The Spine Journal 19 (2019) 261–266

Clinical Study

The impact of prophylactic intraoperative vancomycin powder on microbial profile, antibiotic regimen, length of stay, and reoperation rate in elective spine surgery

Zachary J. Grabel, MD[a,*], Allison Boden, BA[a], Dale N. Segal, MD[a], Stephanie Boden, BA[a], Andrew H. Milby, MD[b], John G. Heller, MD[a]

[a] *Department of Orthopaedic Surgery, Emory University School of Medicine, 59 Executive Park South, Atlanta, GA 30329, USA*
[b] *Department of Orthopaedic Surgery, University of Pennsylvania, 426 B Stemmler Hall, 36th Street and Hamilton Walk, Philadelphia, PA 19104-6081 USA*

Received 31 January 2018; revised 8 May 2018; accepted 24 May 2018

Abstract

BACKGROUND CONTEXT: There is growing concern that the microbial profile of surgical site infection (SSI) in the setting of prophylactic vancomycin powder may favor more resistant and uncommon organisms.

PURPOSE: To demonstrate the impact of prophylactic intraoperative vancomycin powder on microbial profile, antibiotic regimen, length of stay (LOS), and reoperation rate in spine surgical site infection.

STUDY DESIGN AND/OR SETTING: Retrospective cohort study. Patient Sample: the study included 115 postoperative spine patients who were required to return to the operating room for SSI.

OUTCOME MEASURES: The outcome measures were microbial profile, reoperation rate, antibiotic regimen, and LOS for patients with postoperative spine infection who either did (treated) or did not (untreated) receive prophylactic vancomycin powder during their index procedure.

METHODS: A retrospective review of patients who underwent posterior thoracic and/or lumbar spine surgery between 2010 and 2017 was conducted. Those undergoing surgical treatment of SSI were identified, and patients were divided into two groups - those who were treated with intraoperative vancomycin (treated) and those who were not (untreated). The organism profile for each group was compared. The average LOS, reoperation rate, and number of patients requiring more than 1 antibiotic were calculated for each patient in both groups.

RESULTS: There were 5,909 procedures performed. One hundred and fifteen SSIs were identified, resulting in a 1.9% infection rate. Prophylactic vancomycin powder was used in the index procedure for 42 of those cases. 23.8% of cultures in the vancomycin group were polymicrobial and 16.7% were gram-negative compared with 9.6% (p=0.039) and 4.1% (p=0.021) in the untreated group, respectively. In the vancomycin-treated group, 26.1% of patients underwent repeat irrigation and debridement compared with 38.4% in the untreated group (p=0.184). The percentage of patients in the treatment and untreated group who required more than 1 antibiotic was 26.0% and 26.1%, respectively (p=0.984). Mean LOS in the treatment group was 8.0 versus 7.9 for the untreated group (p=0.945)

CONCLUSIONS: In this series, vancomycin powder was associated with a higher prevalence of gram-negative and polymicrobial organisms in patients that ultimately developed postoperative SSI. However, this did not adversely affect the need for multiple reoperations, antibiotic regimen, or LOS for these patients.

Keywords: Antibiotic regimen; Length of stay; Microbial profile; Reoperation rate; Surgical site infection; Vancomycin.

FDA device/drug status: Vancomycin.

Author disclosures: ***ZJG***: Nothing to disclose. ***AB***: Nothing to disclose. ***DNS***: Nothing to disclose. ***SB***: Nothing to disclose. ***AHM***: Nothing to disclose. ***JGH***: Nothing to disclose.

* Corresponding author. Department of Orthopaedics, Emory University School of Medicine, 57 Executive Park South, Room #160-5, Atlanta, GA 30329, USA. Tel.: (404) 778-1567; fax: (404) 778-8192.

E-mail address: zgrabel@emory.edu (Z.J. Grabel).

https://doi.org/10.1016/j.spinee.2018.05.036
1529-9430/

Introduction

Surgical site infection (SSI) following spine surgery is a clinically devastating and resource-intensive complication. The incidence of postoperative spine SSI ranges from 0.7% to 12% [1–3]. Prior literature has demonstrated an

additional cost of $33,705 associated with each spine SSI [4]. The prophylactic use of intraoperative vancomycin powder has been shown in several series to be effective in decreasing the rate of postoperative infection in spine surgery [5–11].

Although the use of intraoperative vancomycin may result in a lower incidence of SSI, there is growing concern that when an SSI does occur in this setting, the microbial profile of these SSIs may favor more resistant and uncommon organisms. A recent study examined positive cultures in postoperative SSI after spine deformity surgery in which intraoperative vancomycin was used in all cases. This investigation revealed the majority of cultures were gram-negative and polymicrobial [12]. Another single institution study similarly examined the microbial trends in patients with postoperative spine SSI (all regions and indications) who were treated with prophylactic local vancomycin and suggested an increase in gram-negative and polymicrobial cultures [13].

The purpose of this study was twofold. First, we sought to compare the microbial profile of SSI in treated patients (intraoperative local vancomycin used) versus untreated patients (no local vancomycin) who underwent elective thoracic and/or lumbar decompression with or without fusion. Second, it examined the effects of local vancomycin powder on the extent of required treatment, including number of reoperations, complexity of antibiotic regimen, and length of stay (LOS). To our knowledge, this has not been documented in the literature.

Methods

Patient selection

Institutional review board approval was obtained before initiation of this study. A retrospective review of patients who underwent posterior thoracic and/or lumbar spine surgery with or without fusion between 2010 and 2017 was conducted. Exclusion criteria included cervical spine procedures, procedures performed through a lateral or anterior approach, and infection as an indication for surgery.

Among this group, a query was performed to identify patients with SSI. We defined a clinically-significant SSI by the need to return to the operating room for an irrigation and debridement procedure. The decision to proceed was made at the discretion of the attending surgeon based on a combination of clinical criteria. Criteria included: wound drainage, wound dehiscence, fevers, evidence of infection on imaging, and elevated infectious laboratory values such as erythrocyte sedimentation rate, C-reactive protein, and white blood cell count. Among this cohort of patients with SSI, patient demographics, comorbidities, previous spine surgery, the use of intraoperative vancomycin, complications, and the onset of SSI after index procedure were recorded.

Surgical details

At our institution, it is standard practice for all patients to receive preoperative and postoperative prophylactic antibiotics. Typically, this consists of weight based intravenous (IV) cefazolin within 1 hour of incision and every 8 hours for 24 hours after surgery. Patients with penicillin allergies receive either IV clindamycin or vancomycin. Subfascial drains are used in most cases but this is based on surgeon preference. Distribution and dosing of vancomycin powder was variable among surgeons, but typical use included wide dispersal of 1 g of vancomycin powder throughout the wound immediately before fascial closure.

Outcome measures and statistical analysis

Patients were divided into two groups—those who were treated with local intraoperative vancomycin (treated) and those who were untreated (nonvancomycin cohort). The organism profile for each group was compared. The average LOS, reoperation rate, and number of patients requiring more than one antibiotic were calculated for each patient in both groups. Patients in the treated and untreated group were then further categorized by culture result (gram-positive, gram-negative, polymicrobial, fungal, and no growth). The average LOS, reoperation rate, and number of patients requiring more than one antibiotic were compared by culture type between the treated and untreated group. Chi-square analysis and two-tailed *t* test were used. Multivariable logistic regression analysis was performed to control for discrepancies in patient characteristics among the vancomycin-treated group and the untreated group. Statistical significance was defined as a p value less than 0.05.

Results

There were 5,909 thoracic and/or lumbar decompression with or without fusion procedures performed between 2010 and 2017. One hundred and fifteen SSIs were identified, resulting in a 1.9% infection rate. Among the SSI cohort, 42 patients had received intraoperative vancomycin. Smoking history, history of diabetes, number of comorbidities, number of postoperative complications, and onset of SSI were not statistically different between the two groups. Mean BMI of patients in the vancomycin group was 32.1 compared with 29.1 in the untreated cohort (p=0.046). The majority of patients in the treatment group underwent fusion procedures (78.6%) as opposed to the untreated group (38.4%; p=0.0003). Only 26.2% of the patients in the vancomycin-treated group had a history of prior spine surgery compared with 46.6% in the untreated group (p=0.031; Table 1). Multivariable logistic regression analysis results are illustrated in Table 2.

Overall, the most common organism cultured was methicillin-sensitive staphylococcus (Staph) aureus (MSSA; 36.5%). Polymicrobial and gram-negative organisms represented 14.8% and 8.7% of cultures, respectively. There

Table 1
Characteristics of patients with SSI who either did or did not (untreated) receive prophylactic intraoperative vancomycin powder during their index procedure

	Vancomycin-treated, n (%)	Untreated, n (%)	p
Smoker	4 (9.5%)	13 (17.8%)	0.228
Mean BMI	32.1	29.1	0.046
Diabetes	12 (28.6%)	18 (24.6%)	0.645
2+comorbidities	30 (71.4%)	47 (64.3%)	0.439
Arthrodesis	33 (78.6%)	28 (38.4%)	0.0003
Prior spine surgery	11 (26.2%)	34 (46.6%)	0.031
Complications	5 (12%)	11 (15%)	0.636
Onset of SSI after index procedure (days)	21	23	0.257

SSI, surgical site infection; BMI, body mass index.

Table 2
Multivariable logistic regression analysis of patient characteristics associated with gram-positive infection in 115 patients with SSI

Patient characteristics		Adjusted odds ratio	95% confidence interval	p
BMI	per 1 kg/m^2	0.94	0.87–1.01	0.08
Fusion	Yes vs no	0.38	0.16–0.92	0.03
Prior spine surgery	Yes vs no	2.99	1.25–7.15	0.01

SSI, surgical site infection; BMI, body mass index.

were 28 cases with no growth from intraoperative cultures (24.3%). Coagulase-negative staphylococcus represented 6.1% of organisms. *Escherichia coli* was the most common gram-negative culture (Table 3).

Table 3
Most common culture results among all SSI patients

Organism	Overall prevalence (n=115)
MSSA	42 (36.5%)
Polymicrobial	17(14.8%)
Gram-negative organism	10 (8.7%)
Coagulase-negative staphylococcus	7 (6.1%)
No growth	28 (24.3%)

MSSA, methicillin-sensitive *Staphylococcus aureus*; SSI, surgical site infection.

A total of 26.1% of culture-positive infections in the vancomycin group were gram-positive organisms, all of which were Staph species. In the untreated group, 64.4% of positive cultures were gram-positive and Staph infections represented 57.5% of infections (p = 0.001). A total of 23.8% of cultures in the vancomycin group were polymicrobial and 16.7% were gram-negative compared with 9.6% (p=0.039) and 4.1% (p=0.021) in the untreated group, respectively. There were two cultures positive for fungus in the nonvancomycin group and none in the treatment group. Approximately one-third (33.3%) of the cultures in the treatment group revealed no growth compared with 19.1% in the nonvancomycin group (p=0.089; Table 4).

In the vancomycin-treated group, 26.1% of patients required an additional irrigation and debridement (I&D) compared with 38.4% in the untreated group (p=0.184). The percentage of patients in the treatment group and nonvancomycin group who required more than one antibiotic was similar (26.0% vs 26.1%, respectively; p=0.984). Mean LOS for the vancomycin treatment group was 8.0 versus 7.9 for the untreated group (p=0.945; Table 5).

Table 4
Cultured organisms from SSI patients who were treated with vancomycin vversus those who were not (untreated) during their index procedure

Organism	Vancomycin-treated, n=42 (%)	Untreated, n=73 (%)	p
Gram-positive organism	**11 (26.1%)**	**47 (64.4%)**	**0.001**
Staphylococcus aureus	**11 (26.1%)**	**42 (57.5%)**	**0.001**
MSSA	8	34	0.003
MRSA	2	1	0.272
Coagulase-negative S. aureus	1	6	0.207
Staphylococcus Intermedius		1	N/A
Group B streptococci		2	N/A
Enterococcus faecalis (group D streptococci; VRE)		3	
Gram-negative organism	**7(16.7%)**	**3 (4.1%)**	**0.021**
Propionibacterium acnes		1	N/A
Escherichia coli	5		N/A
Klebsiella pneumoniae	1		N/A
Proteus	1	1	0.689
Enterobacter aerogenes		1	N/A
Polymicrobial	**10 (23.8%)**	**7 (9.6%)**	**0.039**
Fungal organism		2	N/A
No growth	14(33.3%)	14 (19.1%)	0.089

MSSA, methicillin-sensitive *Staphylococcus aureus*; MRSA, methicillin-resistant *Staphylococcus aureus*; SSI, surgical site infection; VRE, vancomycin-resistant enterococci.

Table 5
Number of patients who required repeat I&D, more than one antibiotic, and mean LOS for vancomycin-treated and untreated patients

	Vancomycin-treated, n=42 (%)	Untreated, n=73 (%)	p
Need for repeat I&D	11 (26.1%)	28 (38.4%)	0.184
>1 antibiotic	11 (26.1%)	19 (26.0%)	0.984
Mean LOS	7.9	8	0.945

I&D, irrigation and debridement; LOS, length of stay.

When broken down by culture type, 18.2% of gram-positive infections in the vancomycin group required repeat I&D and more than one antibiotic compared with 44.7% (p=0.106) and 21.3% (p=0.819) of gram-positive infections in the untreated group, respectively (Table 6A, 6B). Three of the gram-negative infections in the vancomycin treatment group required additional reoperations versus zero in the untreated group. Polymicrobial infections in the vancomycin group required repeat I&D and treatment with more than one antibiotic 60% of the time, respectively, compared with repeat I&D rate of 85.7% (p=0.252) and treatment with multiple antibiotics in 100% (p=0.628) of patients in the untreated group with polymicrobial infection (Table 6A, 6B). Polymicrobial infection resulted in the greatest mean LOS in both the vancomycin-treated and untreated group: 10.3 and 15.1days, respectively (p=0.108; Table 6C).

Discussion

The application of intraoperative vancomycin powder in spine surgery has been reported by many studies to decrease the rate of SSI [5–11]. O'Neil et al. [7] evaluated the infection rate of patients who underwent spine arthrodesis for traumatic spine injuries. The cohort who received intraoperative vancomycin had a 0% rate of infection and the control group had a 13% rate of SSI. Sweet et al. [5] demonstrated a 10-fold decrease in infection rate with intraoperative vancomycin in patients who underwent posterior thoracolumbar fusions. Furthermore, Strom et al. [8]

Table 6A
Number of patients who required repeat irrigation and debridement by culture type

	Vancomycin-treated	Untreated	p
Gram-positive	2 (18.2%)	21 (44.7%)	0.106
Gram-negative	3 (42.9%)	0	N/A
Fungal	N/A	1 (50%)	N/A
Polymicrobial	6 (60.0%)	6 (85.7%)	0.252
No growth	1 (7.1%)	1 (7.1%)	1

Table 6B
Number of patients who required more than one antibiotic by culture type

	Vancomycin-treated	Untreated	p
Gram-positive	2 (18.2%)	10 (21.3%)	0.819
Gram-negative	0	0	N/A
Fungal	N/A	1 (50%)	N/A
Polymicrobial	6 (60.0%)	7 (100%)	0.628
No growth	3 (21.4%)	1 (7.1%)	0.28

Table 6C
Mean length of stay by culture type

	Vancomycin-treated	Untreated	p
Gram-positive	7.8	8.1	0.965
Gram-negative	9.6	6.3	0.489
Fungal	N/A	9	N/A
Polymicrobial	10.3	15.1	0.108
No growth	5	3.9	0.206

demonstrated a similar decrease rate in infection with use of intraoperative vancomycin in patients who underwent posterior cervical fusions. Chiang et al. [9], through meta-analysis, and Heller et al. [10], through retrospective investigation, specifically reported a decreased rate of Staph aureus associated SSIs when intraoperative vancomycin was used. We sought to determine whether SSI in patients who received intraoperative vancomycin may favor more virulent organisms. In addition, this study examined the impact that intraoperative vancomycin has on reoperation rate, antibiotic regimen, and LOS.

The overall infection rate in the present study was 1.9%, which is consistent with prior studies [4,5,14–16]. Staph aureus was the most common organism isolated among all SSIs in our study. This is consistent with the results of Amir Abdul-Jabbar et al.'s [14] investigation, which examined the pathogen profile among 239 spine infections (all spine regions). Interestingly, MSSA was significantly more prevalent in the untreated cohort but there was no difference in prevalence of Coagulase-negative Staph and methicillin-resistant Staph aureus among the two cohorts. This may be attributed to the relatively small number of Coagulase-negative Staph (7) and methicillin-resistant Staph aureus (3) SSIs compared with MSSA (42).

This investigation revealed that gram-negative infections and polymicrobial infections were significantly more prevalent in patients who received intraoperative local vancomycin compared with those who did not. Adogwa et al. [12] and Ghobrial et al. [13] suggested gram-negative infections were more common among patients who received prophylactic vancomycin powder. However, neither of these studies included a control or untreated cohort. In addition, we demonstrated that there was a significantly higher proportion of isolated gram-positive cultures in the untreated cohort compared with those who received vancomycin. We believe this phenomenon is secondary to vancomycin's prophylactic effect against gram-positive organisms. However, it must be noted that more patients in the vancomycin-treated cohort underwent a fusion procedure (Table 1) and multivariable analysis demonstrated that a fusion procedure is independently associated with a lower odds of gram-positive culture in a SSI (Table 2), although there is no clear explanation for this. Furthermore, more patients in the untreated group had a history of prior spine surgery, which was found to be an independent risk factor for gram-positive culture in those with SSI (Table 2). Therefore, patients with a history of previous spine surgery who are not treated with vancomycin powder may be especially susceptible to a gram-positive organism should they develop an SSI.

The overall no-growth rate in our study (24.2%) is consistent with prior studies [12,13]. In contrast to the vancomycin arm in our study, which demonstrated a 33.3% no-growth rate, Amir Abdul-Jabbar et al. [14] revealed a negative culture rate of 2.9% and none of their patients received vancomycin powder. One possibility for a relatively high no-growth rate in the vancomycin arm of our study is that high concentrations of local vancomycin suppressed culture growth. On the contrary, it is possible that we have a cultural bias that favors returning to the operating room in the case of a persistently draining wound, whether infected or otherwise. The notion is that a draining wound not only allows entry to bacteria but the existing hematoma and/or seroma is a fertile culture medium. This may also explain the relatively large percent of cultures without growth in our investigation and aforementioned studies.

Interestingly, there was no significant difference in the need for multiple antibiotics or mean LOS between the vancomycin-treated group and the untreated cohort. There was a pattern toward increased reoperation rate for those who did not receive intraoperative vancomycin, however this was not statistically significant. It is possible that, with a larger sample size, this phenomenon becomes significant in which case another benefit of local application of vancomycin would be that it lowers reoperation rate in those who develop SSI. The reoperation rate, antibiotic regimen, and average LOS were compared by culture type between vancomycin-treated patients and the untreated group to determine if intraoperative vancomycin had an effect on the virulence of the individual organisms (ie, the gram-negative organisms in the vancomycin treatment group causing a higher reoperation rate than those in the untreated group?; Table 5A–C). However, the virulence of each pathogen-type appeared to be no different between the treated and untreated groups. These findings should be comforting to surgeons who use intraoperative vancomycin. That is, when SSI does develop in these patients, the outcomes are not adversely affected in terms reoperation rate, need for multiple antibiotics, and mean LOS.

There are several potential limitations to this study. This was a retrospective study which employed existing documentation in the electronic medical record. In addition, this investigation was conducted at a single institution which serves as a referral center. As a result, the patients in the study may have more comorbidities and may have undergone more complex surgery than patients at other centers. As such, the microbial profile of our patients may not be generalizable. However, the aim of the study was to compare the microbial profile between the treatment and untreated arms, and there was no difference in comorbidities among these groups (Table 1). Another potential limitation is that there was not enough gram-negative or polymicrobial SSIs to accurately perform multivariable logistic regression analysis to control for differences in patient characteristics (ie, BMI; fusion procedure; and history of previous surgery) among the 2 cohorts. Future studies with a larger sample size of gram-negative and polymicrobial cultures are warranted for further investigation. Further investigation is also needed to determine whether the 24% of patients that were culture negative represented cases that were not actually SSIs versus SSIs with undetectable culture growth.

Conclusions

This study demonstrates an association between the use of vancomycin powder and a relative increase in prevalence of gram-negative and polymicrobial organisms in patients ultimately developing SSI following thoracolumbar spine surgery. However, this did not adversely affect the type of care required by the SSI patients, such as the need for multiple reoperations, complexity of antibiotic regimen, or LOS in this series. Continued investigation is needed to evaluate whether the addition of local prophylactic antibiotics with gram-negative coverage coupled with intraoperative vancomycin powder may further affect this microbial profile and serve as a safe and cost-effective means of further reducing the SSI rate in spine surgery.

References

[1] Beiner JM, Grauer J, Kwon BK, et al. Postoperative wound infections of the spine. Neurosurg Focus 2003;15:E14.
[2] Pull ter Gunne AF, Cohen DB. Incidence, prevalence, and analysis of risk factors for surgical site infection following adult spinal surgery. Spine 2009;34:1422–8.
[3] Smith JS, Shaffrey CI, Sansur CA, Berven SH, Fu KM, Broadstone PA, et al. Rates of infection after spine surgery based on 108,419 procedures: a report from the Scoliosis Research Society Morbidity and Mortality Committee. Spine 2011;36:556–63.
[4] Godil SS, Parker SL, O'Neill KR, et al. Comparative effectiveness and cost-benefi t analysis of local application of vancomycin powder in posterior spinal fusion for spine trauma. J Neurosurg Spine 2013;19:331–5.
[5] Sweet FA, Roh M, Sliva C. Intrawound application of vancomycin for prophylaxis in instrumented thoracolumbar fusions: efficacy, drug levels, and patient outcomes. Spine 2011;36:2084–8.
[6] Molinari RW, Khera OA, Molinari III WJ. Prophylactic intraoperative powdered vancomycin and postoperative deep spinal wound infection: 1,512 consecutive surgical cases over a 6-year period. Eur Spine J 2012;21(Suppl 4):S476–82.
[7] 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 2011;11:641–6.
[8] 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 2013;38:991–4.
[9] Chiang HY, Herwaldt LA, Blevins AE, Cho E, Schweizer ML. Effectiveness of local vancomycin powder to decrease surgical site infections: a meta-analysis. Spine J 2014;14:397–407.
[10] Heller A, McIff TE, Lai SM, Burton DC. Intrawound vancomycin powder decreases staphylococcal surgical site infections after posterior instrumented spinal arthrodesis. J Spinal Disord Tech 2015;28: E584–9.
[11] Dennis HH, Wei DT, Darren KZ, Shantakumar JT, Kumar N, Lau LL, et al. Is intraoperative local vancomycin powder the answer to surgical site infections in spine surgery? Spine 2016. [Epub ahead of print].
[12] Adogwa O, Elsamadicy AA, Sergesketter A, et al. Prophylactic use of intraoperative vancomycin powder and postoperative infection: an analysis of microbiological patterns in 1200 consecutive surgical cases. J Neurosurg Spine 2017;27:328–34.
[13] Ghobrial GM, Thakkar V, Andrews E, et al. Intraoperative vancomycin use in spinal surgery: single institution experience and microbial trends. Spine 2014;39:550–5.
[14] Abdul-Jabbar A, Berven SH, Hu SS, Chou D, Mummaneni PV, Takemoto S, et al. Surgical site infections in spine surgery: identification of microbiologic and surgical characteristics in 239 cases. Spine 2013;38:E1425–31.
[15] Khan NR, Thompson CJ, DeCuypere M, Angotti JM, Kalobwe E, Muhlbauer MS, et al. A meta-analysis of spinal. Surgical site infection and vancomycin powder. J Neurosurg Spine 2014;21:974–83.
[16 Glassman SD, Dimar JR, Puno RM, Johnson JR. Salvage of instrumental lumbar fusions complicated by surgical wound infection. Spine 1996;21:2163–9.