Topical Vancomycin as a Tool for the Prevention of Surgical Site Infections in Cranial Neurosurgery: A Retrospective Cohort Study

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BACKGROUND AND OBJECTIVES: Surgical site infections (SSI) in neurosurgery result in prolonged hospitalizations, readmissions, poor outcomes, and even death. Prevention of SSI remains paramount to mitigate the risk of this complication. In this study, we aimed to evaluate the effect of topical use of vancomycin powder during surgical closure in cranial surgery for the reduction of SSI.

METHODS: This is a retrospective cohort study of cranial neurosurgical patients from 2016 to 2022 in Fundación Santa Fe de Bogotá. Baseline clinical and surgical characteristics were collected, as well as vancomycin powder use. The primary outcome of interest was SSI within 90 days after surgery. A *P* value of .05 was considered significant.

RESULTS: We found a total of 1395 patients, of which 1108 met the selection criteria. Surgical site infection was seen in 32 patients (2.9%). Topical use of vancomycin powder during surgical closure was associated with a lower frequency of SSI in cranial surgery n = 10 (2.3%) relative to those who did not use vancomycin n = 22 (3.3%), and it was found to be a protective factor in the multinomial regression, with a statistically significant result (relative risk = 0.397, *P* = .034).

CONCLUSION: The evidence supporting the use of vancomycin powder during surgical closure is currently weak, as the association did not reach statistical significance in the primary analysis. However, a *P* value of less than 0.05 was obtained in the multivariate analysis. To further assess the efficacy of this intervention, additional randomized prospective studies are needed.

KEY WORDS: Neurosurgery, Surgical site infection, Topical vancomycin and cranial surgery.

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Surgical site infections (SSI) are a major cause of morbidity in the clinical setting and are among the most common neurosurgical postoperative complications.[1] It is estimated that SSI prolongs a patient's hospital stay by 10 days and represents an additional cost of approximately $20 000.[2,3] The incidence of SSI varies widely depending on the type of surgery and patient risk.[4] An incidence ranging from 2% to 13% is reported in the literature for spine and skull surgery.[5-7]

There are different risk factors that have been reported to increase surgical site infection, such as cerebrospinal fluid fistula, chronic corticosteroid use (more than 3 months), instrumentation, diabetes mellitus, arterial hypertension, cancer, and smoking.[8,9]

The implications of SSI include multiple reinterventions, instrument removal, long-term antibiotic therapy, and prolonged hospital stay with all the additional potential risks associated with health care.[10] In severe cases, it can result in abscesses, sepsis, and even death.[1,11]

For these reasons, it is essential to work on SSI prevention to improve the quality of care and reduce the use of health care resources.[7] Currently, prophylactic intravenous antibiotics are commonly used in the perioperative setting.[10] In the neurosurgical setting, intravenous cephalosporins have been used due to their high activity against gram-positive bacteria, particularly *Staphylococcus aureus*

ABBREVIATION: SSI, surgical site infections.

and *Staphylococcus epidermidis*, which are the main etiological agents identified in neurosurgical SSI patients.[12] However, the effectiveness of this measure has been limited by progressive antibiotic resistance in these pathogens[11,12]: Up to 60% resistance to cephalosporins has been reported among SSI causative organisms.[13]

Therefore, there is a need to find other methods to prevent SSI. Studies have found that the use of topical vancomycin before surgical closure can be associated with up to a 12-fold decrease in the incidence of SSI.[14] Local application of vancomycin powder to the surgical wound in spinal and intracranial surgery is becoming increasingly popular.[15]

Vancomycin covers a broad spectrum of gram-positive bacteria, is accessible, easy to apply, and reaches high local concentrations while its systemic absorption is almost nil.[5] Because of these high local concentrations, which exceed the minimum inhibitory concentration even for resistant organisms, this intervention has not been found to increase resistance to vancomycin.[5] Several studies suggest that local application of vancomycin to the surgical wound can reduce the incidence of SSI significantly; however, its usefulness is uncertain due to the low quality of most available evidence, and there are currently no large studies that evaluate the effectiveness of topical vancomycin application in skull base surgery in Latin America.[4,6,10,11] For this reason, this study aims to evaluate the effect of topical use of vancomycin powder during surgical closure in cranial surgery for the reduction of SSI over a 6-year period in a Latin American country.

METHODS

Ethics Statement

This study is reported according to the criteria listed in the Strengthening the Reporting of Observational studies in Epidemiology statement. All research protocols were approved by the Institutional Review Board of Fundación Santa Fe de Bogotá. This study did not require informed consent from the patients as the data were collected anonymously, using an alphanumeric code. Identifying information, such as names or patient ID, was not used in this study.

Study Design

This was a single-center, retrospective cohort study conducted at Fundación Santa Fe de Bogotá between January 1, 2016, and May 31, 2022. This study included patients who underwent cranial surgery, and topical vancomycin (generic formulation) was used for surgical closure.

Selection Criteria

Inclusion Criteria

Adult patients (older than 18 years) with a complete clinical history, who complied with a follow-up of up to 90 days after undergoing the surgical procedure (elective and nonelective procedures).

Exclusion Criteria

Patients undergoing cerebrospinal fluid shunt surgery because our clinical care center protocol for hydrocephalus requires the application of intravenous vancomycin before the procedure.

Patients undergoing resection of hypophysial lesions through transsphenoidal approach in whom topical vancomycin is not used due to the type of approach.

Cerebrospinal fluid fistula, although a risk factor for infection, is considered a surgical complication. Consequently, cases with this complication were excluded from this study due to their higher risk of infection, thereby minimizing the potential confounding effect.

Patients who were excluded from this study were those who did not complete the 90-day follow-up, either because they did not continue with the scheduled check-ups or due to non–SSI-related deaths.

All patients in this study underwent surgery following the institutional guidelines for SSI prevention, including the administration of prescribed antibiotic prophylaxis, maintaining normoglycemia before and after the procedure, adhering to operating room hygiene protocols, and ensuring proper skin preparation and disinfection. However, it is important to acknowledge that intraoperative blood glucose levels and temperature may fluctuate because of the lack of continuous monitoring.

At this institution, some neurosurgeons use topical vancomycin on all their patients, whereas others do not use this intervention on any of their patients. Whether a patient received vancomycin powder was determined solely by which neurosurgeon operated on him, regardless of patient characteristics.

The primary end point was the diagnosis of a SSI, as defined by the Center for Disease Control and Prevention criteria,[16,17] which are used for SSI surveillance in Fundación Santa Fe de Bogotá.

Statistical Analysis

The data were initially collected in an Excel database and subsequently stored in RedCap as database software. Statistical analysis of this study was performed using SPSS® version 22 software. A univariate analysis was conducted to describe the demographic and clinical characteristics of the participants. To determine the association between the use of topical vancomycin and the development of SSI, a relative risk with a 95% CI was calculated. To control for potential confounding factors, a multinomial logistic regression model was used. The final model was selected based on its parsimony and absence of collinearity between variables. It is worth noting that the model presented here, despite being the best, may still be affected by the imbalance caused by the frequency of SSI. Statistical significance was defined as $P < .05$.

RESULTS

Participants and Descriptive Data

We found a total of 1395 patients undergoing cranial surgery, of which 1108 met the selection criteria (Table 1). The age range varied between 18 and 94 years, with a median age of 60 years.

Vancomycin powder was placed during surgical site closure in the subgaleal space in 439 patients (39.6%); the remaining 669 patients (60.4%) had conventional closure. The entire study population was followed for a period of 90 days to identify SSI, which occurred in 32 patients (2.9%). SSI rates were 2.3% in the vancomycin group and 3.3% in the control group. There was no significant difference in outcomes observed between patients who received topical vancomycin during skull closure for the prevention of SSI and those who did not (Table 2).

Microbiological analysis of the 32 SSI obtained a total of 10 microorganisms (Table 3). The most frequent causative agents

TABLE 1. Demographic and Clinical Data

Variable	Intervention[a]	Control	Total	*P* value
N	439 (39.6%)	669 (60.4%)	1108	
Age (median)[b]	60	60	60	.263
Sex				
Male	215 (48.9%)	332 (49.6%)	547 (49.4%)	.010
Female	224 (51.1%)	337 (50.4%)	561 (50.6%)	
Comorbidities				
Hypertension	159 (36.2%)	221 (33%)	380 (34.3%)	.829
Diabetes	80 (18.2%)	79 (11.8%)	159 (14.4%)	.003
Smoker	100 (22.7%)	111 (16.5%)	211 (19.0%)	.010
Cancer	53 (12%)	78 (11.6%)	131 (11.8%)	.004
Chronic use of corticosteroids	45 (10.2%)	34 (5%)	79 (7.1%)	.001
Type of surgery				
Oncological	270 (61.5%)	242 (36.1%)	512 (46.2%)	.795
Functional	8 (1.8%)	26 (3.8%)	34 (3.1%)	.000
Trauma	34 (7.7%)	117 (17.4%)	151 (13.6%)	.000
Vascular	69 (15.7%)	125 (18.6%)	194 (17.5%)	.000
Others	58 (13.2%)	159 (23.7%)	217 (19.6%)	.000
Placement of surgical material				
No	335 (76.3%)	529 (79%)	864 (78%)	.284
Yes	104 (23.6%)	140 (21%)	244 (22%)	
Surgical site infection			32 (2.9%)	
Superficial	1 (0.2%)	5 (0.74%)	6 (0.5%)	
Deep	0 (0%)	3 (0.44%)	3 (0.3%)	.346
Organ-specific	9 (2.05%)	14 (2.09%)	23 (2.1%)	

[a]Vancomycin.
[b]Years.

were *S. aureus* (26.2%), *S. epidermidis* (21.4%), and *Pseudomonas aeruginosa* (11.9%).

Finally, we performed a multinominal regression (Table 4) that showed that diabetes mellitus (relative risk [RR] 3.494 CI 95% 1.494-8.175 P:0.004), smoking (RR 3.430 CI 95% 1.5020-7.740 P:0.003), cancer (RR 4.986 CI 95% 1.959-12.689 P:0.001), chronic corticosteroid use (RR 7.393 CI 95% 2. 737-19.971 P:0.000), and placement of surgical material (RR 5.491 CI 95% 2.420-12.467 P:0.000) (such as catheters, reservoirs, titanium plaques) had a statistically significant association with an increased risk of developing SSI after cranial surgery.

TABLE 2. Association Between the Use of Vancomycin Powder and Surgical Site Infection

Use of Vancomycin	SSI	No SSI	Total	RR	*P* value
Vancomycin (+)	10	429	439	0.69	.2137
Vancomycin (−)	22	647	669		
Total	32	1076	1108		

SSI, surgical site infections.

TABLE 3. Causative Agents of SSI in Cranial Surgery

Causal agent	Frequency
Staphylococcus aureus	26.2%
Staphylococcus epidermidis	21.4%
Pseudomonas aeruginosa	11.9%
klebsiella pneumoniae	7.1%
Citrobacter freundii	7.1%
Stenotrophomonas maltophilia	2.4%
Candida albicans	2.4%
klebsiella oxytoca	2.4%
Enterobacter cloacae	2.4%
Candida parapsilosis	2.4%
klebsiella aerogenes	2.4%
Cutibacterium acnes	2.4%
Serratia marcescens	2.4%
Staphylococcus capitis	2.4%

SSI, surgical site infections.

The regression also showed that when adjusting for these risk factors, the use of vancomycin powder has a statistically significant (P = .034) association with a lower risk of SSI (Table 4).

DISCUSSION

The local use of topical vancomycin in cranial surgery remains controversial because while many studies show an association with a decrease in SSI, other studies report no significant benefit.[10,11] Many researchers have expressed the need for studies with larger sample size and a higher level of evidence to establish whether there is indeed a relationship between the 2 variables.[5,18]

For instance, a systematic review and meta-analysis found an overall favorable effect of topical vancomycin on SSI, but the authors pointed out that the strength of the conclusions that can be drawn on the topic is limited by the lack of high-quality evidence to support its use because there are very few prospective randomized studies.[5]

Mallela et al[14] evaluated the application of vancomycin to the subgaleal space in 150 consecutive cases and found a 5% reduction in the incidence of SSI compared with 75 controls.[4] A prospective cohort of 355 patients demonstrated up to a 12-fold reduction in SSI in the vancomycin group compared with those receiving standard of care.[14]

Our study found an SSI rate that was lower for the control group than that observed in previous studies (3.4% vs approximately 6%) and higher for the vancomycin group (2.3% vs approximately 0.5%-1%).[14] We found a reduction of 60% in SSI in the vancomycin group compared with the control group (P = .034).

Patel et al[9] describe that cerebrospinal fluid fistula (OR: 27.41), dexamethasone use (OR: 3.55), and instrumentation (OR: 2.74) are documented risk factors in the literature for presenting with operative site infection.[9,19] Similarly, we found that chronic corticosteroid use and placement of surgical material were risk factors for SSI after cranial surgery, as well as diabetes mellitus, smoking, and cancer.

The most common germs reported in the literature as found in SSI are *S. aureus* and *S. epidermidis*, which are part of the skin microbiota and are believed to be inoculated directly into the surgical wound during surgery.[4] This is directly related to what we found in our study.

To the best of our knowledge, this is the largest patient cohort published in Latin America examining the effectiveness of topical

TABLE 4. Multivariate Analysis by Potential Risk Factors

Variable	SSI (n = 32)	Non-SSI (n = 1076)	RR	95% CI	*P* value
Sex (male)	17	530	0.740	(0.338-1.617)	.450
Hypertension	22	358	2.402	(1.030-5.602)	.043
Diabetes	15	144	3.494	(1.494-8.175)	.004
Smoker	18	193	3.430	(1.520-7.740)	.003
Cancer	11	120	4.986	(1.959-12.689)	.001
Chronic use of corticosteroids	9	70	7.393	(2.737-19.971)	.000
Placement of surgical material	15	229	5.491	(2.420-12.461)	.000
Use of vancomycin powder	10	429	0.397	(0.169-0.933)	.034

SSI, surgical site infections.

vancomycin application in skull surgery. For this reason, we suggest expanding the investigation of the use of topical vancomycin in cranial surgery in the region and, in case our results can be replicated in different institutions, to promote the routine use of vancomycin in cranial surgery.

Limitations

This retrospective study was conducted at a single hospital center, presenting challenges in control of bias related to preoperative, intraoperative, and postoperative conditions. The unknown frequency of vancomycin usage among neurosurgeons in this study introduces a potential limitation of classification bias. However, we consider this limitation to be minimal due to the adherence of all neurosurgeons to a standardized protocol starting from a specific date. Furthermore, the evaluation of other topical antibiotics was not conducted, and patients who underwent cerebrospinal fluid diversion surgery or transsphenoidal pituitary surgeries were excluded. In addition, the exclusion of patients who did not complete the 90-day follow-up might introduce selection bias. Despite its retrospective nature, our study benefits from a robust and comprehensive data collection process. To expand on these findings, we recommend the involvement of multiple centers and the implementation of prospective studies to produce higher levels of evidence.

Future research should focus on conducting prospective randomized studies that control for bias factors, such as blood glucose levels and intraoperative temperature, which are known to increase the risk of SSI. In addition, studies should consider the specific surgical procedures in which topical vancomycin is applied during surgical closure, using a standardized protocol implemented by all neurosurgeons. Furthermore, a follow-up period exceeding 90 days is recommended to assess the long-term outcomes of patients with SSI.

CONCLUSION

The application of topical vancomycin during surgical interventions has shown a modest decrease in the occurrence of SSI, although statistical significance was observed only through multivariate analysis. To address the limitations mentioned above and achieve more robust findings, it is imperative to conduct prospective randomized studies involving larger cohorts of patients. These studies would provide reliable results and facilitate the formulation of evidence-based recommendations regarding the use of vancomycin for SSI prevention.

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REFERENCES

1. Abdullah KG, Attiah MA, Olsen AS, Richardson A, Lucas TH. Reducing surgical site infections following craniotomy: examination of the use of topical vancomycin. *J Neurosurg.* 2015;123(6):1600-1604.
2. Hafez S, Saied T, Hasan E, et al. Incidence and modifiable risk factors of surveillance of surgical site infections in Egypt: a prospective study. *Am J Infect Control.* 2012;40(5):426-430.
3. Erman T, Demirhindi H, Göçer AI, Tuna M, Ildan F, Boyar B. Risk factors for surgical site infections in neurosurgery patients with antibiotic prophylaxis. *Surg Neurol.* 2005;63(2):107-113.
4. Abdullah K, Chen H, Lucas T. Safety of topical vancomycin powder in neurosurgery. *Surg Neurol Int.* 2016;7(Suppl 39)(40):s919.
5. Bokhari R, You E, Zeiler FA, et al. Effect of intrawound vancomycin on surgical site infections in nonspinal neurosurgical procedures: a systematic review and meta-analysis. *World Neurosurg.* 2019;123:409-417.e7.
6. Chiang HY, Herwaldt LA, Blevins AE, Cho E, Schweizer ML. Effectiveness of local vancomycin powder to decrease surgical site infections: a meta-analysis. *Spine J.* 2014;14(3):397-407.
7. Chotai S, Wright PW, Hale AT, et al. Does intrawound vancomycin application during spine surgery create vancomycin-resistant organism? *Neurosurgery.* 2017;80(5):746-753.
8. Cediel EG, Boerwinkle VL, Ramon JF, et al. Length of preoperative hospital stay is the dominating risk factor for surgical site infection in neurosurgery: a cohort data-driven analysis. *Surg Neurol Int.* 2022;13(80):80.
9. Patel S, Thompson D, Innocent S, Narbad V, Selway R, Barkas K. Risk factors for surgical site infections in neurosurgery. *Ann R Coll Surgeons Engl.* 2019;101(3):220-225.
10. Kang DG, Holekamp TF, Wagner SC, Lehman RA. Intrasite vancomycin powder for the prevention of surgical site infection in spine surgery: a systematic literature review. *Spine J.* 2015;15(4):762-770.
11. Ravikumar V, Ho AL, Pendharkar AV, Sussman ES, Kwong-hon Chow K, Li G. The use of vancomycin powder for surgical prophylaxis following craniotomy. *Neurosurgery.* 2017;80(5):754-758.
12. He X, Sun T, Wang J, Li G, Fei Q. Application of vancomycin powder to reduce surgical infection and deep surgical infection in spinal surgery: a meta-analysis. *Clin Spine Surg.* 2019;32(4):150-163.
13. Kim D, Ahn JY, Lee CH, et al. Increasing resistance to extended-spectrum cephalosporins, fluoroquinolone, and carbapenem in gram-negative bacilli and the emergence of carbapenem non-susceptibility in Klebsiella pneumoniae: analysis of Korean Antimicrobial Resistance Monitoring System (KARMS) Data from 2013 to 2015. *Ann Lab Med.* 2017;37(3):231-239.
14. Mallela AN, Abdullah KG, Brandon C, Richardson AG, Lucas TH. Topical vancomycin reduces surgical-site infections after craniotomy: a prospective, controlled study. *Neurosurgery.* 2018;83(4):761-767.
15. Ghobrial GM, Cadotte DW, Williams K, Fehlings MG, Harrop JS. Complications from the use of intrawound vancomycin in lumbar spinal surgery: a systematic review. *Neurosurg Focus.* 2015;39(4):E11.
16. Berriós-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for disease control and prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg.* 2017;152(8):784-791.
17. Russo V, Leaptrot D, Otis M, Smith H, Hebden JN, Wright MO. Health care-associated infections studies project: an American journal of infection control and National Healthcare Safety Network Data Quality Collaboration Case Study—chapter 9 surgical site infection event (SSI) case study. *Am J Infect Control.* 2022;50(7):799-800.
18. Yao R, Tan T, Tee JW, Street J. Prophylaxis of surgical site infection in adult spine surgery: a systematic review. *J Clin Neurosci.* 2018;52:5-25.
19. Nogué M, Rambaud J, Fabre S, Filippi N, Jorgensen C, Pers YM. Long-term corticosteroid use and dietary advice: a qualitative analysis of the difficulties encountered by patient. *BMC Health Serv Res.* 2019;19(1):255-259.

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