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Does the Application of Topical Intrawound Vancomycin Powder Affect Deep Surgical Site Infection and the Responsible Organisms after Spinal Surgery?: A Retrospective Case Series with a Historical Control Group

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Study Design: Retrospective case series with a historical control group.

Purpose: To compare the deep wound infection rates in patients undergoing spinal surgery with the application of topical intrawound vancomycin powder (TIVP) in the surgical site in addition to standard systemic prophylaxis with those in a matched historical cohort of patients for whom TIVP was not used.

Overview of Literature: Surgical site infection (SSI) after spine surgery is debilitating and is responsible for a significant increase in the health care costs, hospital stay, and morbidities. Although the application of TIVP before surgical closure is a promising method for reducing the SSI rate after spine surgery, its use is controversial, and currently, research trials are focusing on identifying its safety, efficacy, and the potential patient population.

Methods: A group of 88 patients who underwent posterior spinal surgery with TIVP administration (treatment group) was compared to a historical control group of 70 patients who had received only standard systemic intravenous prophylaxis (control group) for the analysis of deep SSI rate and the involved organisms.

Results: The overall rate of deep SSIs was 2.5% (4/158). All the SSIs were observed in patients who had posterior instrumentation and fusion for ≥3 levels. In the treatment group, the SSI rate was 3.4% (3/88), and the bacteria isolated were *Escherichia coli* (n=2) and *Pseudomonas aeruginosa* (n=1). In the control group, the infection rate was 1.4% (1/70), and the isolated bacteria were Morganella morganii and *Staphylococcus epidermidis*. No statistically significant association was found between the SSI rates of the treatment and control groups.

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Conclusions: Although the difference in the SSI rates was not statistically significant, the present results suggest that TIVP administration could not reduce the risk of deep SSIs after spinal surgery. Moreover, TIVP administration might also affect the underlying pathogens by increasing the propensity for gram-negative species.

Keywords: Infection; Postoperative complications; Spine; Surgical wound infection; Vancomycin

Introduction

Postoperative wound infection in spinal surgery is a potentially devastating complication that may also cause pseudoarthrosis, adverse neurological sequelae, and death. Despite improvement in the infection control protocols and advances in surgical techniques, the infection rate still ranges 0.7%–11.9% [1].

The type of the surgery influences the prevalence of spinal surgical site infections (SSIs). Instrumentation and fusion procedures have higher rates of infection than procedures without fusion [2]. In order to achieve high intrawound drug concentrations, local antibiotic administration has been utilized in addition to systemic antibiotic prophylaxis. Vancomycin powder reportedly reduced the infection rates from 0.2% to 5.6% [3-5]. Evaniew et al. [6] found no adverse events attributable to intrawound vancomycin in a meta-analysis; however, they also stated that the current quality of evidence was low.

The present study aimed to compare the deep SSI rate in patients who did and did not receive topical intrawound vancomycin during posterior spinal surgery. We hypothesized that there was no difference in the SSI rate based on the application of topical intrawound vancomycin in addition to standard intravenous (IV) prophylaxis.

Materials and Methods

1. Patients

Patient data were retrospectively reviewed for all adult patients who underwent posterior spine surgery between January 2015 and December 2016. The exclusion criteria were as follows: current or recent infection in the previous month, previous history of infections at the surgical site, infection as the indication for surgery, anterior cervical discectomy and fusion procedures, minimally invasive endoscopic spine surgeries, percutaneous biopsies, lumbar discectomies, decompression-only surgeries, rod-lengthening surgeries for early onset scoliosis, and vancomycin allergy.

The patients' medical records were reviewed to determine patient demographics (age, sex, American Society of Anesthesiologists physical status classification), diagnosis (degenerative, deformity, trauma, tumor, and others [congenital, metabolic, inflammatory]), type of surgery (with or without instrumentation), number of levels fused (<3 or ≥3), blood loss during surgery, duration of surgery, duration of hospitalization, presence of SSI, and causative organism.

All the patients received standard systemic antibiotic prophylaxis as per the clinical practice guidelines for antimicrobial prophylaxis in surgery, i.e., 2 g IV cefazolin within 60 minutes before surgical incision followed by 1 g IV cefazolin every 6 hours for 1 day [7]. All the patients were prepared with 10% povidone-iodine solution and disposable draping materials; then, a standard midline incision was performed using the open approach. All the surgical procedures were performed by senior surgeons at two different spine centers. All the wounds were irrigated with at least 2 L of normal saline by gravity prior to skin closure. In the treatment (vancomycin) group, 1 g topical vancomycin powder was applied on the muscles and fascia and subcutaneous tissues following final irrigation. Sub-fascial drains were inserted in all the patients. All the wounds were kept closed for 48 hours. At the time of initial wound inspection, the drains were removed under aseptic conditions by senior surgeons, independent of the collection. Patients were followed up for at least 12 months.

The patients were divided into the following two groups: the treatment (vancomycin) group comprising patients who were administered intrawound topical vancomycin powder from January 2016 to December 2016, at which time it was adapted as a standard protocol; the historical control group comprising those who underwent surgery without the application of topical vancomycin powder

from January 2015 to December 2015, as per the standard protocol at that time. The primary outcome parameter was the incidence of deep SSIs. Cultured organisms and subsequent treatments were also recorded.

The study protocol was approved by the local Institutional Review Board (Acibadem Mehmet Ali Aydinlar University-ATADEK 2018/15) and written informed consent was obtained from all individual participants included in the study.

2. Statistical analyses

Some patients had more than one measure in the dataset; therefore, univariate analyses were performed, considering the clustered structure of the data. Chi-square test statistics and Mann-Whitney *U*-test for clustered data were used to evaluate the categorical and continuous variables, respectively. If any of the cell had an expected count <5, Fisher exact test was performed. Clustered Data Statistical Software (Department of Biostatistics, Ankara University, Ankara, Turkey) was used for the statistical analyses. The type-I error rate was taken as α=0.05 for statistical significance.

Results

Total 158 patients were included in the study. The treatment group consisted of 88 patients, and the control

Table 1. Comparison between the treatment and control groups

Characteristic	Control group (Vancomycin -)	Treatment group (Vancomycin +)	*p*-value
Total no. of patients	70	88	
Age (yr)	49.31±22.77	50.77±22.47	
Sex			
Male	26 (37.1)	40 (45.5)	
Female	44 (62.9)	48 (54.5)	
American Society of Anesthesiologists physical status classification			0.307
I	42 (60.0)	42 (47.7)	
II	18 (25.7)	27 (30.7)	
III	10 (14.3)	17 (19.3)	
IV	0	2 (2.3)	
Diagnosis			0.649
Deformity	10 (14.3)	9 (10.2)	
Degenerative	37 (52.9)	53 (60.2)	
Trauma	9 (12.9)	8 (9.1)	
Tumor	6 (8.6)	11 (12.5)	
Others	8 (11.4)	7 (8.0)	
Instrumentation			**0.001**
Yes	56 (80.0)	85 (96.6)	
No	14 (20.0)	3 (3.4)	
Vertebral fusion			0.227
<3	21 (30.0)	19 (21.6)	
≥3	49 (70.0)	69 (78.4)	
No. of vertebral fusion	4 (0–18)	4 (0–18)	0.226
Surgery duration (min)	270 (90–600)	330 (120–600)	**0.004**
Blood loss (mL)	275 (0–4,509)	400 (50–6,000)	**0.001**
Hospitalization period (day)	3 (0–38)	4 (1–18)	**0.019**

Values are presented as number (%), mean±standard deviation, mean (minimum–maximum). Bold type is considered statistically significant (p<0.05).

group comprised 70 patients. Overall, the groups were statistically similar with respect to patient demographics (Table 1).

Performance of instrumentation was significantly more in the treatment group than in the control group (96.6% and 80%, respectively; p=0.001). The surgical duration was significantly longer in the treatment group (330 versus 270 minutes, respectively; p<0.05). The mean blood loss was also significantly higher in the treatment group (p<0.05). Surgical characteristics are shown in Table 1.

The overall rate of SSIs was 2.5% (4/158) (Table 2). In the treatment group, three patients had deep SSIs (3.4%), and all patients had >3 levels of instrumentation and fusion. The bacteria that were isolated were *Escherichia coli* in two cases and *Pseudomonas aeruginosa* in one case. In the control group, only one patient developed a deep SSI (1.4%), similar to that in a patient with 3 levels of instrumentation and fusion. The infection was polymicrobial SSI, and the bacteria that were isolated were *Morganella morganii* and *Staphylococcus epidermidis*. In all the cases of SSIs (control and treatment group), the surgical duration was >300 minutes, and blood loss was >500 mL. The average patient age was >35 years. Three cases were degenerative, while the other was congenital in nature. Infections were diagnosed between 7 and 21 days postoperatively. All the patients were treated with surgical debridement and IV antibiotics, and two additionally required vacuum-assisted closure (Table 3). No additional SSIs were reported at the final follow-up for either group, and there were no adverse events related to the intrawound vancomycin treatment.

Discussion

The results of the present study showed no significant decrease in the incidence of postoperative deep SSI in patients who underwent spinal surgery with the application local vancomycin powder. None of the patients experienced any side effects due to vancomycin use. In addition, the bacteria that were isolated were *E. coli* in two patients and *P. aeruginosa* in one patient in treatment group, and *M. morganii* and *S. epidermidis* in control group.

Our findings contradict the results of studies that favor topical vancomycin administration to decrease SSI rates. Furthermore, we found that all the bacteria isolated from SSIs in the treatment group were gram-negative bacteria.

Table 2. Deep surgical site infections after spine surgery in the treatment and control groups

Infection	Control group (Vancomycin -)	Treatment group (Vancomycin +)	Total	*p*-value
(-)	69 (98.6)	85 (96.6)	154 (97.5)	0.431
(+)	1 (1.4)	3 (3.4)	4 (2.5)	
Total	70 (100.0)	88 (100.0)	158 (100.0)	

Values are presented as number (%).

Table 3. Patients with deep surgical site infection and their treatments

	Group	Age (yr)	Sex	Diagnosis	# of fusion levels	ASA status	Surgery duration (min)	Blood loss (mL)	Site	Culture	Treatment
1	Control	62	F	Degenerative	3	III	360	500	Deep	*Morganella morganii* *Staphylococcus epidermidis*	Debridement IV antibiotics VAC
2	Treatment	79	F	Degenerative	7	I	300	600	Deep	*Escherichia coli*	Debridement IV antibiotics
3	Treatment	74	F	Degenerative	8	I	450	600	Deep	*Pseudomonas aeruginosa*	Debridement IV antibiotics VAC
4	Treatment	35	F	Others (congenital deformity)	10	I	450	1,500	Deep	*E. coli*	Debridement IV antibiotics

ASA status, American Society of Anesthesiologists physical status classification; F, female; IV, intravenous; VAC, vacuum-assisted closure.

Local delivery of antibiotics has advantages, such as achievement of high concentrations directly at wound site and avoidance of systemic toxicity [8-10]. The prophylactic administration of local intrawound vancomycin has become a routine practice following its use by Sweet et al. [4]. Several other retrospective studies have reported that intrawound vancomycin use is safe and effective for decreasing postoperative SSI rates [5,11-14]. However, Martin et al. [15,16] found no association between intrawound vancomycin administration and SSI rates. In their review on the effect of local vancomycin administration on the SSI rate, Kang et al. [17] concluded that there is limited evidence supporting the intrasite administration of vancomycin powder in surgical wounds. To our knowledge, two randomized trials have been conducted on this subject, and the researchers found no significant difference in the SSI rate of the control and treatment groups [18,19]. Our findings support these studies; however, considering that several retrospective studies have reported contradictory findings, it is clear that there is insufficient data to reach a definitive conclusion.

The leading cause of SSIs in spinal surgery is the presence of gram-positive bacteria, especially *Staphylococcus aureus* [2]. However, we found that gram-negative bacteria were the cause of SSI in our treatment group. Similarly, Hey et al. [20] found *P. aeruginosa* to be the most common causative agent by means of SSIs in topical intrawound vancomycin powder administered patients. The small sample size of the present study may be why our patients did not have any gram-positive SSI. However, considering that gram-negative infections form a small part of SSIs, their role as major causative agents in the treatment group makes this finding more significant. Ghobrial et al. [21] hypothesized that intraoperative vancomycin application caused selective pressure that increased the prevalence of gram-negative and polymicrobial wound infections and found that although *S. aureus* was still the most common cultured organism in SSI among patients who underwent spinal surgery with intraoperative vancomycin, more gram-negative organisms were isolated than in the historical control group (60.7% versus 21%, p=0.0001). They concluded that increased gram-negative and polymicrobial infections may require additional antibiotics, further complicating the SSIs [21]. In a recent randomized prospective study, Mirzashahi et al. [19] showed that intrawound vancomycin had a significant effect on the infection germ type in case of SSIs.

Our study is limited by its retrospective design and relatively low sample size. With 88 patients in the treatment group and 70 in the historical control group, the effect size was 0.403 (according to Table 1, blood loss). The type-I error rate was 0.05, and the achieved power of this study was 0.806; thus, no real statistical comparison was possible. Moreover, the treatment and control groups were not equally matched for instrumentation; it is known that instrumentation (as well as related increased blood loss and surgical time) is associated with increased SSIs [22,23], and all the SSIs in our study were found in patients who underwent instrumentation, similar to the findings in the literature. Although this difference needs to be acknowledged, it is noteworthy that there was no reduction in the SSI rate of the treatment group (an increased rate was observed), and the microbiological spectrum was entirely different. These differences cannot be explained by a relatively higher instrumentation rate (as well as the associated increased blood loss and surgical time). Finally, this study focused only on deep SSIs because they are considered more serious, important, and challenging; the definition is less subjective, as well [23].

Although most retrospective studies have reported that local vancomycin decreases the SSI rates, few retrospective studies, including ours and the randomized controlled trials, have found no beneficial effects. In this study, we found an increased incidence of gram-negative agents in SSIs. This stresses on the need of more rigorous evidence in supporting of or against the benefit of using local antibiotics, specifically vancomycin, because this may iatrogenically increase gram-negative infections while aiming to reduce gram-positive infections.

Conclusions

Although the sample size was relatively small, and the statistical analysis showed no significant difference, the results of this study have demonstrated that topical intrawound vancomycin powder administration could not reduce the risk of deep SSIs after spinal surgery. Moreover, all deep SSIs were caused by gram-negative bacteria in the treatment group; therefore, the application of topical intrawound vancomycin powder might have influenced the underlying pathogens by increasing the propensity for gram-negative species. However, future randomized trials are needed to confirm the present findings.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Conception and design: PA, SY, SA, EA; data acquisition: PA, VNN, SA; drafting of the manuscript: PA, SB, SA; analysis of data: SY; critical revision: SA, SP, EA; and supervision: SP, EA.

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