

Vancomycin Use in Posterior Lumbar Interbody Fusion of Deep Surgical Site Infection

Shiyong Wang, Rubin Yao, Zhongjie Li, Xiangdong Gong, Jitao Xu, Fajun Yang, Kaishun Yang

Department of Spinal Surgery, First Affiliated Hospital of Dali University, Dali, Yunnan, People's Republic of China

Correspondence: Kaishun Yang, Department of Spinal Surgery, First Affiliated Hospital of Dali University, Dali, Yunnan, People's Republic of China, Tel +86-872-2201044, Email yangkaishunyks5@126.com

Objective: To retrospectively analyze if the use of topical intraoperative vancomycin powder reduces deep surgical site infection (DSSI) after posterior lumbar interbody fusion.

Methods: All spinal surgeries for lumbar degenerative disease and underwent posterior fixation interbody fusion between January 2013 and December 2018 were reviewed. A total of 891 patients were included, of which 527 patients (treatment group) received intraoperatively topical vancomycin powder; the others were served as control group. The primary outcomes were the overall incidence of DSSI and the effect of vancomycin on its development. The secondary outcome was risk factors for DSSI. Data on the baseline characteristics, postoperative complications, perioperative risk factors, and one-year postoperative prognoses were extracted from the medical records.

Results: A total of 20 patients met the diagnostic criteria for DSSI (2.24%), of which 7 patients (1.33%) in the treatment group and 13 patients (3.57%) in the control group. There was a significant difference in the incidence of DSSI between the groups ($P = 0.026$). Multivariate logistic regression analysis with stepwise backward elimination showed that the local use of vancomycin powder was an independent protective factor for DSSI (odds ratio (OR): 0.25, $P = 0.01$), whereas high body mass index (BMI) (OR : 1.21, $P = 0.005$), drinking (OR : 5.19, $P = 0.005$), urinary tract infections (OR : 4.49, $P = 0.021$), diabetes mellitus (OR : 4.32, $P = 0.03$), and blood transfusions (OR : 3.67, $P = 0.03$) were independent risk factors for DSSI.

Conclusion: The intraoperative usage of vancomycin powder could reduce effectively decreases the incidence of DSSI after posterior lumbar interbody fusion for degenerative lumbar diseases. High BMI, diabetes mellitus, drinking, and urinary tract infections were independent risk factors for DSSI, whereas the local use of vancomycin protected against these factors.

Keywords: posterior lumbar interbody fusion, vancomycin, deep surgical site infection, risk factors

Introduction

DSSI after spinal surgery is an uncommon but devastating complication with the reported incidence as high as 11.3%.¹ It is well documented that the factors of risk infection are including longer operation time, posterior surgical approach, previous surgery, and application of spinal instruments.² While many efforts has been made to control the incidence of DSSI such as the unprecedented development of antimicrobial agents, the widespread use of minimally invasive surgery, and continuous improvements in postoperative care techniques, the decrease in the incidence of SSIs is low.³⁻⁵ In clinical practice, various methods have been adopted to prevent or reduce the development of DSSI, including blood glucose control, treatment of urinary tract infections, smoking cessation, nutritional supplementation, preoperative skin debridement, antibiotic prophylaxis, while DSSI is still a substantial reason of prolonging hospital stay, increasing medical costs, rate of reoperations, pseudoarticulation formation and death.⁶⁻⁸ Therefore, control of DSSI after spinal surgery is urgent considering the quality of patients' life and the financial burden.

Recently, intraoperative application of vancomycin powder to spinal incisions has been reported effectively reducing surgical site infection rates and topical use increased vancomycin concentration without increasing drug-related side effects.⁹ A previous study evaluated the release characteristics in vivo and antibacterial ability of vancomycin, they found that the vancomycin concentration could be detected at 0.5 h and increased rapidly until reaching the peak at 2 h, and it could be still detected 7 days after the surgery.¹⁰ Besides, no death, local infection or other complications occurred.

The majority of the aforementioned literatures highlighting surgical site infection have historically been in the field of multiple spinal diseases and surgeries, and directly sprinkle vancomycin powder before closing the incision, but the results varied. We therefore explored if the use of topical intraoperative vancomycin powder reduces DSSI after posterior lumbar interbody fusion.

Materials and Methods

Inclusion/Exclusion Criteria and Data Collection

The study protocol was approved by the institutional review board at Spinal Surgery Department of our hospital. The inclusion criteria included patients with degenerative diseases of the lumbar spine (spondylolisthesis, spinal stenosis, disc herniation, degenerative scoliosis, discogenic low back pain, and lumbar instability); patients undergoing posterior lumbar interbody fusion; patients who were followed-up for more than one year. The exclusion criteria included lumbar fractures, spinal inflammatory diseases, patients with degenerative diseases of the lumbar spine who underwent decompression only (percutaneous endoscopic discectomy or minimally invasive transforaminal lumbar discectomy), and patients followed-up for less than one year.

A total of 891 patients with posterior lumbar interbody fusion and fixation met the inclusion criteria and finally included in this study from January 2013 to December 2018. In our cohort, 364 patients did not receive local vancomycin (control group) and 527 patients received local vancomycin (treatment group). According to the Centers for Disease Control and Prevention (CDC) criteria,¹¹ deep surgical site infection (DSSI) is defined as an infection that occurred within 30 days (without implants) or within one year (with implants) after surgery involving deep soft tissue.

Patient demographics (age, gender, height, weight), smoking status, alcohol drinking status, presence of diabetes, hypertension, hyperuricemia, urinary tract infection (laboratory tests or urological diagnosis), surgical factors (number of spinal levels, intraoperative blood loss, duration of operation, postoperative drainage volume, number of internal fixations), preoperative hospital stay, number of blood transfusions, and catheter dwell time were recorded. All patient's records were evaluated for signs of DSSI within one year after discharge.

Surgery and Local Use of Vancomycin

All patients underwent posterior lumbar decompression and interbody fusion after preoperative examination and exclusion of surgical contraindications. During surgery, pedicle screws were used for fixation, and autogenous bone was implanted into the intervertebral space, or one cage was implanted after bone graft (allograft bone was used in cases in which autogenous bone was insufficient). Systemic antibiotic prophylaxis with second-generation cephalosporins was performed in all patients 30–60 min before skin resection. Patients allergic to penicillin or cephalosporins received clindamycin. Antibiotics were repeated once when blood loss exceeded 1500 mL or surgical time exceeded 3 h. Antibiotics were continually administered up to 24–48 h after surgery for all patients. After discectomy and decompression, the incision and intervertebral space were washed with sterile saline. After intervertebral bone grafting and cage implantation, the incision was soaked with povidone-iodine for at least three min (except for dural rupture) and washed with 3000 mL of sterile saline. When no active bleeding was detected, two negative pressure drainage tubes were placed deep in the incision, and the incision was closed layer by layer.

In the treatment group, approximately 250 mg of vancomycin powder was mixed with the bone graft. Then, the graft was implanted into the intervertebral space and cage, and 250 mg of vancomycin powder was applied directly to the surgical bed. In cases in which more than two levels were fused, the intraoperative dose of vancomycin was increased to 1000 mg, and the other should use only 500 mg.

The drainage tubes were maintained under negative pressure after surgery to reduce the risk of hematoma formation. The drainage tubes were removed after the drainage volume was less than 50 mL/day, and radiographs and three-dimensional computed tomography (3DCT) reconstruction of the lumbar spine were reviewed.

Statistical Analysis

The effects of the local use of vancomycin powder on DSSI and its potential risk factors were analyzed. Categorical and continuous data were analyzed using the chi-square and independent-sample *t*-tests. In multivariate analysis, relative risk, 95% confidence intervals, and independent risk and protective factors were determined by multivariate logistic regression with stepwise backward elimination. A *P*-value of less than 0.05 was considered statistically significant.

Results

Patient Characteristics and the Incidence of DSSI

The demographics and clinical characteristics of two groups are shown in Table 1. There were no significant differences in demographics and clinical characteristics between patients with and without SSIs in the control group, except for BMI (25.69 ± 1.95 vs 23.20 ± 3.39 kg/m², $P = 0.001$).

The incidence of DSSI was significantly lower in the treatment group ($P = 0.026$, chi-square test, Figure 1). A total of 20 patients (2.24%) were present with DSSI, including 13 (3.57%) in the control group and 7 (1.33%) in the treatment group (Table 2).

Microbiological Analyses

Among the 20 infected patients, the bacterial culture was negative in 11 patients and positive in nine patients. In the treated group, cultures were positive for *Escherichia coli* (three cases) and Gram-positive cocci (one case). In the control group, cultures were positive for Gram-negative bacteria (three cases) and Gram-positive bacteria (two cases) (Table 3). No vancomycin-resistant strains were found.

Multivariate Logistic Regression Analysis of DSSI

Multivariate analysis of all patients showed that the local use of vancomycin was a protective factor for DSSI ($OR: 0.25$, $B: -1.38$, $P = 0.01$), whereas high BMI ($P = 0.005$), drinking ($P = 0.005$), diabetes mellitus ($P = 0.03$), urinary tract infection ($P = 0.021$), and blood transfusions ($P = 0.03$) were independent risk factors for DSSI.

In the subgroup analysis, the independent risk factors for DSSI in the control group were high BMI ($P = 0.01$), diabetes mellitus ($P = 0.006$), number of surgical levels ($P = 0.005$), postoperative drainage volume ($P = 0.014$). And in the treatment group were surgical duration ($P = 0.025$) and perioperative blood transfusion ($P = 0.002$) (Table 4).

Table 1 Demographic and Clinical Characteristics of Lumbar Fusion Patients Treated or Not with Vancomycin Intraoperatively. Factors Included in the Study and Intra-Group Comparison Between the Two Groups

Patient Factors		Control Group		P	Treatment Group		P
		DSSI	Non-DSSI		DSSI	Non-DSSI	
Gender	Male, n (%)	8 (61.5%)	148 (42.2%)	0.166	2 (28.6%)	232 (44.6%)	0.641
	Female, n (%)	5 (38.5%)	203 (57.8%)		5 (71.4%)	288 (55.4%)	
Age (years)		57.08±8.29	52.82±9.63	0.117	62.29±5.68	56.02±19.58	0.398
Body mass index (kg/m ²)		25.69±1.95	23.20±3.39	0.001*	24.97±4.08	23.28±3.33	0.186
Smoking (yes)		5 (38.5%)	95 (27.1%)	0.366	2 (28.6%)	123 (23.7%)	1.000
Alcohol abuse (yes)		4 (30.8%)	45 (12.8%)	0.063	2 (28.6%)	66 (12.7%)	0.498
Diabetes mellitus (yes)		3 (23.1%)	21 (6.0%)	0.062	1 ((14.3%)	28 (5.4%)	0.848
Hypertension (yes)		5 (38.5%)	84 (23.9%)	0.231	3 (42.9%)	121 (23.3%)	0.444
Hyperuricemia (yes)		1 (7.7%)	23 (6.6%)	1.000	2 (28.6%)	57 (58.2%)	0.387
Urinary tract infection (yes)		2 (15.4%)	23 (6.6%)	0.498	2 (28.6%)	36 (6.9%)	0.143
Preoperative hospital stay (days)		7.85±4.95	5.91±3.04	0.185	6.29±2.69	6.12±3.74	0.909
Number of surgical levels (n)		1.62±0.87	1.35±0.56	0.292	1.43±0.54	1.35±0.57	0.715
Intraoperative blood loss (mL)		442.31±299.20	417.98±270.00	0.751	378.57±186.76	313.82±231.71	0.462
Surgical duration of operation (min)		181.15±38.58	184.15±60.63	0.860	130.00±16.58	161.38±47.22	0.002*
Postoperative drainage volume (mL)		261.62±222.92	438.50±325.88	0.053	572.00±270.19	445.69±464.99	0.474
Number of internal fixations (n)		8.38±1.85	7.80±1.69	0.226	7.29±0.76	7.47±1.91	0.800
Blood transfusion (n)		5 (38.5%)	100 (28.5%)	0.436	5 (71.4%)	127 (24.4%)	0.016*
Postoperative catheter dwell time in dwelling (days)		1.77±1.17	2.55±1.71	0.103	2.86±2.97	2.76±3.41	0.940

Note: *Significantly different at $p < 0.05$.

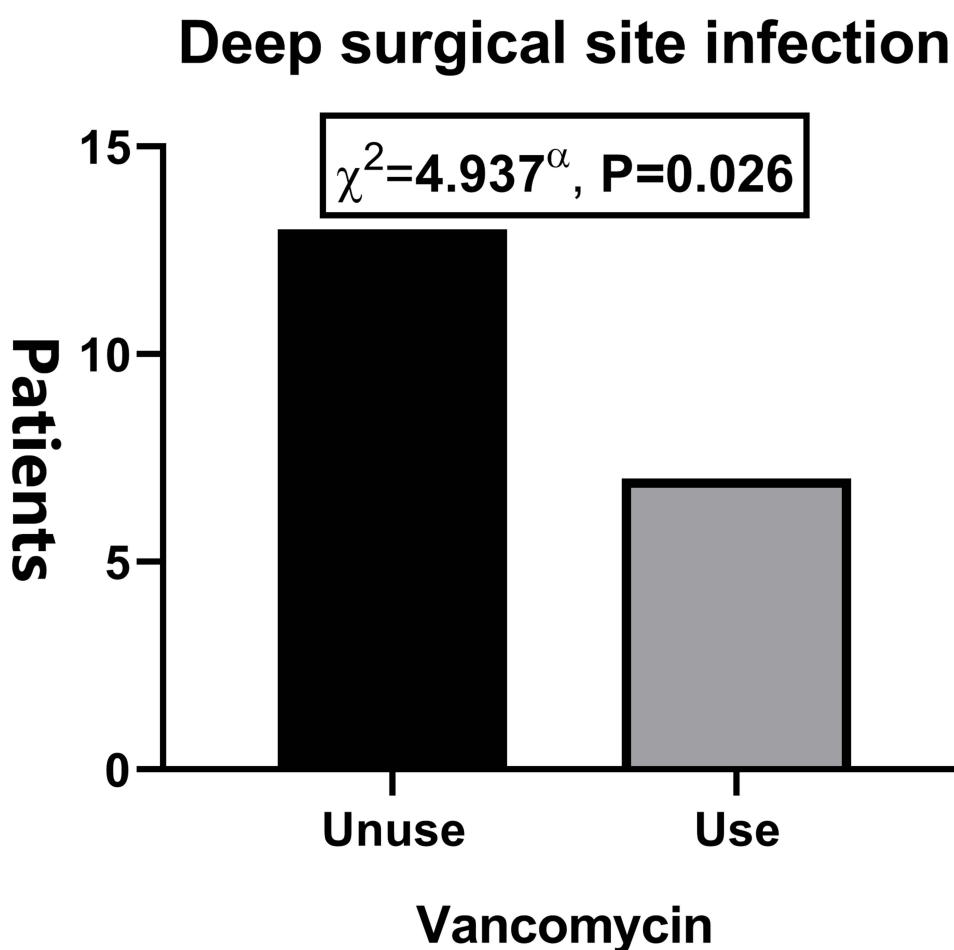


Figure 1 The rate of deep surgical site infection between two group.

Discussion

Spinal surgeons are focused on developing and implementing strategies to reduce and prevent the occurrence of DSSI. *Staphylococcus aureus* cultures in the nasal cavities, preoperative chlorhexidine showers, antibacterial treatments in the surgical sites, preoperative intravenous antibiotic prophylaxes, intraoperative temperature monitoring, intrawound vancomycin, postoperative drainage, and other measures are used to prevent DSSI.¹² Intravenous vancomycin is effective in preventing infections with methicillin-resistant *Staphylococcus aureus* (MRSA); however, this treatment is not routinely adopted because it is associated with hypotension, ototoxicity, nephrotoxicity, and an increased risk in the development of drug-resistant microorganisms in the oropharyngeal, respiratory, and urogenital tract.¹³ Due to vancomycin being absorbed into the blood from the wound with very poor efficiency and not detected in the serum of most patients, the risk of development of drug-

Table 2 Effect of Intrawound Vancomycin on the Rate of Deep Surgical Site Infection

		Local Vancomycin Treatment		Total	P	χ^2
		No	Yes			
DSSI Rate	Yes	13 (65.0%)	7 (35.0%)	20 (100%)	0.026	4.937
	No	351 (40.30%)	520 (59.70%)	871 (100%)		
		13/364 (3.57%)	7/527 (1.33%)	20/891 (2.24%)		

Table 3 Microorganisms in the Surgical Site

Infectious Agent	Patients (n)	Control Group	Treatment Group
<i>Escherichia coli</i>	4	1	3
<i>Enterobacter cloacae</i>	1	1	0
<i>Klebsiella pneumoniae</i>	1	1	0
Multidrug-resistant <i>Staphylococcus epidermis</i>	1	1	0
<i>Staphylococcus haemolyticus</i>	1	1	0
Gram-positive coccus	1	0	1
Negative microbial culture	11	8	3

Note: Microbiological culture in 20 patients with surgical site infections after lumbar fusion.

Table 4 Multivariate Logistic Regression Analysis of Risk Factors for Deep Surgical Site Infections

	Risk Factors	OR (95% CI)	B (SE)	Wald (df)	P
Total sample	Vancomycin (0: no, 1: yes)	0.25 (0.087–0.718)	−1.38 (0.54)	6.64 (1)	0.010
	Body mass index (kg/m ²)	1.21 (1.061–1.381)	0.191 (0.07)	8.05 (1)	0.005
	Alcohol abuse (0: no, 1: yes)	5.19 (1.65–16.30)	1.65 (0.58)	7.96 (1)	0.005
	Diabetes mellitus (0: no, 1: yes)	4.23 (1.15–15.55)	1.44 (0.67)	4.70 (1)	0.030
	Urinary tract infection (0: no, 1: yes)	4.49 (1.25–16.10)	1.50 (0.65)	5.32 (1)	0.021
Control group	Blood transfusion (n)	3.67 (1.135–11.867)	1.30 (0.599)	4.72 (1)	0.030
	Body mass index (kg/m ²)	1.28 (1.061–1.549)	0.25 (0.10)	6.64 (1)	0.010
	Diabetes mellitus (0: no, 1: yes)	9.65 (1.921–48.516)	2.27 (0.82)	7.58 (1)	0.006
	Number of surgical levels (n)	4.17 (1.553–11.193)	1.43 (0.50)	8.03 (1)	0.005
	Postoperative drainage volume (mL)	0.996 (0.992–0.999)	−0.004 (0.002)	5.99 (1)	0.014
Treatment group	Surgical duration (min)	0.97 (0.941–0.996)	−0.032 (0.014)	5.05 (1)	0.025
	Perioperative Blood transfusion (n)	16.75 (2.858–98.164)	2.82 (0.90)	9.76 (1)	0.002

resistant microorganisms in the oropharyngeal, gastrointestinal, and respiratory tracts is low, and high concentrations of vancomycin in the surgical site, which can effectively inhibit the growth of bacteria, may help prevent DSSI.⁸

In our cohort, 0.5 g and 1.0 g of vancomycin were applied to patients with one/two segments and more than two segments, respectively. Armaghani's study speculated that our study could achieve effective local vancomycin concentrations of a bacteriostatic concentration, and the serum vancomycin concentration was lower. Moreover, approximately 250 mg of vancomycin powder was mixed with autologous bone and implanted into the intervertebral space, delaying drug release into the bloodstream and increasing drug concentration in the intervertebral space, reducing the occurrence of DSSI under the condition of ensuring safety.

The effect of vancomycin on osteogenesis is a concern of many researchers and clinicians. In this study, approximately 250 mg of vancomycin powder was mixed with autologous bone, and the effect on bone graft fusion should be paid more attention to. Mendoza et al¹⁴ performed posterolateral lumbar spinal fusion in rats and found that the local administration of a standard dose (14.3 mg/kg) and a high dose (143 mg/kg) did not inhibit fusion, and the use of bone morphogenetic protein might have reduced the effect of vancomycin on bone fusion. Moreover, vancomycin (3.5 mmol/L) induced a temporary decrease in osteoblast proliferation but did not significantly affect the osteoblast metabolic activity.¹⁵ Vancomycin concentrations in our study were lower than those used in the above studies. In the cases that continued to give negative pressure suction, vancomycin applied locally would be lost some during wound irrigation, and fusion was successful in all treated patients. Therefore, the amount and method of vancomycin used in our study did not significantly affect interbody fusion.

Vancomycin affects the shape and viability of dural fibroblasts in vitro in a concentration-dependent manner.¹⁶ However, Sweet et al⁸ showed that vancomycin was safe to be poured into the incision when the dura was exposed.

There were no cases of epidural rupture or pseudoepidural cyst formation due to local vancomycin administration in our cohort. In patients with cerebrospinal fluid leakage after dural rupture, vancomycin was not applied locally, and autologous bone mixed with vancomycin was implanted into the intervertebral space and cage. No serious complications related to cerebrospinal fluid leakage were found in the perioperative period, and the drainage tube was removed after 7–10 days. A dural tear is an independent risk factor for SSI,¹⁷ and whether or not vancomycin can be used locally for those patients, how to use it, and at what dose and its effectiveness still need to be further studied.

We also found an anomaly in the treatment group, in which a short operative time was a risk factor for DSSI. In contrast, previous studies have suggested that prolonged surgery increases the risk of SSI.¹⁸ Besides, various factors were associated with DSSI in this study, BMI, drinking, urinary tract infections, diabetes mellitus, and blood transfusions, which were independent risk factors for DSSI. The reasons are analyzed as follows: age, BMI, intraoperative blood loss, postoperative drainage volume, and the frequency of blood transfusions in infected were higher than in the uninfected patients, but the operation time was significantly shorter. This may be related to the fact that surgeons speed up surgical procedures and shorten surgical time to reduce the risk of surgery and anesthesia in elderly patients and high BMI. However, that might neglect more delicate manipulation, resulting in poor hemostasis and in increased perioperative bleeding and blood transfusions. Previous research has found that advanced age, high BMI, blood transfusions, and bleeding are risk factors for SSI.^{18–21} Therefore, shortening surgical times while ignoring the delicate operation and hemostatic control may be counterproductive in such patients. Besides, it has been reported that smokers presented a 3-fold greater incidence of SSI of 17.8%, patients with diabetes of 14.3% compared with 7.8% among patients who did not have diabetes, male with a 2-fold increased risk compared with female (8.8% vs 4.9%).²²

The local application of vancomycin may affect the microbiota of the surgical site. In our cohort, bacteria cultured from pus in the treated group were mainly Gram-negative *Escherichia coli*. Several bacterial species were identified in the surgical site in the control group, including methicillin-resistant *Staphylococcus epidermidis* (MRSE). In this respect, a controlled study of 380 patients found that the local application of 1.0–2.0 g of vancomycin did not significantly decrease the rate of SSIs ($P = 0.2$) but changed the predominant bacterial species colonizing the wound.²³ Therefore, the amount of vancomycin used in our study (0.5–1.0 g) was enough to change the bacterial composition in the surgical site. Although this treatment approach had no adverse clinical outcomes and decreased the incidence of infections with MRSE and MRSA, the emergence of vancomycin-resistant bacteria, SSIs with Gram-negative bacteria and fungi, and vancomycin-related side effects should be monitored. A literature review showed that using 1.0–2.0 g of vancomycin in the surgical bed reduced the risk of SSIs; however, there were 23 (0.3%) adverse events.²⁴ Thus, further studies are necessary to find a balance between treatment efficacy and drug toxicity.

Conclusion

The results of this study have demonstrated that topical intrawound vancomycin powder administration could significantly reduce the risk of DSSI after posterior lumbar interbody fusion for degenerative lumbar diseases. However, future randomized trials are needed to confirm the present findings.

Abbreviations

DSSI, Deep surgical site infection; BMI, Body mass index; SSI, Surgical site infection; CDC, Centers for disease control and prevention; CT, Computed tomography; MRSE, Methicillin-resistant *Staphylococcus epidermidis*; MRSA, Methicillin-resistant *Staphylococcus aureus*.

Ethics Approval and Consent to Participate

This study was conducted with approval from the Ethics Committee of First Affiliated Hospital of Dali University. This study followed the Declaration of Helsinki. Written informed consent was obtained from all study participants.

Disclosure

The authors report no conflicts of interest in this work.

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