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ORIGINAL PAPER

Topical vancomycin for surgical prophylaxis in non-instrumented pediatric spinal surgeries

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Abstract

Study design Retrospective cohort study.

Objective To determine if topical vancomycin irrigation reduces the incidence of post-operative surgical site infections following pediatric spinal procedures.

Summary of background data Surgical site infections (SSIs) following spinal procedures performed in pediatric patients represent a serious complication. Prophylactic use of topical vancomycin prior to closure has been shown to be effective in reducing incidence of SSIs in adult spinal procedures. Non-instrumented cases make up the majority of spinal procedures in pediatric patients, and the efficacy of prophylactic topical vancomycin in these procedures has not previously been reported.

Methods This retrospective study reviewed all non-instrumented spinal procedures performed over a period from 05/2014–12/2016 for topical vancomycin use, surgical site infections, and clinical variables associated with SSI. Topical vancomycin was utilized as infection prophylaxis, and applied as a liquid solution within the wound prior to closure.

Results Ninety-five consecutive, non-instrumented, pediatric spinal surgeries were completed between 01/2015 and 12/2016, of which the last 68 utilized topical vancomycin. There was a 11.1% SSI rate in the non-topical vancomycin cohort versus 0% in the topical vancomycin cohort ($P = 0.005$). The number needed to treat was 9. There were no significant differences in risk factors for SSI between cohorts. There were no complications associated topical vancomycin use.

Conclusions Routine topical vancomycin administration during closure of non-instrumented spinal procedures can be a safe and effective tool for reducing SSIs in the pediatric neurosurgical population.

Keywords Antibiotics · Spine infection · Non-instrumented spine · Infection prophylaxis · Surgical site infection · Surgical prophylaxis · Topical vancomycin · Vancomycin powder · Pediatric spinal surgery

Introduction

Surgical site infections (SSIs) following spinal procedures performed in pediatric patients represent a serious complication and are associated with increased morbidity [1] and increased 30-day readmission rates [2]. Additionally, in adult patients undergoing spinal procedures, the risk of mortality is doubled following SSIs [3]. Prophylactic use of topical vancomycin prior to closure has been extensively explored in adult populations undergoing spinal procedures and has been shown to be effective in reducing incidence of SSIs [4–6].

Despite the efficacy of prophylactic topical vancomycin in adult spinal surgeries, there has not been widespread adoption in pediatric spinal surgeries. Within the pediatric population, there have only been two reports of utilization of topical vancomycin, both of which were restricted to instrumented cases for spinal deformity repair [7–9]. While the use of instrumentation increases the risk of surgical site infection [10], non-instrumented cases make up the majority of spinal procedures

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in pediatric patients, and the efficacy of prophylactic topical vancomycin in these procedures has not previously been reported. We present the first study of prophylactic topical vancomycin during non-instrumented spinal surgery for the prevention of SSIs in the pediatric population.

Materials and methods

This was a retrospective study examining the use of intra-operative prophylactic vancomycin irrigation for the prevention of SSIs following non-instrumented spinal procedures performed at Lucille Packard Children's Hospital Stanford (LPCH). This study was approved by the Stanford Institutional Review Board. Inclusion criteria for procedures analyzed in this study included all consecutive spinal procedures performed by senior authors (GL or SC) at LPCH between 5/2014 and 12/2016. Procedures that included instrumentation were excluded from this study. Utilization of topical vancomycin was adopted at different time points by each provider over the study period, but once adopted was then standard practice for every non-instrumented spinal procedure.

Data utilized in this study were extracted from the electronic medical record. Operative data extracted included operative date, diagnosis, procedure, length of operation, use of intra- and peri-operative steroid, use of intra and peri-operative antibiotics, whether the surgery was emergent, and whether the operative wound was clean or contaminated. The following patient demographics were extracted: age, BMI, and gender. The following potential SSI risk factors were collected: existing coronary artery disease, previous surgery, cancer, immunosuppression, diabetes, and hypertension. Finally, the post-operative period was scrutinized for SSI. SSIs were determined using the CDC guidelines and included any operative-wound related infection (superficial, deep, meningitis, etc.) that occurred within 3 months of the operative date. For patients who underwent multiple procedures included in this cohort, the SSI was linked to the most recent surgery.

All operations in this study were performed with standard-of-care antibiotic prophylaxis, including pre- and post-operative antibiotic prophylaxis of intravenous ceftriaxone or cefazolin of 50 mg/kg (up to a maximum of 2 g) given within 30 min before the incision as per guidelines. Patients with known penicillin allergies were treated with 15 mg/kg of vancomycin intravenously. Topical vancomycin was not used in any patient with known allergy or adverse reaction to the medication.

Operations done in the intervention group included an additional prophylactic use of a solution of 1 g of vancomycin diluted in 10–20 cm^3 of normal saline used for surgical intra-wound irrigation prior to incision closure. Irrigation was chosen as a means of vancomycin delivery in order to maximize surface area covered. Following vancomycin irrigation, wounds were closed in a standard multi-layer fashion using sutures or staples as indicated.

Statistical analysis was performed using a 2-sample, unpaired, *t* test to compare variables between the control and vancomycin-treated groups. We performed an ad-hoc cost-analysis by comparing SSI and vancomycin costs between the control and intervention group. To do so, we calculated the total costs associated with vancomycin and surgical site infections between the two groups by multiplying the unit costs of vancomycin and surgical site infection by the number of observed instances between the groups. The unit cost of a pediatric surgical site infection was approximated through a thorough review of relevant literature as $25,962 [10]. The unit cost of irrigation with 1 g vancomycin was determined using institutional data to be $49.4.

Results

In our study, 95 consecutive, non-instrumented, pediatric spinal surgeries were included, 27 in the control group followed by 68 in the intervention group treated with intra-operative prophylactic vancomycin irrigation. In total, there were 87 lumbar cases, 5 thoracic cases, and 3 cervical cases. Case etiologies are detailed in Fig. 1. Simple tethered cord was defined as a single-level laminotomy to section the filum in the setting of a low lying spinal cord. Lumbar drains were placed for baclofen trials.

We matched demographic characteristics between the control and vancomycin-treated groups and tested for significant differences in known SSI risk factors. There were no significant differences in demographic SSI risk factors, including age, BMI, history of cancer, diabetes, hypertension, or immunosuppression (Table 1). Additionally, we examined surgical procedure characteristics including whether the procedure was performed emergently, whether the wound was contaminated, and the length of operation, and found no significant differences between the control and intervention groups.

The primary outcome of interest in this study was the incidence of SSI between the control surgical procedures and the procedures treated with prophylactic vancomycin. We identified three SSIs among all patients included, of which three occurred in the control group and zero occurred in the vancomycin-treated operations (Tables 2). This corresponds to a SSI incidence of 11.1% in the control group and 0% in the vancomycin-treated group, with an absolute risk reduction associated with vancomycin use of 11.1% ($P = 0.005$, 5% CI = 3.4%, 95% CI = 18.7%). Based on the absolute risk reduction of 11.1%, we calculated a number of spine operations needed to treat nine operations. Of the infections in the non-treated cohort, there were two patients with culture indeterminate clinical infections where no

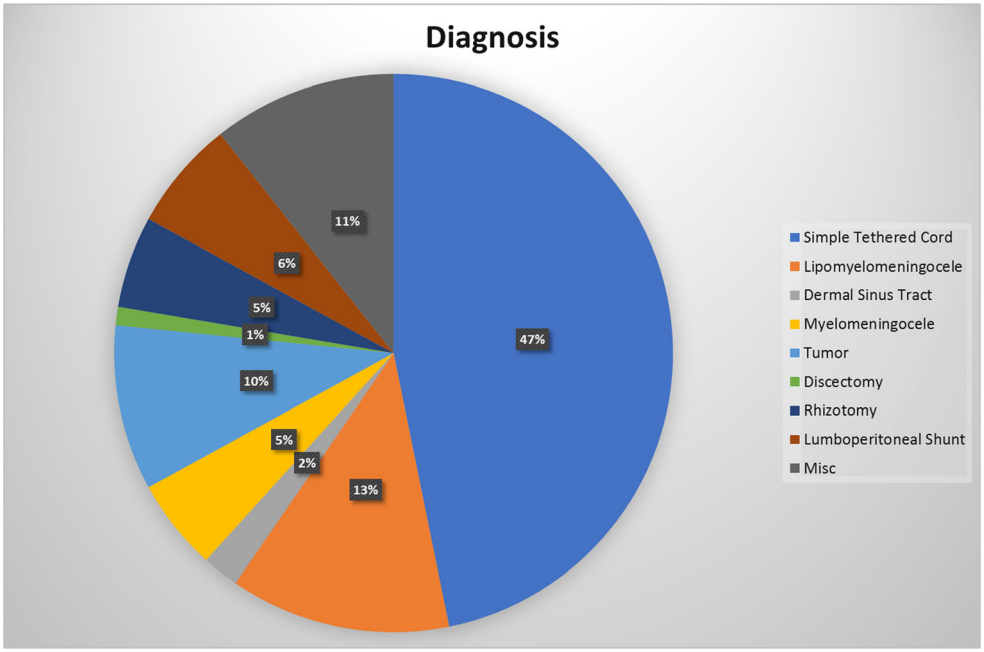

Fig. 1 Surgical diagnosis. Percentage representation of surgical diagnosis of all patients included in the cohort

organism could be isolated from culture, likely secondary to antibiotic initiation prior to wound culture sampling. Of note, IV vancomycin was administered to 11 patients in the control cohort (none of which developed infection) and two patients in the topical vancomycin cohort. There were no adverse events associated with topical vancomycin use observed in any of the 68 patients in the intervention cohort.

A secondary goal of this study is an ad-hoc cost-analysis of the use of vancomycin for spinal operations in pediatric patients. In the control group, we calculated total SSI-associated costs by multiplying the observed number of infections by a unit cost of $25,962, which was determined by Featherall et al., as the approximate additional cost associated with SSI following a spinal neurosurgical procedure [10]. This calculation yielded a total cost of $77,886 in the control group, or $2884 per procedure. In the intervention group, no SSIs were observed and therefore total cost was solely determined by the unit cost of vancomycin multiplied by the number of cases, yielding a total cost of $3359, or $49.4 per operation (Table 3).

Table 1 Demographics and operative characteristics between vancomycin-treated and control patients

	Vancomycin ($N=68$)	Control ($N=27$)	P value
Age (years)	6.3 ± 6.8	5.4 ± 7.3	0.61
Intra-operative steroids	9	2	0.43
Peri-operative steroids	7	1	0.30
Body mass index Average	18.0 ± 4.5	17.1 ± 3.1	0.41
Sex (male)	28	15	0.21
Cancer	6	0	0.11
Diabetes	0	0	NA
Hypertension	0	0	NA
Immunosuppression	3	0	0.27
Emergent	5	2	0.99
Contaminated	2	2	0.33
Average length of Operation	168.8 ± 103.0	144.0 ± 90.0	0.28
SSI	0	3	*0.005***

**$P < 0.01$

Discussion

In this study, we describe the results of the first retrospective series of consecutive pediatric non-instrumented spinal surgeries treated with topical vancomycin with the goal of prophylactic SSI prevention. Prophylactic topical vancomycin has been extensively studied in adult spinal surgery literature [4–6]; however, there is a dearth of evidence on the efficacy in pediatric populations. The observed incidence of SSIs in pediatric populations varies based on the diagnosis and procedure; however, reported rates include 0.5 to 41.7% following spinal deformity surgery [1], 18% following myelomeningocele repair [11], and 5.8% following tethered cord release [12]. Given the known effects of SSIs in increasing hospital length-of-stay, morbidity, and mortality, reducing the incidence of SSIs represents a meaningful opportunity to improve post-operative outcomes and quality of life following spinal surgery in children. In our single institution retrospective study, we demonstrated that the use of topical

Table 2 Characteristics of observed surgical site infections

Patient no.	Diagnosis	Age	Sex	BMI	Operative details	Vanco. use	Organism cultured
1	Myelomeningocele	0 (Perinatal)	M	13.5	Closure of myelo-meningocele	No	*Enterobacter cloacae*
2	Lipomyelo-meningocele	0.41	M	17.07	Lumbarsacral laminectomy for repair of lipomyelo-meningocele	No	Indeterminate
3	Tethered cord	0.25	F	16.38	Lumbar laminectomy L5 for repair of lipomyelo-meningiocele	No	Indeterminate

vancomycin reduced SSI incidence in pediatric patients undergoing non-instrument spinal surgery from 11.1 to 0.0%.

Previous studies of topical vancomycin for SSI prophylaxis in pediatric spinal surgery have predominantly focused on populations undergoing instrumented procedures for spinal deformity repair. Gans et al. examined the use of topical vancomycin powder in a consecutive series of 87 pediatric patients undergoing instrumented thoracic and lumbar surgery for spinal deformity repair. This study demonstrated the safety of vancomycin use in this setting through an analysis of postoperative serum creatinine and vancomycin concentrations and incidence of nephrotoxicity or other adverse reactions. All patients experienced minimal changes in serum creatinine, undetectable levels of systemic vancomycin, and no nephrotoxicity or other vancomycin-related complications [8]. Armaghani et al. examined the safety of topical vancomycin use in 25 patients undergoing instrumented spinal fusion for spinal deformity [7]. They found low, sub-therapeutic serum levels of vancomycin (mean 2.5 μg/ml POD0) coupled with high supratherapeutic drain output levels (mean 403 μg/ml POD0) demonstrating likely local efficacy with low risk of systemic toxicity. Though we did not measure serum and local wound vancomycin levels, we can assume lower systemic levels given the higher utilization and wound surface area in pediatric deformity surgery versus non-instrumented pediatric spinal procedures and our lack of any nephrotoxicity or other systemic vancomycin-related complications.

An additional goal of our study was to examine the potential cost-lowering effect of vancomycin for SSI prophylaxis in pediatric spinal surgeries. Literature on the cost of wound complications SSIs following spinal surgeries has reported costing ranging from $26,977 to $961,722 following wound complications [13–15]. Although the aforementioned studies are not directly applicable to our population as they focused on instrumented spinal fusions and our study analyzed surgical infections following non-instrumented procedures, it is clear that surgical site infections in pediatric populations have the potential to significantly increase costs. In our study, we estimated a cost savings of $74,527 in comparing our vancomycin-treated group with the control group. This translates to a potential savings of $238,516 savings per 100 patients.

When considering prophylactic use of vancomycin, the potential for adverse reactions must be considered. When delivered intravenously, some of the known adverse reactions associated with vancomycin include an anaphylactoid reaction known as "red man syndrome", nephrotoxicity, hepatoxicity, and rash [16, 17]. The instance of these events following topical application of vancomycin are unclear; however, our results coincide with previous studies of topical vancomycin use during pediatric spinal surgeries which showed no such adverse events [7, 8]. Given the rising incidence of antibiotic resistant bacteria, we should also consider the risk of increasing the proportion of vancomycin-resistant bacterial strains when considering prophylactic use of vancomycin. However, a recent study on 1200 adult patients given topical vancomycin for SSI prophylaxis found no cases of acquired vancomycin resistance [18]. Similarly, in our cohort, there was 1-g negative infection and two culture indeterminate infections, but no vancomycin-resistant infections.

This study is limited by retrospective and single-institution design. Despite these limitations, this study reflects the first investigation of the efficacy of topical vancomycin for preventing SSIs in non-instrumented pediatric spinal procedures. Ideally, prospective multicenter randomized controlled trials are needed to compare the efficacy of adding topical vancomycin to existing standard of care methods of SSI prevention in pediatric patients undergoing spinal surgeries. An additional consideration for the use of topical vancomycin is whether local administration provides significantly greater infection prophylaxis than intravenous-only vancomycin delivery. Tubaki et al. compared intravenous antibiotics alone versus intravenous antibiotics in combination with intra-wound vancomycin and found no significant difference in the infection rate [19]. Future studies on the efficacy of intra-wound vancomycin could address this question by adding a

Table 3 Cost analysis

Treatment	Unit cost	Control group	Vancomycin group	Total cost
Spine infection	$25,962	3	0	$77,886
1 g vancomycin	$49.4	0	68	$3359

comparison arm of patients who received exclusively vancomycin intravenous prophylaxis and compare this group with patients treated with both local vancomycin and standard of care intravenous prophylaxis.

Compliance with ethical standards

Conflict of interest The authors of this manuscript have no financial interest in the subject under discussion.

IRB approval This work was approved by the Stanford IRB.

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