Safety of Topical Vancomycin for Pediatric Spinal Deformity

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Study Design. Retrospective cohort analysis.

Objective. To establish if drain levels exceed the minimum inhibitory concentrations for common pathogens (methicillin-resistant *Staphylococcus aureus*, methicillin-sensitive *Staphylococcus aureus*, and *Propionibacterium acnes*—2 μg/mL; *Staphylococcus epidermidis*, *Enterococcus faecalis*—4 μg/mL). Evaluate the safety of topical vancomycin in pediatric patients undergoing spinal deformity surgery and determine if postoperative serum levels approach toxicity (25 μg/mL).

Summary of Background Data. The application of topical vancomycin powder has decreased postoperative wound infections in retrospective analyses in the adult population with minimal local and systemic risks. The safety and efficacy of vancomycin powder has not been completely evaluated in the pediatric population after deformity surgery.

Methods. Topical vancomycin powder (1 g) was applied during wound closure after instrumented posterior spinal fusion. All patients received intravenous perioperative antibiotics and a subfascial drain was used. Serum and drain vancomycin levels were collected immediately postoperatively and during the first 2 postoperative days (PODs). Complications were recorded.

Results. The study population consisted of 25 patients with a mean age of 13.5 years (9.5–17.1 yr) and mean ± standard deviation body weight of 44.5 ± 18 kg. Underlying diagnoses included: adolescent idiopathic scoliosis (12), neuromuscular scoliosis (10), and kyphosis (3). Mean serum vancomycin levels trended downward from 2.5 μg/mL (POD 0) to 1.9 μg/mL (POD 1) to 1.1 μg/mL (POD 2). Mean drain levels also trended downward from 403 μg/mL (POD 0) to 251 μg/mL (POD 1) to 115 μg/mL (POD 2). No vancomycin toxicity or deep wound infections were observed. One patient with neuromuscular scoliosis developed a superficial wound dehiscence that was managed with dressing changes.

Conclusion. Topical application of vancomycin powder in pediatric spinal deformity surgery produced local levels well above the minimum inhibitory concentration for common pathogens and serum levels below the toxicity threshold (25 μg/mL). There were no deep wound or antibiotic related complications.

Key words: pediatric deformity, infection, vancomycin, toxicity, complications, safety.

Level of Evidence: 3

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Surgical site infections pose a burden on both patients and hospitals. Patients who have a surgical site infection are 5 times more likely to be readmitted to the hospital.1 The cost of multiple debridements and long-term antibiotics after a surgical site infection for pediatric spine deformity surgery can average around $150,000.2 In addition, the morbidity, pain, and suffering to the child and the family after infection cannot be quantified in dollars. The rate of infection after pediatric deformity surgery may range from 1% to 5%; however in children with neuromuscular disease the rate can be as high as 24%.1,4

Factors that can increase the risk of surgical site infection after pediatric deformity surgery include inappropriate timing of antibiotics, previous spine surgery, medical comorbidities, age, longer fusions (>10 vertebrae), blood loss, and obesity.4 The most common organisms involved in deep surgical site infections are gram positive,5–7 specifically *Staphylococcus epidermidis* may be involved in 50% of infections8. However, in the neuromuscular population gram negative pathogens may be more common.5,10

In response to the additional morbidity and cost of infection after spinal surgery, local antibiotics have been used with success.11–15 The hypothesis is that local administration of antibiotics will create supratherapeutic levels in an area that...
may be devoid of vasculature after surgery due to extensive soft-tissue dissection, with little to no systemic effect. In the adult population, application of vancomycin powder has decreased rates of deep infection after instrumented spinal fusion in elective cases as well as in the trauma population. To date, there has only been 1 study evaluating the safety of vancomycin powder in pediatric spine deformity, which demonstrated the safety of 500 mg of local vancomycin in patients weighing more than 25 kg.

Intravenous vancomycin can have adverse effects that include anaphylaxis, renal failure, and ototoxicity. There is a single case report of circulatory collapse after local vancomycin administration. Local application of antibiotics with highly concentrated levels may inhibit osteoblast function and increase the rate of pseudarthrosis. In addition, there is also concern that the local levels of antibiotics may diminish rapidly when drains are used postoperatively. Sweet et al found supratherapeutic levels of vancomycin in spinal wounds that were well above the minimum inhibitory concentration (MIC) for common organisms with no appreciable serum levels for at least 3 days postoperatively in the adult population. The local levels in the wound were less than that which may impact osteoblast function and thus demonstrated safety in the adult population. To our knowledge, no study has quantified the local vancomycin levels after spinal deformity surgery in a pediatric population.

In 2012, the overall surgical site infection rate at our institution was 5.5% for posterior spinal fusion in pediatric patients (idiopathic and neuromuscular deformity). This data in combination with the observation of a 0% infection rate in adult spine trauma patients after application of vancomycin powder, prompted a study of the safety of vancomycin powder in the pediatric population. The goal of our study was to evaluate the local and serum levels associated with intra-wound vancomycin application in pediatric patients undergoing spinal deformity surgery. We hypothesized that the local levels of vancomycin will be well above the MIC for common organisms but below levels concerning for local or systemic toxicity for days after spinal surgery.

**MATERIALS AND METHODS**

With institutional review board approval, a retrospective review was performed of pediatric patients undergoing posterior spinal fusion for deformity at a tertiary referral children’s hospital during a 3-month period in 2013. Inclusion criteria consisted of patients younger than 18 years who had undergone posterior spinal fusion for deformity who received local vancomycin powder with postoperative laboratory data including serum and drain vancomycin levels. Exclusion criteria included patients who did not have spinal deformity, had less than 6 months of follow-up and incomplete serum or drain vancomycin level data. Patient demographics were recorded including age, sex, weight, diagnosis, deformity (scoliosis or kyphosis), and primary versus revision surgery.

All patients received prophylactic preoperative antibiotics within 60 minutes of incision that included 25 mg/kg cefazolin followed by the same dose every 8 hours until drain removal. If the patient had penicillin allergy, clindamycin 10 mg/kg was administered. Neuromuscular patients also received gentamicin 2.5 mg/kg. All patients were prepped with DuraPrep (3M, St. Paul, MN) and an Ioban (3M) drape was placed over the skin prior to incision. Fusion levels were determined by preoperative templating. Prior to skin closure, 2 L of normal saline was used to irrigate the wound and a single 10 French Jackson-Pratt subfascial drain (Cardinal Health, Dublin, OH) was placed. Prior to fascia closure, a total of 1 g of vancomycin powder (Hospira Inc., Lake Forest, IL) was applied to the subfascial and suprafascial layers of the wound. The wounds were closed with absorbable suture in the fascia and subcutaneous tissues and the skin closed with a running monofilament suture. A sterile dressing was applied that remained in place until discharge. Drains were removed when the output was less than 30 mL per 8-hour shift or at postoperative day (POD) 3. Prophylactic antibiotics were discontinued at the time of drain removal.

Daily postoperative vancomycin serum and drain levels, drain outputs, operative time, estimated blood loss, numbers of levels fused, and fusions to the pelvis were obtained from chart review. Any adverse reactions or infections within the follow-up period after surgery were also obtained through chart review from clinic notes.

**RESULTS**

A total of 25 patients were included in the study. The average age was 13.5 years (range, 9.57–17.1 yr) with a mean ± standard deviation (SD) weight of 44.5 ± 18 kg. The mean postoperative follow-up was 9.2 months. The predominant diagnosis was adolescent idiopathic scoliosis. An average of 13 levels were fused (range, 9–17) with 9 fusions extended to the pelvis. The mean ± SD estimated blood loss was 934 ± 619 mL and mean ± SD operating room time was 468 ± 104 minutes. Complete demographic data is presented in Table 1.

Postoperatively, serum vancomycin levels were collected and showed an expected downtrend with respect to time (Figure 1). Immediate postoperative serum levels averaged 2.5 μg/mL and decreased to 1.9 μg/mL on POD 1 and 1.1 μg/mL on POD 2. One patient who weighed 18 kg had a serum vancomycin level of 10 μg/mL on POD 1 but did not demonstrate any systemic effects and was discharged without issue. Similarly, a decrease over time was seen with the local vancomycin levels but the levels remained elevated throughout the time the drain was in place (Figure 2). On POD 0 the average vancomycin levels in the wound were 403 μg/mL followed by 251 μg/mL on POD 1 and 115 μg/mL on POD 2. Of note, the minimum concentration detectable by our lab was 2 μg/mL. Table 2 depicts the relationship of the time from wound closure with serum and drain vancomycin levels. Drain outputs were measured daily until discontinued. The mean ± SD of drain output were 367 ± 139 mL on POD 1369 ± 163 mL on POD 2, and 206 ± 115 mL on POD 3.

There were 2 complications in our cohort (8%), 1 incidental dural tear that was treated by primary closure, and 1 superficial wound dehiscence. The latter occurred in an...
11-year-old female with cerebral palsy who was treated successfully with oral trimethoprim and sulfamethoxazole along with dressing changes and her wound ultimately closed by secondary intention. To date, there have been no deep infections defined as requiring operative debridement and/or intravenous antibiotics.

**DISCUSSION**

In this study of pediatric patients undergoing operative treatment of spinal deformity with local application of vancomycin powder, we found that serum levels never exceeded therapeutic levels (15–20 μg/mL) and intrawound vancomycin levels far exceeded MIC for common organisms after POD 2 (methicillin-resistant *Staphylococcus aureus*, methicillin-sensitive *Staphylococcus aureus*, *Propionibacterium acnes* is 2 μg/mL; *Staphylococcus epidermidis*, *Enterococcus faecalis* is 4 μg/mL). These results suggest that intrawound application of 1 g of vancomycin powder is safe and provides a local antibiotic concentration that continues to be supratherapeutic for at least 2 days postoperatively.

Sweet et al. were one of the first groups to study both serum and local levels of vancomycin after adult instrumented spinal surgery. In patients who received intrawound vancomycin, they demonstrated nearly undetectable serum levels and persistently supratherapeutic local levels after POD 3 without evidence of renal toxicity or a significant incidence of pseudarthrosis. Their study added crucial evidence of the poor systemic absorption of vancomycin in the adult population but also provided information regarding the safety of vancomycin powder in the local environment. In our cohort of children and adolescents, we demonstrated similar supratherapeutic local levels with a time-dependent decline, using

### TABLE 1. Baseline Demographic and Clinical Characteristics of Study Population (N = 25)

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>Age, mean (min–max), yr</td>
<td>13.5 (9.6–17.1)</td>
</tr>
<tr>
<td>Follow-up, mean (min–max), mo</td>
<td>9.2 (6.4–13.7)</td>
</tr>
<tr>
<td>Primary surgery</td>
<td>23</td>
</tr>
<tr>
<td>Revision surgery</td>
<td>2</td>
</tr>
<tr>
<td>Fusion levels, mean (min–max)</td>
<td>13 (9–17)</td>
</tr>
<tr>
<td>Fusion to pelvis</td>
<td>9</td>
</tr>
<tr>
<td>EBL, mean ± SD, mL</td>
<td>934 ± 619</td>
</tr>
<tr>
<td>OR time, mean ± SD, min</td>
<td>468 ± 104</td>
</tr>
<tr>
<td>Weight, mean ± SD, kg</td>
<td>44.5 ± 18</td>
</tr>
</tbody>
</table>

**Diagnosis**

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
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<tbody>
<tr>
<td>AIS</td>
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<tr>
<td>Cerebral palsy</td>
<td>7</td>
</tr>
<tr>
<td>Syndrome</td>
<td>3</td>
</tr>
<tr>
<td>Spina bifida</td>
<td>1</td>
</tr>
<tr>
<td>Tumor</td>
<td>1</td>
</tr>
<tr>
<td>Neurogenic</td>
<td>1</td>
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</table>

**Deformity**

<table>
<thead>
<tr>
<th>Deformity</th>
<th>Count</th>
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</thead>
<tbody>
<tr>
<td>Scoliosis</td>
<td>22</td>
</tr>
<tr>
<td>Kyphosis</td>
<td>3</td>
</tr>
</tbody>
</table>

SD indicates standard deviation; EBL, estimated blood loss; OR, operating room; AIS, adolescent idiopathic scoliosis.

![Figure 1](Vancomycin Serum Levels)

**Figure 1.** Vancomycin serum levels are near undetectable after 24 hours after surgery. Values trend downward in a time-dependent manner (R² = 0.11).

![Figure 2](Vancomycin Drain Levels)

**Figure 2.** Local levels of vancomycin decrease in a time-dependent manner (R² = 0.35).

### TABLE 2. Vancomycin Levels Postoperatively (N = 25)

<table>
<thead>
<tr>
<th>POD</th>
<th>Serum Vancomycin Level, Mean (Range), μg/mL</th>
<th>Drain Vancomycin Level, Mean (Range), μg/mL</th>
<th>Time From Wound Closure, Mean (Range), hr</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>2.5 (1–6)</td>
<td>403 (25–800)</td>
<td>2.5 (0.7–6)</td>
</tr>
<tr>
<td>1</td>
<td>1.9 (0–10)</td>
<td>251 (34–422)</td>
<td>15.5 (9–24)</td>
</tr>
<tr>
<td>2</td>
<td>1.1 (0–2)</td>
<td>115 (11–334)</td>
<td>39.3 (35–49)</td>
</tr>
</tbody>
</table>

POD indicates postoperative day.

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**Spine**

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the same doses of vancomycin powder as used in adults. However, in contrast to the adult patients studied by Sweet et al., vancomycin was detectable in the serum likely due to the reduced body weight of the pediatric cohort. The maximum serum level detected (10 μg/mL) was well below potentially toxic levels (25 μg/mL).

Our results are similar to those of Gans et al.16 a retrospective study where 500 mg of vancomycin powder was applied locally after pediatric spinal deformity surgery. Postoperatively, they noted negligible changes in serum creatinine and undetectable serum vancomycin levels. Despite using a higher dose (1 g), our study confirmed that postoperative serum vancomycin levels remain low and do not approach the toxicity threshold even for small children. In addition, we demonstrated that the local wound environment maintains supratherapeutic vancomycin levels for at least 2 days postoperatively and likely longer given the time-dependent decrease in the levels observed (Figure 2). Despite the higher dose, the maximum local vancomycin levels observed in this study (800 μg/mL) did not approach levels that have been shown to adversely impact osteoblast function (greater than 5000 μg/mL).21 These findings suggest that the higher dose of intrawound vancomycin (1 g) in pediatric patients will provide supratherapeutic wound levels without altering bone biology.

The cost of 1 g of vancomycin at our institution is $44.00. In the adult population, it has been noted that the application of vancomycin powder may lead to a cost savings of more than $400,000 per 100 spinal fusions performed.22 Given the similar infection rate between high-risk adult patients and patients with pediatric deformity, the use of vancomycin powder would be expected to be similarly cost-effective.

CONCLUSION

Previously, surgeons have relied upon data from adult studies with respect to the potential safety of topical vancomycin in pediatric patients. By using a uniform dose of vancomycin powder and correlating this to both local and systemic levels, we have demonstrated that systematic use of vancomycin is safe in pediatric patients while providing a local environment that is toxic to the most common gram-positive pathogens responsible for early infections. Unfortunately, despite the uniform dose of vancomycin and variable patient characteristics, our data is insufficient to develop a pharmacokinetic model that provides dose recommendations based upon patient weight or fusion levels. A weakness of the study is the retrospective collection of data regarding complications and infections. Also, with short-term follow-up, we are unable to assess delayed presentations of infections presumably associated with biofilm production and sessile organisms that are resistant to the mechanism of action used by vancomycin.21 In addition, although there were no deep infections and only 1 superficial wound dehiscence, the small sample size and variable diagnoses prevent us from describing the efficacy of vancomycin powder.

Future directions include prospective randomized trials comparing standard intravenous antibiotic prophylaxis in combination with topical vancomycin powder to intravenous antibiotics alone in pediatric patients undergoing spinal deformity surgery. In addition as more patients receive intrawound vancomycin, we will begin to evaluate if the incidence of delayed wound infections caused by pathogens organized in biofilm,23 such as Propionibacterium acnes or Staphylococcus epidermidis, are reduced by the supratherapeutic levels of antibiotic present in the early postoperative period.

Key Points

- Nontoxic vancomycin serum levels were observed in pediatric patients with the use of 1 g of topical vancomycin.
- Intrawound levels of vancomycin exceeded the MIC of common organisms by more than 50 times at postoperative day 2 and likely remain elevated without approaching toxic levels to bone and soft tissue.
- No systemic effects of vancomycin or infections were observed.

References