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Comparing Topical Vancomycin Vs Control Procedure Focus on Staphylococcus Event in Spinal Surgery Procedures: A Systematic Review and Meta-Analysis

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ABSTRACT

This study aimed to evaluate the effectiveness of topical vancomycin powder versus standard prophylaxis in preventing gram-positive bacterial infections, specifically Streptococcus species, in spinal surgery patients through a systematic review and meta-analysis. A comprehensive search was conducted across the PubMed, Cochrane Library, Scopus, and ScienceDirect databases. The search strategy incorporated the terms "Spine Surgery," "Topical Vancomycin," "Surgical Site Infection," "Gram-positive," and "Staphylococcus." Studies were included if they involved adult patients undergoing spinal surgery, evaluated topical vancomycin powder applied directly to surgical wounds before closure, compared it to control groups receiving standard systemic antibiotic prophylaxis alone, and reported surgical site infection rates with a focus on gram-positive organisms. Reviewers independently identified studies, extracted data, and assessed study quality using the Newcastle–Ottawa Scale. Risk ratios with 95% confidence intervals were calculated. Statistical heterogeneity was assessed using the I^2 statistic. Nine comparative studies involving 9,745 patients were analyzed. Streptococcus infections occurred in 44 of 3,943 patients (1.11%) in the vancomycin group versus 115 of 5,802 patients (1.98%) in the control group (risk ratio, 0.49; 95% confidence interval, 0.34–0.70; I^2 = 4%). Topical vancomycin powder significantly reduced Streptococcus infections by 51% in spinal surgery patients, demonstrating consistent protective effects against gram-positive pathogens with minimal heterogeneity across studies.

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INTRODUCTION

Surgical site infections (SSIs) remain one of the most significant complications following spinal surgery, with reported incidence rates ranging from 0.7% to 15%, depending on the surgical approach, patient comorbidities, and use of instrumentation (Daher et al., 2024). These infections impose substantial clinical and economic burdens, often requiring prolonged hospitalization, additional surgical interventions, and extensive antibiotic therapy, while significantly impacting patient outcomes and quality of life. The microbiological landscape of spinal SSIs is predominantly characterized by gram-positive organisms, with Staphylococcus aureus accounting for approximately 45.2% of infections, followed by Staphylococcus epidermidis at 31.4%, and methicillin-resistant pathogens comprising 34.3% of all spinal SSIs (Li et al., 2022). This gram-positive predominance, particularly involving staphylococcal species, has driven considerable interest in targeted antimicrobial prophylaxis strategies that can effectively address these specific pathogens while maintaining favorable safety profiles.

The concept of local antibiotic application has evolved significantly over the past two decades, with topical vancomycin powder emerging as a particularly promising intervention for preventing gram-positive SSIs in spinal surgery (Bokhari et al., 2019). Vancomycin's

broad-spectrum activity against gram-positive bacteria, including methicillin-resistant Staphylococcus aureus (MRSA) and coagulase-negative staphylococci, makes it an ideal candidate for topical application (Khanna et al., 2019). When applied directly to the surgical wound, vancomycin powder achieves local tissue concentrations ranging from 263 to 2,938 μg/mL on the day of surgery, representing concentrations nearly 1,000-fold higher than the minimum inhibitory concentration for MRSA and coagulase-negative Staphylococcus species (Li et al., 2022). However, despite widespread adoption of this practice, the clinical evidence remains contentious, with recent randomized controlled trials producing conflicting results regarding its efficacy in reducing overall SSI rates (Daher et al., 2024). While some studies demonstrate significant reductions in staphylococcal infections, concerns have been raised about potential selection pressure favoring gram-negative organisms and the development of vancomycin resistance (Gande et al., 2019; Tafish et al., 2021).

Therefore, this study aims to evaluate the effectiveness of topical vancomycin powder versus standard prophylaxis in preventing gram-positive bacterial infections, specifically Staphylococcus species, in spinal surgery patients through systematic review and meta-analysis. Given the inconsistent findings in individual studies and the critical importance of evidence-based infection prevention strategies in spinal surgery, a comprehensive systematic review and meta-analysis is warranted to definitively establish the role of topical vancomycin in preventing gram-positive SSIs, particularly those caused by Staphylococcus species.

METHOD

This systematic review and meta-analysis was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Studies were eligible for inclusion if they involved adult patients (≥18 years) undergoing any type of spinal surgery, regardless of surgical approach or indication. The authors included randomized controlled trials and cohort studies that evaluated topical vancomycin powder applied directly to the surgical wound before closure as the intervention, compared to control groups receiving either no topical antibiotic prophylaxis, placebo, or standard systemic antibiotic prophylaxis alone. Eligible studies reported surgical site infection rates as a primary or secondary outcome, with particular focus on infections caused by gram-positive organisms, specifically *Staphylococcus aureus* and *Staphylococcus epidermidis*, and on infection classification as deep or superficial when available. Excluded studies comprised case reports, case series without control groups, those involving pediatric populations (<18 years), non-spinal orthopedic procedures, studies using systemic vancomycin as the intervention, and analyses focusing exclusively on gram-negative bacterial infections without corresponding gram-positive data.

A comprehensive search was performed in electronic databases, including PubMed, the Cochrane Library, Scopus, and ScienceDirect. The search strategy incorporated the keywords “Spine Surgery,” “Topical Vancomycin,” “Surgical Site Infection,” “Gram-positive,” and “Staphylococcus.” All identified records were imported into reference management software for organization, and duplicates were removed through automated and

manual screening. Titles and abstracts were independently reviewed to identify potentially eligible studies, and full texts were evaluated by two reviewers according to the inclusion and exclusion criteria.

The methodological quality and risk of bias were assessed using the Newcastle–Ottawa Quality Assessment Scale (NOS) for cohort studies. Each study was independently evaluated and rated, and the results were categorized as good, fair, or poor quality according to the NOS criteria.

Quantitative data were analyzed using meta-analytic techniques. For dichotomous outcomes, data were extracted as the number of events (n) and total participants (t) in each group (vancomycin and control). Effect sizes were calculated as risk ratios (RR) with 95% confidence intervals (CI). Statistical heterogeneity across studies was assessed using the I^2 statistic. All statistical analyses were conducted using RevMan version 5.4.1.

RESULTS AND DISCUSSION

Results

Data identification and selection process

A comprehensive search was conducted across PubMed, Cochrane Library, Scopus, and ScienceDirect which yielded a total of 332 records. After removing 21 duplicates, 311 unique records remained for screening. During the title and abstract screening phase, 17 records were assessed, of which 3 were excluded due to irrelevance. This left 12 articles for full-text review. Of these, there 2 articles were excluded. A total of 10 studies met the inclusion criteria and were included in the final analysis. All 10 studies were further included in the meta-analysis. (Figure 1)

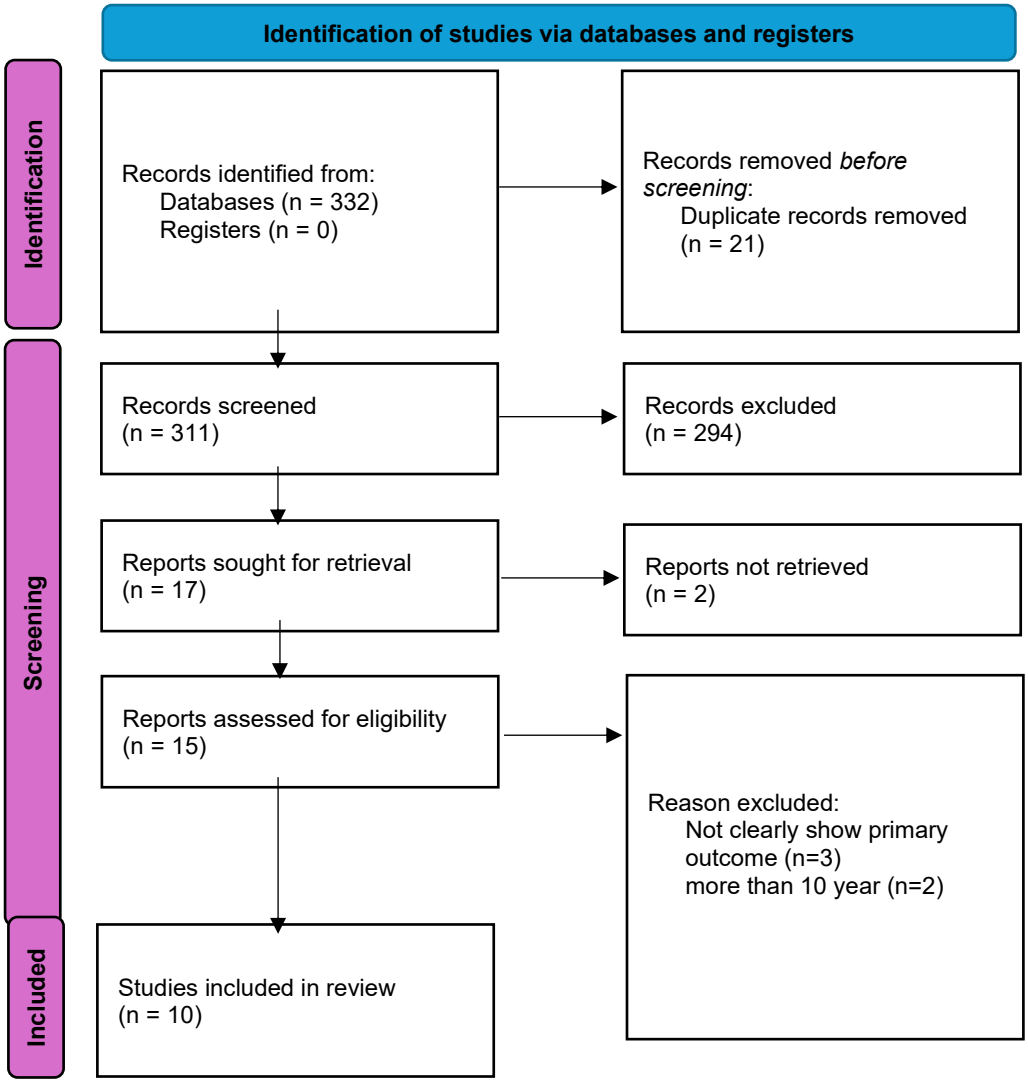


Figure 1. PRISMA Flow diagram for Selection Study

Source: Processed by researcher (2024)

Study characteristics

A total of nine comparative studies met our inclusion criteria and were included in this meta-analysis (Table 1). Eight studies employed retrospective cohort designs, while one utilized a prospective cohort approach (Chotai et al., 2017). The studies were conducted between 2015 and 2022, with sample sizes ranging from 389 patients (Dennis et al., 2016) to 2,859 patients (Horii et al., 2018). All studies evaluated posterior spinal surgery procedures, including instrumented fusions and arthrodesis, with patient populations primarily involving adults undergoing various spinal procedures for degenerative diseases, deformity correction, and trauma. One study specifically focused on pediatric patients under 18 years (Garg et al., 2018). Topical vancomycin dosing protocols varied considerably across studies, ranging from 250 mg (Wang et al., 2022) to 2 grams (Gaviola et al., 2016), with most studies applying 1-2 grams of vancomycin powder directly to the surgical wound, instrumentation, and surrounding tissues before closure. Control groups consistently

received standard intravenous antibiotic prophylaxis, predominantly cefazolin, without any topical antibiotic application. (Tabel 1)

Table 1: Study Characteristics

Study (Author, Year)	Study Design	Participant Characteristics	Sample Size (Intervention/Control)	Intervention Details	Control Group Details
Lemans et al., 2019	Retrospective Cohort	Adult patients undergoing open, posterior, instrumented spinal surgery at any level	379/257	1-2 grams vancomycin powder applied to all layers of surgical wound, instrumentation, dura, and bone graft before closure	Standard antimicrobial prophylaxis with IV cefazolin only
Horii et al., 2018	Retrospective Cohort	Patients ≥15 years undergoing posterior instrumented spinal surgery	694/2165	1-2 grams intraoperative vancomycin powder spread throughout local wound before closure	No intrawound vancomycin powder
Wang et al., 2022	Retrospective Cohort	Patients with lumbar degenerative disease undergoing posterior fixation interbody fusion	527/364	250 mg vancomycin powder mixed with bone graft + 250 mg applied directly to surgical bed (up to 1000 mg for >2 levels)	Standard antimicrobial prophylaxis without topical vancomycin
Garg et al., 2018	Retrospective Cohort	Pediatric patients (<18 years) undergoing posterior spinal fusion	228/310	Topical vancomycin powder 500-2000 mg applied to surgical site before closure	No topical vancomycin
Lee et al., 2016	Retrospective Cohort	Patients undergoing posterior lumbar surgery	275/296	1 gram vancomycin powder applied directly to wound before closure	Standard prophylactic IV antibiotics only
Dennis et al., 2016	Retrospective Cohort	Instrumented spine surgery patients, single institution, Singapore. Exclusions: recent infection, systemic antibiotics, immunosuppressants, immunodeficiency	117/272	1g intraoperative local vancomycin powder applied to wound before closure + standard prophylaxis (IV cefazolin)	Standard prophylaxis alone (IV cefazolin 1g pre-surgical + 1g q8h × 48h)
Heller et al., 2015	Retrospective Cohort	Posterior instrumented spinal arthrodesis patients, single surgeon, Kansas Medical Center	342/341	0.5-2g vancomycin powder (dose based on patient size/levels) applied directly to wound + standard AMP (IV cefazolin)	Standard AMP alone (IV cefazolin 20mg/kg pre-op, q4h intraop, 1g q8h × 24h postop)
Gaviola et al., 2016	Retrospective Cohort	Multilevel spinal fusion (≥3 levels) patients, age ≥18 years,	116/210	2g topical vancomycin powder sprinkled	IV cefazolin 2g alone

Study (Author, Year)	Study Design	Participant Characteristics	Sample Size (Intervention/Control)	Intervention Details	Control Group Details
		Vermont Medical Center		on soft tissues, implants, and bony elements + IV cefazolin 2g	
Chotai et al., 2017	Prospective Cohort	Elective spine surgery patients (degenerative and oncological), Vanderbilt Medical Center	1215/1587	1g vancomycin powder per 10cm wound length applied to muscle, fascia, subcutaneous tissues + standard prophylaxis (IV cefazolin 1g)	Standard prophylaxis alone (IV cefazolin 1g pre-op, q8h × 24h)

Study results

Vancomycin Powder versus Control on Streptococcus Infection Events in Spine Surgery

Nine studies involving 9,745 patients provided data on Streptococcus infection outcomes following spinal surgery (Table 2, Figure 2). The pooled analysis demonstrated that topical vancomycin powder significantly reduced Streptococcus infection rates compared to control groups, with 44 infections occurring among 3,943 patients (1.11%) in the vancomycin group versus 115 infections among 5,802 patients (1.98%) in the control group. The meta-analysis revealed a statistically significant risk reduction with a pooled risk ratio of 0.49 (95% CI: 0.34-0.70, p<0.001), indicating that topical vancomycin powder reduces the risk of Streptococcus infections by approximately 51% compared to standard prophylaxis alone. Heterogeneity between studies was minimal (I^2 = 4%), suggesting consistent treatment effects across different study populations and surgical settings, which strengthens the reliability of this finding for clinical practice.

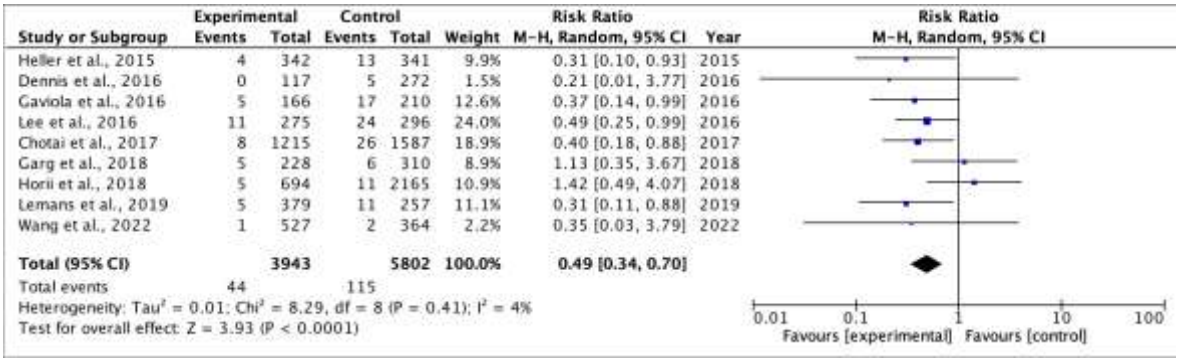


Figure 2. Forest plot comparing the effect of intrawound Vancomycin powder versus control on Streptococcus infection events in spine surgery

Source: Results of meta-analysis by researchers (2024)

Table 2. Comparing the effect of intrawound Vancomycin powder versus control on Streptococcus infection

Outcome	Studies, *n*	Participants	Erythromycin, *n*/total (%)	Azithromycin, *n*/total (%)	RR [95% CI]	I^2
Streptococcus infection events	9	9745	44/3943 (1.11)	115/5802 (1.98)	0.49 [0.34, 0.70]	4%

Source: Results of meta-analysis by researchers (2024)

Quality of studies

The quality of studies is presented in Table 3.

Table 3: Risk of Bias Assessment

First Author, Year	Selection Bias				Confounding Bias	Measurement Bias			Total Score	Risk Level
	Representative Sample Size	Selection of A comparison Group	Ascertainment of Exposure by Secure Record	Outcome Not Present at Beginning of Study		Assessment of Outcome	Follow Up Length	Follow-up Rate ≥ 90%		
Lemans, 2019	1	1	1	1	1	1	1	1	**8**	**Medium Risk**
Horii, 2018	1	1	1	1	1	1	1	0	**7**	**Medium Risk**
Wang, 2022	1	1	1	1	1	1	1	1	**8**	**Medium Risk**
Garg, 2018	1	1	1	1	0	1	1	0	**6**	**High Risk**
Lee, 2016	1	1	1	1	1	1	1	0	**7**	**Medium Risk**
Dennis, 2016	1	1	1	1	1	1	1	1	**8**	**Medium Risk**
Heller, 2015	1	1	1	1	1	1	1	1	**8**	**Medium Risk**
Gaviola, 2016	1	1	1	1	1	1	1	0	**7**	**Medium Risk**
Chotai, 2017	1	1	1	1	0	1	1	1	**7**	**Medium Risk**

Source: Assessed using the Newcastle-Ottawa Scale (NOS) by researchers (2024)

Discussion

This systematic review and meta-analysis provides compelling evidence that topical vancomycin powder significantly reduces gram-positive bacterial infections, specifically Streptococcus species, in spinal surgery by approximately 51%. The remarkably low heterogeneity ($I^2 = 4\%$) across nine studies involving nearly 10,000 patients demonstrates consistent protective effects across diverse surgical populations and institutional practices. These findings contribute to the growing body of evidence supporting targeted antimicrobial prophylaxis strategies for gram-positive pathogens in spine surgery, though they also highlight important considerations regarding the broader spectrum of surgical site infection prevention.

Our results align closely with recent systematic reviews and meta-analyses that have consistently demonstrated the efficacy of topical vancomycin against gram-positive organisms. Ushirozako et al. (2021) reported a significant reduction in SSI rates after posterior spinal surgery using propensity score-matched analysis, finding an odds ratio of 0.486 (95% CI: 0.243-0.972) for vancomycin-treated patients (Ushirozako et al., 2021). Similarly, Li et al. (2022) found that vancomycin powder was particularly effective against gram-positive bacteria (OR: 0.35; 95% CI: 0.23-0.56) and MRSA infections (OR: 0.20; 95%

CI: 0.10-0.43) in their comprehensive meta-analysis of 22 studies (Li et al., 2022). The consistency of our findings with these larger analyses reinforces the robustness of the protective effect against gram-positive pathogens, while also supporting the mechanistic rationale for vancomycin's targeted antimicrobial spectrum.

However, our analysis reveals an important microbiological consideration that warrants careful interpretation. While our results demonstrate effectiveness against Streptococcus infections, recent studies have raised concerns about potential shifts in bacterial ecology following topical vancomycin use. Hu et al. (2023) reported that while vancomycin reduced overall SSI rates, the proportion of gram-negative bacteria increased from 30.1% to 46.4% in vancomycin-treated patients who developed infections (Hu et al., 2023). This selective pressure phenomenon has been corroborated by multiple investigations, including Gande et al. (2019) who found increased rates of gram-negative and polymicrobial infections in their meta-analysis of vancomycin powder use (Gande et al., 2019). These findings suggest that while vancomycin effectively targets gram-positive pathogens, it may inadvertently create ecological niches for resistant gram-negative organisms, potentially complicating the management of breakthrough infections.

The clinical significance of our findings is substantial, particularly when considered within the context of infection prevention strategies and healthcare economics. Recent cost-effectiveness analyses have demonstrated that topical vancomycin can generate significant healthcare savings. A Brazilian study by Ramos et al. (2021) found cost savings of approximately $75,460 USD per 100 spinal fusion procedures when using topical vancomycin, with infection rates decreasing from 9.8% to 2.4% (Ramos et al., 2021). Furthermore, high-quality randomized controlled trials, such as the prospective double-blind study by Zhang et al. (2024), have confirmed both the safety and efficacy of intrawound vancomycin powder in reducing SSI rates without significant adverse effects (Zhang et al., 2024). These economic and safety considerations support the clinical implementation of topical vancomycin, particularly in high-risk populations where the absolute risk reduction would be most pronounced.

Several methodological strengths enhance the credibility of our findings, including the comprehensive search strategy, rigorous inclusion criteria focusing on comparative studies, and the use of appropriate statistical methods with assessment of heterogeneity. The low I^2 statistic indicates that our results are not significantly influenced by study-specific factors, suggesting broad applicability across different surgical populations and institutional practices. However, important limitations must be acknowledged. The predominance of retrospective cohort studies (8 of 9 included studies) introduces potential selection bias and confounding factors that may influence the observed treatment effects. Additionally, the significant variation in vancomycin dosing protocols (ranging from 250mg to 2g) across studies makes it difficult to establish optimal dosing recommendations. Most concerning is the potential for publication bias, as studies reporting positive outcomes may be more likely to be published than those showing neutral or negative results.

The theoretical and practical implications of our findings extend beyond immediate clinical application to broader infection prevention strategies and antimicrobial stewardship considerations. The demonstrated efficacy against gram-positive pathogens supports the

continued use of topical vancomycin in high-risk spinal procedures, particularly those involving instrumentation or patients with multiple comorbidities. However, clinicians must remain vigilant for breakthrough infections caused by gram-negative organisms and should consider broader-spectrum empirical antibiotic coverage when infections occur despite vancomycin prophylaxis. Future research should focus on optimizing dosing protocols, identifying patient populations most likely to benefit from topical vancomycin, and developing combination prophylaxis strategies that address both gram-positive and gram-negative pathogens. Additionally, large-scale randomized controlled trials with longer follow-up periods are needed to definitively establish the safety profile and to better understand the long-term implications of selective antimicrobial pressure in spinal surgery patients

CONCLUSION

This meta-analysis found that topical vancomycin powder significantly reduced gram-positive bacterial infections, particularly Streptococcus species, by 51% among spinal surgery patients across nine studies encompassing 9,745 participants, with minimal heterogeneity observed. These findings confirm the clinical efficacy of vancomycin powder as a complementary measure to standard antibiotic prophylaxis, especially for high-risk or instrumented procedures. However, clinicians should remain cautious regarding potential increases in gram-negative infections associated with its use. Future research should focus on long-term microbial resistance patterns, optimal dosing protocols, and comparative effectiveness across specific spinal surgery subtypes to refine its clinical application.

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