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Original Research

Intranasal Testing and Treatment for *Staphylococcus aureus* With Intravenous Vancomycin and Intranasal Povidone-iodine Prior to Posterior Spinal Fusion: A Retrospective Cohort Study Between Two High-volume Children's Hospitals

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ABSTRACT

Background: The impact of surgical site infections in spinal surgery can be profound. Several studies have demonstrated that *S. aureus* carriers have an increased risk of surgical site infection (SSI). The current literature shows decreased SSI in the adult population with povidine-iodine (PI) nasal treatment for decolonizing the nares of patients infected with *S. aureus*. The goal of this research study was to analyze the isolated effect of presurgical *S. aureus* nasal testing and PI application prior to spinal surgery.

Methods: This is a retrospective cohort study of children 8 to 18 years of age who underwent posterior spinal fusion from 2018 to 2020 at two standalone academic pediatric hospitals. Both hospitals had the same preoperative surgical bundle except that Group B included testing for *S. aureus* and treatment preoperatively if positive. In addition, all patients in Group B received PI nasal decolonization on the day of surgery.

Results: The overall infection rate between both hospitals was identified as 3.4%, with no difference between the two groups. The infection rate was lowest for adolescent idiopathic scoliosis, with a rate of 1.3% and highest for neuromuscular scoliosis, with a rate of 8.2%. Hospital-wide bacterial rates in Group A compared to Group B were higher for all *S. aureus* species (33.8% vs 30.1%, $P = 0.0004$), methicillin-sensitive *S. aureus* (24.6% vs 13.1 %, $P < 0.001$) but lower for methicillin-resistant *S. aureus* (9.2% vs 17%, $P = 0.02$). Postoperative infection culture rates or bacterium types were not significantly different between the two groups.

Conclusions: The treatment of patients with PI nasal decolonization in the pediatric spinal fusion cohort did not show a decrease in postoperative infections. The PI nasal testing and treatment was $308.25 per patient and $189,580.75 over the study period. Elimination of intranasal testing and *S. aureus* treatment result in cost savings and eliminates an unpleasant patient experience.

Key Concepts:

(1) The treatment of patients with povidine-iodine (PI) nasal decolonization in a pediatric spinal fusion cohort did not show a decrease in postoperative infections.
(2) Elimination of intranasal testing and *Staphylococcus aureus* treatment in a pediatric spinal fusion cohort results in cost savings and reduces an unpleasant experience for the patient.
(3) Increased surgical time during posterior spinal fusion in a pediatric cohort of patient did not lead to an increased rate of surgical site infection (SSI).

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(4) Across the cohort of pediatric patient undergoing posterior spinal fusion (PSF), the rate of infection for adolescent idiopathic scoliosis (AIS) patients was 1.3% compared with 8.2% infection rate in patients with neuromuscular scoliosis (NMS).

Level of Evidence: Level III

Introduction

The impact of surgical site infections (SSIs) is dramatic. A 3% overall mortality rate can be directly attributed to SSI, with likely more with SSI as an indirect cause [1]. Within the field of spinal surgery, the implications of SSI are even more pronounced, with one-third of patients experiencing incomplete recoveries and a 2.3% one-year mortality rate [2]. Several studies have demonstrated that *Staphylococcus aureus* carriers have an increased risk of SSI, with the SSI rate up to 9 times higher among *S. aureus* carriers than in noncarriers [3–9]. The intranasal colonization of *S. aureus* is a common target of eradication protocols. Multiple studies have shown effectiveness of intranasal mupirocin presurgical treatment in eliminating *S. aureus* colonization [4,10–12]. More recent research into *S. aureus* intranasal elimination has focused on use of povidone-iodine (PI) nasal swabs. This treatment has the benefit of decreased risk of staphylococcal antibiotic resistance [13,14], has eliminated mupirocin-related adverse reactions, demonstrates a reduced need for strict patient compliance in application, and increases savings to patients with respect to out-of-pocket costs [15]. Several studies have demonstrated the efficacy of the PI nasal treatment in decolonizing the nares of adult patients colonized with *S. aureus* [16–18], and the use of a presurgical PI nasal treatment has resulted in a reduction of SSI within several clinical trials [19–21]. The use of an evidence-based care bundle has demonstrated significant impact and cost-effectiveness as a preventative intervention for orthopaedic spine surgery with regards to reducing SSI [22,23]. The surgical care with a treatment-bundled approach typically uses a variable combination of perioperative antibiotics, intrawound vancomycin, betadine irrigation, chlorhexidine scrub (CHG), and a *S. aureus* nasal swab protocol. The use of a *S. aureus* nasal swab protocol, with either mupirocin or PI, is a standard part of some care bundles. Although the composite clinical effectiveness indicates reduced rates of SSI, there is a paucity of research into the isolated effect of each infection control measure in reducing SSI in pediatric patients. In order to investigate the direct effect of one of these measures, similar pediatric patient cohorts would need to be identified and the impact of a specific SSI infection control measures analyzed.

In 2018, standardized surgical bundles were implemented at two large pediatric hospitals in a single healthcare system (Table 1). The goal of this research study was to analyze the isolated effect of presurgical *S. aureus* nasal screening, with preoperative vancomycin treatment if positive and day-of-surgery PI nasal decolonization prior to pediatric spinal surgery within the context of an evidence-based surgical care bundle.

Materials and methods

This study was a dual-center retrospective cohort study consisting of two cohorts at standalone high-volume academic pediatric hospitals. Both cohorts of patients underwent posterior spinal fusion (PSF) between the years 2018 and 2020. This study received institutional review board approval from the children's hospital system where all data were collected. The first cohort (Group A) consisted of patients who received the standard preoperative treatment bundle in addition to the *S. aureus* nasal screening within 6 months of surgery and preoperative treatment with intravenous vancomycin if positive for *S. aureus*. Additionally, all patients in Group A received PI nasal decolonization on the day of surgery regardless of prior nasal screening results. The second cohort (Group B) consisted of patients who received the standard preoperative treatment bundle without *S. aureus* screening or treatment. Both pediatric hospitals used the same

Table 1.
Surgical bundle.

Group A	Group B
Soap and water bath (night before surgery)	Soap and water bath (night before surgery)
4% CHG solution bath (the night before surgery)	4% CHG solution bath (night before surgery)
2% CHG wipe bath (the day of surgery)	2% CHG wipe bath (day of surgery)
No razor	No razor
Clippers used for hair removal	Clippers used for hair removal.
Nasal MRSA screening within 6 months of surgery; if positive, treat with vancomycin	No MRSA screening
Betadine nasal swab used intraoperative for patients receiving implants	No
Prophylactic antibiotic timing (within 60 min of incision for all, except vancomycin and fluroquinolones within 120 min of incision)	Prophylactic antibiotic timing (within 60 min of incision for all, except vancomycin and fluroquinolones within 120 min of incision)
Standardized antibiotics	Standardized antibiotics
Ancef: standard antibiotic	Ancef: standard antibiotic
Ancef + vancomycin: MRSA-positive patient	Ancef + vancomycin: MRSA-positive patient
Vancomycin: true penicillin allergy	Vancomycin: true penicillin allergy
Ancef + gentamycin: NMS	Ancef + gentamycin: NMS
Posterior spinal fusion surgery only	
Standardized irrigation with betadine or CHG	Standardized irrigation with betadine or CHG
Vancomycin powder prior to wound closure	Vancomycin powder prior to wound closure
Standardized wound dressing	Standardized wound dressing
Mepilex/AquaCell dressing: AIS	Mepilex/AquaCell dressing: AIS
Portable wound vac: NMS	Portable wound vac: NMS

AIS, adolescent idiopathic scoliosis; CHG, chlorhexidine scrub; NMS, neuromuscular scoliosis; MRSA, methicillin-resistant Staphylococcus aureus.

surgical treatment bundle to their PSF surgery patients apart from the *S. aureus* nasal screening, preoperative intravenous vancomycin treatment, and day-of-surgery PI decolonization.

A search of the electronic medical records at each institution identified the patients undergoing these procedures during the study dates. We included all pediatric patients aged 8–18 years undergoing primary posterior spinal surgery. Any patient who had prior spinal surgery, immunodeficiency, malignancy, or did not have record of at least 90 days of follow-up was excluded from our study. Demographic makeup of the two cohorts was collected including sex, age, and type of scoliosis. Scoliosis type was defined as adolescent idiopathic scoliosis (AIS), neuromuscular scoliosis (NMS), or other scoliosis. NMS was defined as scoliosis caused by disorders of the brain, spinal cord, or muscular system such as cerebral palsy, spina bifida, muscular dystrophy, etc. Other scoliosis was defined as scoliosis caused by any other diagnosis or syndromes causing scoliosis such as Down syndrome, other chromosomal abnormalities, Marfan syndrome, skeletal dysplasias, etc. Surgical information such as length of surgery, postoperative infection, and bacteria isolated from infection were also collected. SSIs were defined using the definition from the Centers for Disease Control (CDC) National Healthcare Safety Network (NHSN) standard measurements. Infections were classed as superficial incisional SSI, deep incisional SSI, or organ space SSI using the NHSN criteria [24]. Hospital-wide antibiograms were compared between both hospitals to evaluate local bacterial rates. The cost of nasal cultures and PI nasal swabs were also collected.

Statistical analysis

Continuous variables were summarized as median (Q1, Q3), whereas categorical variables were reported as frequency (percentage). Unadjusted comparisons of patient characteristics between the two pediatric hospitals were made using a Wilcoxon rank-sum test (for continuous variables) or Fisher's exact test (for categorical variables). Postoperative SSI rates were calculated based on patient characteristics (hospital site, sex, age, scoliosis diagnosis, and length of surgery). Logistic regression models were used to compare the occurrence of postoperative SSI between the two hospitals and to identify any other univariate predictors. Multivariable models were adjusted for length of surgery, sex, and scoliosis diagnosis. Odds ratio (OR) estimates and 95% confidence intervals (CIs) were calculated from the fitted models and can be interpreted as the multiplicative increase in the odds of postoperative SSI. *P* values less than 0.05 were considered as statistically significant, and all statistical tests were two-sided. Statistical analyses were performed using R statistical software (version 4.1.2; R Foundation for Statistical Computing, Vienna, Austria).

Results

Demographics

A total of 1040 patients were identified and included in the study, with 610 patients in Group A and 430 in Group B (Table 2).

The cohort consisted of 683 females (66%) and 357 males (34%) with more females identified in Group A (62% vs 70%, $P = 0.007$). The majority of patients, 51%, had the diagnosis of other scoliosis with a greater number in Group B ($P < 0.001$). The median age was 14 years old and equal between both groups ($P = 0.61$). Multivariable regression analysis did not show that patient age or sex was an independent risk factor for infection.

Infections

The overall infection rate between both hospitals was identified as 3.4% with no difference between the two groups (Table 3 and Table 4).

The infection rate was lowest for AIS with a rate of 1.3% in the cohort and highest at 8.2% for NMS. NMS diagnosis was the only significant predictor for infection in unadjusted and multivariable analyses. *S. aureus* species were the most common cause of post-operative infections in Group A and B (68.2% vs 38.5%, $P = 0.0879$). Hospital-wide bacterial rates in Group A compared to Group B were higher for all *S. aureus* species (33.8% vs 30.1%, $P = 0.0004$), methicillin-sensitive *S. aureus* (MSSA) (24.6% vs 13.1 %, $P < 0.001$) but lower for methicillin-resistant *S. aureus* (MRSA) (9.2% vs 17%, $P = 0.0200$) (Table 5).

Postoperative infection culture rates or bacterium types were not significantly different between the two groups (Table 6).

Preoperative nasal cultures for *S. aureus* were only obtained in Group A. Eight patients had a positive culture for a positivity rate of 1.3%. Only 4 patients who developed a postoperative infection (12%) had positive nasal cultures for the same bacteria. All four had MSSA infections. No

Table 2.
Patient characteristics by hospital site.

	Group A (N = 610)	N	Group B (N = 430)	*P* value
Age (years)	14 (11, 16)	430	14 (12, 15)	0.61
Sex		430		0.007
Female	380 (62%)		303 (70%)	
Male	230 (38%)		127 (30%)	
Diagnosis		430		0.006
AIS	200 (33%)		111 (26%)	
NMS	122 (20%)		73 (17%)	
Other	288 (47%)		246 (57%)	
Length of surgery (min)	344 (274, 465)	422	222 (181, 292)	<0.001

Continuous variables were summarized as median (Q1, Q3), whereas categorical variables were reported as frequency (percentage). P values result from a Wilcoxon rank-sum test (for continuous variables) or Fisher's exact test (for categorical variables).
AIS, adolescent idiopathic scoliosis; NMS, neuromuscular scoliosis.

Table 3.
Postoperative surgical site infections by patient characteristics.

Variable	N	No. of SSIs	SSI rate
Overall	1040	35	3.4%
Hospital site			
Group A	610	22	3.6%
Group B	430	13	3.0%
Age (years)			
< 13	353	14	4.0%
13–14	279	8	2.9%
> 14	408	13	3.2%
Sex			
Female	683	21	3.1%
Male	357	14	3.9%
Diagnosis			
AIS	311	4	1.3%
NMS	195	16	8.2%
Other	534	15	2.8%
Length of surgery (min)			
< 241	345	12	3.5%
241–346	341	11	3.2%
> 346	344	12	3.5%

Continuous variables (age and length of surgery) were categorized by tertiles.
AIS, adolescent idiopathic scoliosis; NMS, neuromuscular scoliosis; SSI, surgical site infection.

Table 4.
Prediction of postoperative surgical site infections.

Variable	Unadjusted analysis			Multivariable analysis		
	N	Odds ratio (95% CI)	*P* value	N	Odds ratio (95% CI)	*P* value
Hospital site	1040			1030		
Group A		Reference			Reference	
Group B		0.83 (0.40, 1.65)	0.61		0.74 (0.33, 1.62)	0.46
Age (years)	1040	0.99 (0.90, 1.08)	0.76	1030	0.99 (0.90, 1.08)	0.77
Sex	1040			1030		
Female		Reference			Reference	
Male		1.29 (0.63, 2.54)	0.47		1.30 (0.64, 2.58)	0.45
Diagnosis	1040			1030		
AIS		Reference			Reference	
NMS		6.86 (2.47, 24.23)	<0.001		7.03 (2.53, 24.88)	<0.001
Other		2.22 (0.80, 7.84)	0.16		2.24 (0.81, 7.92)	0.15
Length of surgery (10-min increase)	1030	1.00 (0.97, 1.02)	0.71	1030	1.00 (0.97, 1.02)	0.71

AIS, adolescent idiopathic scoliosis; CI, confidence interval; NMS, neuromuscular scoliosis.
Reference categories: Hospital A, female (sex), and AIS (diagnosis).
Multivariable models were adjusted for length of surgery.

patient with positive nasal cultures for MRSA developed a postoperative infection with MRSA.

In conducting a post hoc power analysis, we used an assumption that the *S. aureus* testing and treatment in Group A should eliminate all *S. aureus* infections. Considering that Group A had 12 infections with *S. aureus*, this assumption would change their calculated infection rate from 22 to 10 for their 610 cases or 1.64%. Comparing the 1.64% infection rate in Group A, with the 3.0% infection rate in Group B, and after a power analysis, 2058 patients would be required for a power of 0.80 and α of 0.05. With the 1040 patients available to our study, the power would be 0.74, with an α of 0.05.

Table 5.
Hospital biograms 2018 to 2020.

Variable	N	Group A	Group B	*P* value
Hospital bacteria infections	7851	4590	3261	
Bacteria type				
Escherichia coli		1624 (35.4%)	1181 (36%)	0.4470
Klebsiella pneumonia		293 (6.4%)	207 (6.3%)	0.9782
Proteus mirabilis		123 (2.7%)	121 (3.7%)	0.0095
Salmonella species		0 (0.0%)	85 (2.6%)	0.0001
Pseudomonas aeruginosa		462 (10.1%)	370 (11.3%)	0.0692
Staphylococcus aureus (MSSA)		1130 (24.6%)	427 (13.1%)	0.0001
Staphylococcus aureus (MRSA)		422 (9.2%)	553 (17.0%)	0.0200
Staphylococcus (combined)		1552 (33.8%)	980 (30.1%)	0.0004
Enterococcus faecalis		383 (8.3%)	158 (4.8%)	0.0001
Streptococcus pneumoniaea		153 (3.3%)	159 (4.9%)	0.0006

Rates represented as percentage (%).
P values result from a chi-squared test for continuous variables.
MSSA, methicillin-sensitive Staphylococcus aureus; MRSA, methicillin-resistant Staphylococcus aureus.

Length of surgery

The length of surgery in Group A was longer than in Group B, with a mean of 344 min vs 222 min ($P < 0.001$). Length of surgery was not identified as a significant risk factor for infection (OR = 1.00, $P = 0.71$). After adjusting for length of surgery in multivariable analysis, there was still no significant difference in odds of infection for Group B compared to Group A (OR = 0.74, $P = 0.46$).

Costs

The *S. aureus* nasal culture cost at both institution was $295 per patient. All patients were tested in Group A for a total cost of $189,580.75 over the study period. The PI nasal swab at our institution cost $13.25, for a total cost of $8082.50. Intravenous vancomycin treatment at our institution was $40 per patient, for a total cost of $1560. Group A's total

Table 6.
Postoperative infection cultures.

Variable	N	Group A	Group B	*P* value
Positive cultures	31	22	9	0.4854
Bacteria type				
Escherichia coli		2	0	0.5193
Klebsiella pneumonia		1	2	0.5412
Proteus mirabilis		5	1	0.3771
Pseudomonas aeruginosa		1	1	1.0000
Staphylococcus aureus (MSSA)		12	6	0.7332
Staphylococcus aureus (MRSA)		3	0	0.2790
Streptococcus pneumoniaea		0	1	0.3714
Haemophilus parainfluenzae		1	0	1.0000
Morganella morganii		1	0	1.0000
Polymicrobial		5	1	0.3771

P values result from a Fischer's exact test for categorical variables.
MSSA, methicillin-sensitive Staphylococcus aureus; MRSA, methicillin-resistant Staphylococcus aureus.

added cost of nasal cultures, PI nasal swabs and intravenous vancomycin was $189,580.75 over the study period of 3 years.

Discussion

Postoperative infections have a major impact on patients, their families, and society. The cost to treat a postoperative infection after a PSF can be as much as $114,763 [25]. These costs do not take into consideration indirect costs such as time missed from school for the patient and time missed from work for the families, which can add to the patient and family burden.

Hospital systems worldwide have developed and implemented surgical bundles in hopes of decreasing postoperative infection rates. Poe-Kochert et al. [26] showed that implementing a surgical bundle in pediatric patients undergoing PSF can reduce infection rates significantly [26]. It is difficult to test the efficacy of each bundle component as they are usually implemented at the same time. These bundle components also have not been widely tested in the pediatric setting. We believe that this is the first study to evaluate the effectiveness of universal *S. aureus* screening with intravenous vancomycin treatment based on positivity and preoperative nasal decolonization with PI in pediatric patients undergoing PSF surgery.

Interestingly, our study did not find a decrease in the rate of infections after universal preoperative MRSA nasal screening with appropriate preoperative intravenous vancomycin treatment and day-of-surgery decolonization with PI nasal swabs. Many studies in adults have shown a significant decrease in rate of postoperative infections with these measures prior to orthopaedic surgery, including total joint arthroplasty and spinal surgery [5–18]. These studies notably examined multiple components of our own surgical bundle, including CHG baths prior to surgery. As such, it is possible that the CHG baths along with other components of the bundle can decrease the risk of *S. aureus* in children without the need for nasal decolonization.

This study also did not show a decrease in *S. aureus* infections with universal preoperative nasal MRSA screening, preoperative intravenous vancomycin treatment if positive, and day-of-surgery PI nasal treatment. The hospital bacterial biogram showed a significantly higher overall infection rate of MSSA in Group A but a higher overall infection rate of MRSA in Group B. Despite these differences, there was no significant difference in MRSA and MSSA postoperative infection rates between the two hospitals.

The infection rates found in this study are comparable to other studies of PSF in pediatric patients [15–27], with the two hospitals in our study demonstrating a 1.3% infection rate in patients with AIS and 8.2% infection rate in patients with NMS.

S. aureus nasal screening and PI nasal decolonization are costly and may be uncomfortable for some patients. Patients have reported discomfort and nasal dryness after PI nasal decolonization [27]. The cost of the two treatments was $188,032.50 over the three-year study period. Eliminating nasal screening and nasal decolonization in pediatric patients can decrease costs both to patients and institutions and may reduce discomfort to patients, although this topic was not studied in this paper.

This study was performed in a large health system that has two standalone academic pediatric hospitals. Comparing two hospitals in a single system allowed for standardization and control of multiple other variables that can lead to postoperative infections, such as antibiotic prophylaxis, wound closure type, wound dressing, etc. All other surgical bundle components were standardized with the only difference being the *S. aureus* screening, vancomycin treatment, and PI nasal swabs. The large patient population of 1040 pediatric patients undergoing PSF also strengthens the study.

This study does have a number of important weaknesses. First, this was a retrospective study, which is known to have multiple limitations. Although we have a large patient population in the study, only a post hoc power analysis was performed and found to be underpowered. Second, the hospital in Group A performed two measures that attempted to decrease the incidence of SSI, preoperative *S. aureus* nasal screening, and treatment as well as day-of-surgery PI nasal decolonization. Ideally, only one measure would have been changed in order to assess the individual effect on the outcome. Additionally, the hospital in Group A discontinued the use of nasal MRSA screening and PI nasal treatment after seeing no change in the infection rate compared to Group B; thus, the population of the study is limited to this study period. The populations at the two facilities were not completely homogeneous with a difference in patient sex distribution and type of scoliosis. Finally, other studies have shown that longer surgical times can lead to an increased risk of infection [28]. This was not seen in our study after multivariable analysis, though Group A had significantly longer surgical times than Group B. Even with these limitations, our large study population and standardized surgical treatment allow for strong comparison between the two treatment groups.

Conclusion

Universal *S. aureus* screening, and preoperative intravenous vancomycin treatment if positive, and day-of-surgery PI nasal swabs as part of a surgical treatment bundle increased treatment cost by $308.25 per pediatric patient without a reduction in postoperative infections. Hospitals should consider removing these aspects of the surgical treatment bundles in pediatric patients undergoing PSF surgery.

Author contributions

Jason Malone: Writing – review and editing, Writing – original draft, Methodology, Investigation, Conceptualization. **Alex Lee-Norris:** Writing – review and editing, Writing – original draft. **Austin Wynn:** Writing – original draft. **Kaitlin Maher:** Writing – review and editing. **John Lovejoy:** Writing – review and editing. **Ryan Illgenfritz**: Writing – review and editing. **Margaret Baldwin:** Writing – review and editing. **Adriana Cadilla:** Writing — review and editing. **Kathryn Farrell:** Writing — review and editing, Data curation. **Emily Craver:** Formal analysis.

Consent for publication

The author(s) declare that no patient consent was necessary as no images or identifying information are included in the article.

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Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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