridium difficile infections.27 The approximately 500,000 SSIs that occur each year account for up to $10 billion in US health care expenditures.25 Such infections have a profound impact on patients, their families, health care providers, and the overall health care system.

The rates of infection following spinal fusion have been estimated to be between 2% and 13%,1,19,41 and a number of risk factors have been investigated. Although not uniform, there is fairly consistent evidence that obesity/increased body mass index, advanced age, malnutrition, longer operation times, diabetes, smoking, blood transfusion, cancer, and history of a previous SSI are associated with an increased risk of SSI.5,34,35,38,41,42,54 The most common organisms involved in SSI after spine surgery are gram-positive organisms, such as Staphylococcus aureus and Staphylococcus epidermidis.9,8,32 The use of preoperative antibiotics to target these bacteria, including intravenous cephalosporins and thoracic skin preparation, is a

Abbreviations used in this paper: CI = confidence interval; NOS = Newcastle-Ottawa Quality Assessment Scale; OCEBM = Oxford Centre for Evidence Based Medicine; RR = relative risk; SSI = surgical site infection.
routine measure in controlling SSIs. Despite specifically targeting gram-positive organism cell wall synthesis, the routine use of intravenous vancomycin has not been shown to be more effective than intravenous cephalosporins in preventing SSIs.1,2

The use of vancomycin powder has been investigated in cardiothoracic surgery,26,51 orthopedic surgery,21 vascular surgery,20 and spine surgery.2,15,29,36,37,46,47,49 The evidence thus far in spinal surgery is mixed, with some papers reporting a protective benefit2,15,29,36,37,46,47,49 and others showing no benefit.15,26,29,37,50 We combined data from existing studies to maximize the collective power to determine whether a protective benefit truly exists or not.

Methods

This study was conducted using the Assessment of Multiple Systematic Reviews (AMSTAR) measurement tool,43 and reporting was performed according to the guidelines defined by Meta-analysis Of Observational Studies in Epidemiology (MOOSE)48 and Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA).2,15,29,36,37,46,47,49 The research question for this study was: “Does intrawound vancomycin powder reduce the rate of SSIs in spine surgery?”

Search Strategy

The systematic search strategy involved a search using multiple electronic databases, bibliographies of relevant articles, and consultation with the senior author (P.K.). In April 2014, we electronically searched PubMed/MEDLINE, Clinicaltrials.gov, The Cochrane Library, Web of Science, and Scopus to find English-language articles (excluding “gray literature”) with no timeframe restrictions. The following terms in various combinations were used: “vancomycin powder,” “spine surgery,” “neurosurgery,” “surgery,” and “surgical site infection.” Two independent researchers (N.R.K. and J.M.A.) along with librarians at the University of Tennessee Health Science Center conducted independent literature searches. If there was any question as to the eligibility of an article, consensus was reached through discussion with the senior author (P.K.). When necessary, additional contact was made with the authors of the included articles to confirm data.

Inclusion Criteria, Data Extraction, End Points, Definitions

The goals of the search were to find articles that met the following inclusion criteria: 1) described a group of adult patients (> 18 years of age) who had vancomycin powder applied during their spine surgery; 2) described a control group not treated with vancomycin powder; 3) had the use of vancomycin powder as the main treatment difference between the two groups; and 4) reported the number of patients and number of infections for each group. Thus, uncontrolled studies, case reports, and pediatric reports were excluded.

Two separate individuals (N.R.K. and P.K.) screened all potential articles and extracted data independently. The data extracted from each article included: 1) the indication for surgery (i.e., trauma, degenerative, tumor, etc.); 2) the total number of participants per group; 3) the number of surgeons treating the group under study; 4) the authors’ definition of an SSI; 5) the dose and method of application of the vancomycin powder; 6) details on the use of perioperative antibiotics, drains, and skin preparation; 6) any complications related to the use of vancomycin powder; and 7) any potential conflict of interest as reported by the authors. The level of evidence for each study was evaluated using the Oxford Centre for Evidence Based Medicine (OCEBM) guidelines.19 Study quality (i.e., assessment of bias within individual studies) was determined using the Jadad scale for randomized controlled trials39 and the Newcastle-Ottawa Quality Assessment Scale (NOS)51 for controlled observational cohort studies. Disagreements among any of the above data points were resolved through discussion among the authors.

Meta-Analysis

For each study, the numbers of infections in patients treated with vancomycin powder and in the controls were identified and a relative risk (RR) was calculated. An RR < 1 indicates protection against SSI when using vancomycin powder. The overall risk ratio was computed using the method of DerSimonian and Laird.6

A random effects meta-analysis was performed on the selected studies. A random effects model—in contrast to a fixed effects model—does not assume that the RR is the same across studies and yields a more conservative estimate of effect. In cases of 2 or more zero cells, the assumption of continuity correction was not used and the corresponding point estimates were designated as “not estimable.” We assessed heterogeneity using the I2 statistic, which returns a value between 0% and 100%, with higher values denoting increasing heterogeneity. We regarded an I2 value between 30% and 60% as moderate heterogeneity.2,5,16

Subgroup analysis was performed to determine whether vancomycin powder was beneficial and to what degree in patients who underwent instrumented operations compared with those who did not. Publication bias (i.e., assessment of bias across studies) was graphically evaluated using a funnel plot.44,45,46 Statistical analysis was conducted using Stata/SE version 13.1 software.

Results

Our search strategy initially identified 335 articles (Fig. 1). After excluding duplicate studies and articles not directly related to our hypothesis, a total of 21 articles remained. Of these 21 articles, 11 were excluded for the following reasons: 1) 1 study was excluded because it was a case report;26 2) 2 studies were excluded because they were cost analyses;44,45 3) 1 study was excluded because it was an editorial;15 4) 4 articles were excluded because they were review articles;12,13,40,52 and 5) 3 studies had no control group.10,11,32 Thus, 10 studies were eligible for analysis.

Characteristics of Eligible Studies

There was 1 prospective randomized control trial (OCEBM Level II evidence) and 9 retrospective cohort
studies (Level III; Table 1). Six studies contained only patients who had undergone instrumented operations. The overall quality of the 9 observational studies was good. The average number of stars using the NOS was 6.22 ± 0.83 out of a maximum of 9 stars. Many of the retrospective cohort studies2,29,36,37,46,49 did not explicitly state that they controlled for confounding factors. One of the 2 studies by Strom et al. did control for instrumentation.47 The 1 randomized controlled trial50 in this analysis was not blinded; therefore, it received 3 out of 5 points using the Jadad criteria.

Meta-Analysis

Five of the 10 studies showed vancomycin to be protective overall in preventing SSIs (Table 2). Although the paper by Heller et al. concluded that vancomycin powder decreased the risk of S. aureus SSI, it did not decrease the overall risk of SSI (2-tailed Fisher's exact test, p < 0.081). Similarly, Hill et al. showed a decreased deep infection rate with vancomycin powder, but they did not count superficial (suprafascial) wound infections, which effectively negated the protective benefit (two-tailed Fisher's exact test, p = 0.20). There were 2574 patients and 106 infections (4.1%) in the pooled control group compared with 2518 patients and 33 infections (1.3%) in the pooled treatment group, giving an absolute risk reduction and relative risk reduction of 2.8% and 68%, respectively. The overall RR was 0.34 (95% CI 0.17–0.66, p = 0.021; Fig. 2) and the number needed to treat was 36 patients. In other words, an SSI is 2.99 times more likely when not using intrawound vancomycin powder in spine surgery. Thirty-six patients treated with vancomycin powder would be needed to prevent 1 SSI.

Subgroup Analysis: Instrumented vs Noninstrumented

The instrumented analysis contained 9 of the studies included in the overall meta-analysis; however, 3 of the 9 studies (Pahys et al.,47 Strom et al.,47 and Tubaki et al.50) had values different from the overall analysis because they contained both instrumented and noninstrumented patients. There were a total of 4338 patients from the 9 studies. In the treatment group there were 27 SSIs in 2146 patients (1.26%) compared with the control group, which had 91 SSIs in 2192 patients (4.15%), giving an absolute risk reduction and relative risk reduction of 2.89% and 70%, respectively. The overall RR was 0.32 (95% CI 0.15–0.69, p = 0.023), and the number needed to treat was 35 patients (Fig. 3).

Three studies with a total of 454 patients contained infection results on noninstrumented surgeries. In the treatment group there was 1 SSI in 222 patients (0.45%) compared with 4 SSIs in 232 patients (1.72%) in the control group, giving an absolute risk reduction and relative risk reduction of 1.27% and 74%, respectively. However, the study by Pahys et al.37 could not be included in the meta-analysis because there were zero infections in the treatment and control groups. With the remaining 2 studies, the overall RR was 0.238 (95% CI 0.02–2.36, p = 0.226) (Fig. 4).

Publication Bias

The absence of any studies in the right, lower quadrant of the funnel plot suggests that small, negative studies have not been published in the literature (Fig. 5). Given the small number of included studies (n = 10), this may be a spurious finding. While publication bias may exist, formal statistical testing for it was not performed.
<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>Grade (OCEBM)</th>
<th>Quality of Evidence (no. of stars)*</th>
<th>Type of Study</th>
<th>Study Population</th>
<th>No. of Surgeons/Institutions</th>
<th>Definition of Outcome</th>
<th>Skin Prep</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweet et al., 2011</td>
<td>3</td>
<td>selection (4), comparability (0), outcome (2)</td>
<td>retrospective cohort</td>
<td>instrumented thoracolumbar surgery for trauma, degenerative pathology, scoliosis, &amp; tumor; open &amp; MIS procedures</td>
<td>3/1</td>
<td>deep infection only</td>
<td>betadine</td>
</tr>
<tr>
<td>O’Neill et al., 2011</td>
<td>3</td>
<td>selection (4), comparability (0), outcome (2)</td>
<td>retrospective cohort</td>
<td>instrumented surgery at all levels for trauma only</td>
<td>multiple (1 group treated all by 1 surgeon, the other by multiple)/1</td>
<td>superficial or deep</td>
<td>chlorhexidine</td>
</tr>
<tr>
<td>Caroom et al., 2013</td>
<td>3</td>
<td>selection (4), comparability (0), outcome (2)</td>
<td>retrospective cohort</td>
<td>instrumented cervical fusions for spondylotic myelopathy</td>
<td>1/1</td>
<td>not provided</td>
<td>Duraprep for control group, ChloraPrep for vancomycin group</td>
</tr>
<tr>
<td>Pahys et al., 2013</td>
<td>3</td>
<td>selection (4), comparability (0), outcome (2)</td>
<td>retrospective cohort</td>
<td>instrumented &amp; noninstrumented cervical surgery for all indications</td>
<td>1/1</td>
<td>superficial &amp; deep requiring debridement</td>
<td>unclear; alcohol foam added to control group 2 &amp; vancomycin group</td>
</tr>
<tr>
<td>Strom et al., 2013</td>
<td>3</td>
<td>selection (4), comparability (1), outcome (3)</td>
<td>retrospective cohort</td>
<td>instrumented &amp; noninstrumented lumbar surgery, almost all degenerative; very few MIS procedures</td>
<td>1/1</td>
<td>superficial &amp; deep requiring debridement</td>
<td>unclear</td>
</tr>
<tr>
<td>Strom et al., 2013</td>
<td>2</td>
<td>Jadad scores: randomization 2, blinding 0, follow-up 1</td>
<td>prospective randomized trial</td>
<td>open spine surgery at any level, excluding MIS</td>
<td>unknown/1</td>
<td>not provided</td>
<td>betadine</td>
</tr>
<tr>
<td>Tubaki et al., 2013</td>
<td>2</td>
<td>Jadad scores: randomization 2, blinding 0, follow-up 1</td>
<td>prospective randomized trial</td>
<td>open spine surgery at any level, excluding MIS</td>
<td>unknown/1</td>
<td>not provided</td>
<td>betadine</td>
</tr>
<tr>
<td>Heller et al., 2013</td>
<td>3</td>
<td>selection (4), comparability (0), outcome (2)</td>
<td>retrospective cohort</td>
<td>instrumented surgery at any level for all indications</td>
<td>1/1</td>
<td>superficial or deep w/in 90 days requiring additional operation &amp; having positive cultures</td>
<td>betadine (patients instructed to wash themselves w/chlorhexidine the night before)</td>
</tr>
<tr>
<td>Hill et al., 2014</td>
<td>3</td>
<td>selection (4), comparability (0), outcome (2)</td>
<td>retrospective cohort</td>
<td>all &gt;18 yrs of age needing posterior spine surgery</td>
<td>2/1</td>
<td>superficial or deep w/in 1 month or longer from surgery</td>
<td>unclear</td>
</tr>
<tr>
<td>Martin et al., 2014</td>
<td>3</td>
<td>selection (4), comparability (0), outcome (1)</td>
<td>retrospective cohort</td>
<td>instrumented thoracolumbar surgery for deformity; no MIS</td>
<td>9/1</td>
<td>deep (but only if it occurred w/in 30 days of surgery)</td>
<td>chlorhexidine</td>
</tr>
</tbody>
</table>

* NOS or Jadad. MIS = minimally invasive surgery.
<table>
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<tr>
<th>Authors &amp; Year</th>
<th>Periop Antibiotics</th>
<th>Drain Used Postop?</th>
<th>Dose &amp; Distribution of Vancomycin</th>
<th>Results*</th>
<th>Conclusions</th>
<th>COI Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sweet et al., 2011</td>
<td>2 g cefazolin w/in 1 hr of incision &amp; continued for 24 hrs postop</td>
<td>yes, but not all patients</td>
<td>2 g: 1 g mixed w/ bone graft, 1 g distributed in deep &amp; superficial tissues</td>
<td>vancomycin 2/911 (0.2%), control 21/821 (2.6%)</td>
<td>vancomycin powder decreases risk of SSI</td>
<td>no</td>
</tr>
<tr>
<td>O’Neill et al., 2011</td>
<td>1 g cefazolin w/in 1 hr of incision &amp; continued for 24 hrs postop; if allergic then 900 mg clindamycin given</td>
<td>yes</td>
<td>1 g distributed in deep &amp; superficial tissues</td>
<td>vancomycin 0/56 (0%), control 7/54 (13%)</td>
<td>vancomycin powder decreases risk of SSI</td>
<td>yes</td>
</tr>
<tr>
<td>Caroom et al., 2013</td>
<td>cefazolin, clindamycin, or vancomycin; antibiotic continued until 24 hrs after drain was removed on postop Day 2</td>
<td>yes</td>
<td>1 g applied subfascial</td>
<td>vancomycin 0/40 (0%), control 11/72 (15%)</td>
<td>vancomycin powder decreases risk of SSI</td>
<td>no</td>
</tr>
<tr>
<td>Pahys et al., 2013</td>
<td>cefalosporin w/in 1 hr of skin incision &amp; 24 hrs postop</td>
<td>yes, in control group 2 &amp; vancomycin group</td>
<td>500 mg subfascial</td>
<td>vancomycin 0/195, control Group 1 9/483 (1.8%), control Group 2 2/1323 (0.3%)</td>
<td>vancomycin powder did not contribute to lowering the risk of SSI</td>
<td>yes</td>
</tr>
<tr>
<td>Strom et al., 2013</td>
<td>cefazolin, if allergic then vancomycin</td>
<td>yes</td>
<td>1 g spread throughout</td>
<td>vancomycin 0/156 (0%), control 11/97 (11.3%)</td>
<td>vancomycin powder decreases risk of SSI</td>
<td>no</td>
</tr>
<tr>
<td>Strom et al., 2013</td>
<td>cefazolin, if allergic then vancomycin</td>
<td>yes</td>
<td>1 g spread throughout</td>
<td>vancomycin 2/79 (2.5%), control 10/92 (10.9%)</td>
<td>vancomycin powder decreases risk of SSI</td>
<td>no</td>
</tr>
<tr>
<td>Tubaki et al., 2013</td>
<td>noninstrumented: 750 mg cefuroxime before incision followed by 750 mg cefuroxime every 8 hrs for 1 day; instrumented: same, but antibiotics continued every 8 hrs postop until drain removed</td>
<td>yes, but not all patients</td>
<td>1 g spread throughout</td>
<td>vancomycin 7/433 (1.6%), control 8/474 (1.7%)</td>
<td>vancomycin powder does not decrease risk of SSI</td>
<td>no</td>
</tr>
<tr>
<td>Heller et al., 2013</td>
<td>20 mg/kg cefazolin 1 hr before surgery then every 4 hrs during surgery, then 24 hrs postop; if allergic or an MRSA carrier then 1 g of vancomycin was used</td>
<td>unknown</td>
<td>0.5–2 g (depending on weight of patient &amp; no. of levels)</td>
<td>vancomycin 9/342 (2.6%), control 18/341 (5.3%)</td>
<td>although vancomycin powder decreased risk of S. aureus SSI, the overall risk of SSI was not reduced (Fisher exact test, p = 0.081)</td>
<td>no</td>
</tr>
<tr>
<td>Hill et al., 2014</td>
<td>1–2 g cefazolin (vancomycin if allergic) before surgery &amp; 24 hrs postop</td>
<td>unknown</td>
<td>1–2 g spread throughout</td>
<td>vancomycin 5/150 (3.3%), control 11/150 (7.3%)</td>
<td>vancomycin powder decreased deep SSI, but overall risk of SSI was not reduced (Fisher exact text, p = 0.20)</td>
<td>yes</td>
</tr>
<tr>
<td>Martin et al., 2014</td>
<td>cefazolin (dose not provided) w/in 1 hr of incision &amp; continued for 24 hrs postop; if allergic, then 900 mg clindamycin given</td>
<td>yes, in most patients</td>
<td>2 g spread throughout</td>
<td>vancomycin 8/156 (5.1%), control 8/150 (5.3%)</td>
<td>vancomycin powder does not decrease risk of SSI</td>
<td>yes</td>
</tr>
</tbody>
</table>

* None of the patients experienced complications with vancomycin powder. COI = conflict of interest; MRSA = methicillin-resistant Staphylococcus aureus.
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Discussion

The development of an SSI in spine surgery is a significant complication, often requiring reoperation, extended hospital stay, and weeks of intravenous antibiotics. The current protocol of preoperative intravenous antibiotics has been shown to provide coverage for fewer than half of the staphylococcal organisms found in hospitals.24,33 The pharmacokinetics of intrawound vancomycin powder provide high minimal inhibitory concentration levels at the site of the wound without the development of the systemic toxicity, such as hypotension and nephrotoxicity, noted with high doses of intravenous vancomycin.49 For these reasons, and the fact that it is minimally time-consuming, easy to administer, and inexpensive, the use of vancomycin powder has gained the attention of many spine surgeons.

Although 5 of the 10 studies did not support the use of vancomycin powder, our meta-analysis suggests that it does decrease the risk of a spinal SSI. Patients without vancomycin powder were more than 3 times more likely to develop an SSI. In our subgroup analysis, vancomycin

![Forest plot of all studies (instrumented and noninstrumented) with their respective RRs and 95% CIs, events (infections), treatments (vancomycin powder), and overall RR.](image)

![Forest plot of studies with only instrumented patients.](image)
powder remained statistically beneficial in the instrumented cohort (p = 0.023), but not in the noninstrumented group (p = 0.226).

None of the papers in our study reported a single complication with the use of vancomycin powder. The recent case report by Mariappan et al. makes a weak argument that vancomycin powder led to circulatory collapse in a 52-year-old woman with breast cancer who underwent a thoracic fusion and stabilization with vertebrectomy, during which 2 liters of blood were lost.28 At our own institution, we have anecdotally observed a number of postoperative sterile seromas in patients who received vancomycin powder, all of them treated with percutaneous aspiration with no recurrence. A high incidence of sterile seromas was also described in a recent study by Ghobrial et al.11

Literature Review

Sweet et al. first demonstrated that 2 grams of vancomycin powder decreased SSIs in a retrospective cohort of 1732 patients with instrumented thoracolumbar fusions performed by 3 surgeons at 1 institution in 2010.49 One year later, O’Neill et al. confirmed this finding in a series of 110 patients in whom 1 gram of vancomycin powder was used with instrumented fusions.36 Three subsequent studies in both instrumented2,46 and noninstrumented47 patient populations have found a similar protective benefit. The latest publication by Hill et al.17 reported a decrease in the deep infection rate in 300 patients treated by 2 surgeons, one of whom administered 1–2 grams of vancomycin into the wound at closure (n = 150) and the other did not (n = 150). Both surgeons used the same preoperative intravenous antibiotic regimen, but no information was provided about method of surgical site prepping. These investigators provide clear definitions of superficial (suprafascial) and deep (subfascial) infections. Although the authors focused on the deep infections—6 (4%) in the control group compared with none in the treatment group—they inexplicably disregarded the 5 superficial infections that occurred in each group, despite the fact that they included a picture in their paper that clearly showed the vancomycin powder applied to all layers of the wound. With these 5 additional superficial infections in each group, the number of infections in the control group (n = 11) compared with the treatment group (n = 5) no longer reached statistical significance (2-tailed Fisher’s exact test, p = 0.20). The same group of authors has published a corollary cost-savings report presumably using many of the same patients, touting a savings of more than $500,000 with the use of vancomycin powder.8

There are several studies that have not shown any benefit with vancomycin powder, including 1 recent prospec-
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tive randomized controlled trial.50 Martin et al. reviewed 306 patients undergoing deformity surgery and found no difference in SSI between the treated (2 grams of vancomycin powder) and control groups.29 Pahys et al. found no difference when using 500 mg of vancomycin powder in addition to alcohol foam for skin preparation and a superficial wound drain in a series of 1001 instrumented and noninstrumented fusions.37 Heller et al. showed that 0.5 to 2 grams of vancomycin powder decreased the risk of staphylococcal infections compared with the control group, but upon closer inspection the overall risk (including staphylococcal species) did not change.55

The randomized (nonblinded) controlled trial by Tubaki et al.,50 the first of its kind, deserves special mention as it is the first randomized trial of the effectiveness of vancomycin powder. The authors found no reduction in SSI (1.7% control vs 1.6% treatment) with vancomycin powder in 907 patients with both instrumented (n = 606) and noninstrumented (n = 301) spinal surgery performed by a group of senior surgeons over an 18-month period at a single institution (Ganga Hospital, India). Exclusion criteria included prior history of infection at the surgical site, biopsy or minimally invasive spinal procedures, follow-up of less than 12 weeks, or an allergy to vancomycin. The paper appears to be internally valid and generalizable. It is noteworthy that the only inclusion criterion was “open spine surgery at any level” and there was no a priori sample size calculation made. Also, the authors do not provide the breakdown of the indication for surgery, such as spondylosis, trauma, tumor, infection, etc., and we assume that the vast majority of the noninstrumented patients were treated for degenerative pathology. Ultimately, having a baseline infection rate that is quite low (1.7%) makes it very difficult without a large number of patients to show a benefit with vancomycin powder, if one truly exists. And even if it did lower the infection risk, this benefit would likely be too small to be considered cost-effective.

Implications of Our Findings

The evidence for the use of vancomycin powder is far from clear. We believe that vancomycin powder may have a benefit in institutions whose baseline infection rate is high (around 5% or greater) or in higher risk patients such as those with 1 or more known risk factors (for example, an obese diabetic patient requiring a multilevel thoracic fusion). The indiscriminate application of vancomycin to any patient undergoing a posterior spinal operation, such as reported in the randomized trial included in our analysis,50 is probably not appropriate. In fact, the infection rate in the control population in that paper was a very respectable 1.7%. All of the articles that reported an infection rate in the control group of more than 10% showed a reduction in the infection rate with vancomycin powder.2,30,46,47

Our findings are, in some ways, similar to those for antibiotic-impregnated shunt systems for hydrocephalus.25 Both can potentially prevent a costly complication with long-term consequences, both should be used if the baseline infection rate is high or in “high-risk” patients, and both are relatively inexpensive (1 gram of vancomycin powder costs $40 at our institution), require no change to the operation or additional operative time, and are extremely low-risk interventions. None of the papers for this meta-analysis reported any deleterious side effect with vancomycin powder. Although our meta-analysis supports the use of vancomycin powder, it can only be viewed as a weak recommendation given the heterogeneity among the included studies (discussed below) and the presence of a randomized trial that did not find a benefit. At this time, surgeons on both sides of the debate could effectively argue for or against the use of vancomycin powder in spine surgery.

Limitations of the Study

The strength of the recommendations from a meta-analysis is only as robust as the quality of articles from which it is derived. The papers that were eligible for this analysis were nearly all Level III studies (retrospective observational cohort trials), with the exception of 1 Level II prospective randomized controlled trial. The quality of all the studies was acceptable. More studies are needed and are undoubtedly forthcoming. The randomized trials that are currently underway at our own institution (clinical trial no. NCT01977989) and at Vanderbilt University (clinical trial no. NCT01566422) will provide clarity on this topic.

There was considerable heterogeneity among the included studies, which could confound our results. There were differences in the type of surgery (e.g., open vs minimally invasive, instrumented vs noninstrumented), spinal level, indications, perioperative antibiotics, skin preparation, and the method of vancomycin powder application. Another significant limitation was the nonuniform definition of an SSI and the variable follow-up time, particularly the paper by Martin et al.,29 in which only infections that occurred within 30 days of surgery were counted.

Conclusions

Surgical site infection is an important quality performance metric to improve upon. In this meta-analysis of 10 studies with more than 2000 patients in both the treatment and control groups, the use of intrawound vancomycin powder in open spine surgery (i.e., not minimally invasive) decreased the overall risk of SSI by one-third with no reported complications. We can only weakly endorse our recommendation on the use of intrawound vancomycin powder in spine surgery. The evidence is inconclusive as to which patient population actually benefits, but we postulate that vancomycin powder should be used in institutions with a high baseline infection rate (assuming other potential sources of SSI have been addressed) or in those patients believed to be “high-risk.”

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Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.
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References
1. Anderson DJ, Kaye KS, Classen D, Arias KM, Podgorny K, Bauer, Camillo. Study supervision: Klimo, Khan, DeCuypere. Critically revising the article: Klimo, Khan. De-Cuyper, Angotti, Kalobwe. Approved the final version of the manuscript: Klimo, Khan, De-Cuyper.

34. Olsen MA, Mayfield J, Lauryssen C, Polish LB, Jones M, Vest

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46. Strom RG, Pacione D, Kalhorn SP, Frempong-Boadu AK: Decreased risk of wound infection after posterior cervical fusion with routine local application of vancomycin powder. Spine (Phila Pa 1976) [epub ahead of print], 2013

47. Strom RG, Pacione D, Kalhorn SP, Frempong-Boadu AK: Lumbar laminectomy and fusion with routine local application of vancomycin powder: decreased infection rate in instrumented and non-instrumented cases. Clin Neurol Neurosurg 115:1766–1769, 2013


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