

Prophylactic Intraventricular Vancomycin for Prevention of External Ventricular Drain-Related Infections: A Retrospective Cohort Study**Malavsinh Jadeja¹, Neelesh Bhatnagar², Ram Velash Meena³, Govind Mangal⁴, Alka Chhabra⁵, Seema Partani⁶**¹Assistant Professor, Department of Critical Care Medicine, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India²Professor and Head, Department of Neuroanaesthesiology, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India³Assistant Professor, Department of Anaesthesiology, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India⁴Professor and Head, Department of Neurosurgery, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India⁵Professor and Head, Department of Anaesthesiology, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India⁶Professor, Department of Anaesthesiology, Geetanjali Medical College and Hospital, Geetanjali University, Udaipur, Rajasthan, India

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Corresponding Author: Dr. Ram Velash Meena

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Abstract:**Background:** External ventricular drain (EVD)-related infection (ERI) is a significant complication of neurosurgical care, contributing to morbidity, prolonged hospitalization, and increased healthcare costs. Although intraventricular vancomycin can achieve high cerebrospinal fluid concentrations, its prophylactic role and potential effect on microbial patterns remain insufficiently characterized.**Objective:** To evaluate the feasibility and preliminary association of adjunctive intraventricular vancomycin with intravenous cephalosporin, compared with intravenous cephalosporin alone, in reducing ERI among adults undergoing EVD placement.**Methods:** In this retrospective cohort study, 90 adults undergoing EVD placement were allocated equally to receive intraventricular vancomycin 10 mg daily for 7 days plus intravenous ceftriaxone or ceftazidime, or intravenous cephalosporin alone. The primary outcome was ERI within 30 days. Secondary outcomes included ICU and hospital length of stay, microbial profile, EVD duration and replacement, mortality, and adverse events.**Results:** ERI occurred in 3/45 patients (6.7%) receiving vancomycin versus 12/45 (26.7%) controls (absolute risk reduction, 20.0%; 95% CI, 5.2–34.8%; RR, 0.25; 95% CI, 0.08–0.81; $p=0.02$). All infections in the vancomycin group were caused by gram-negative organisms compared with 2/12 (16.7%) in controls ($p=0.02$). Hospital and ICU stays were significantly shorter with vancomycin. Transient chemical ventriculitis occurred in 2 patients (4.4%). Mortality was 11.1% versus 26.7% ($p=0.10$).**Conclusion:** Adjunctive intraventricular vancomycin was associated with lower ERI rates and shorter hospital and ICU stays but with a shift toward gram-negative infections. Given the small, retrospective sample, these findings are preliminary and hypothesis-generating. Larger multicenter studies are warranted to confirm efficacy, safety, and microbial consequences.**Keywords:** External Ventricular Drain; EVD-Related Infection; Ventriculitis; Intraventricular Vancomycin; Antimicrobial Prophylaxis; Cerebrospinal Fluid Infection; Retrospective Cohort Study; Pilot Study.**DOI:** 10.25258/ijpqa.17.10.2

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Introduction

External ventricular drain (EVD) placement is a common, potentially life-saving procedure for acute hydrocephalus, intracranial pressure monitoring, and cerebrospinal fluid diversion in conditions such as subarachnoid haemorrhage,

traumatic brain injury, and intraventricular haemorrhage. [1,2] Despite standardized insertion and maintenance protocols, EVD-related infection (ERI) remains an important complication, increasing morbidity, ICU and hospital stay, and

healthcare costs. Reported ERI rates range from 0.8% to 27%, with systematic reviews estimating approximately 8–10%.[3]

Coagulase-negative staphylococci and *Staphylococcus aureus* are the predominant pathogens, although gram-negative bacilli are increasingly recognized, particularly with prolonged catheterization and repeated manipulation.[4,5] Diagnosis remains challenging because fever, altered consciousness, and CSF abnormalities may also reflect the underlying neurological illness or non-infectious inflammation.[6,7]

IDSA and Neurocritical Care Society guidelines recommend periprocedural antimicrobial prophylaxis during EVD insertion but discourage prolonged systemic prophylaxis throughout catheterization.

Antimicrobial-impregnated catheters and standardized insertion and maintenance practices are recommended, while intraventricular antibiotics are generally reserved for established ventriculitis or meningitis.[8,9]

Vancomycin is a potential prophylactic agent because of its activity against common gram-positive EVD pathogens, including methicillin-resistant staphylococci. Fu et al. (2017) reported lower ERI rates with pre-emptive intrathecal vancomycin (10 mg daily for 7 days). However, selective suppression of gram-positive organisms may alter microbial ecology and promote gram-negative infections. Previous studies have reported conflicting findings regarding the efficacy and safety of prophylactic intraventricular vancomycin.[10,1,2]

The present pilot study was designed to evaluate whether adjunctive intraventricular vancomycin with intravenous cephalosporin is associated with lower ERI rates compared with intravenous cephalosporin prophylaxis alone and to characterize the microbial spectrum and clinical outcomes associated with each strategy. To our knowledge, no retrospective cohort study has specifically compared intraventricular vancomycin plus intravenous cephalosporin with intravenous cephalosporin alone using CDC defined infection criteria.

Materials and Methods

Study Design and Setting: The study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations.

Participants: Adult patients (age ≥ 18 years) who underwent EVD placement for acute hydrocephalus, intracranial pressure monitoring, or cerebrospinal fluid diversion during the study period were retrospectively identified from institutional medical records.

Exclusion criteria included pre-existing central nervous system infection, receipt of intrathecal or intraventricular antibiotics within the preceding 7 days, known allergy to vancomycin or cephalosporins, pregnancy or breastfeeding, or life expectancy of less than 72 hours.

Treatment Exposure Classification: Patients were retrospectively grouped according to the prophylactic antimicrobial therapy documented in their medical records. The intraventricular vancomycin group received intraventricular vancomycin in addition to intravenous cephalosporin, while the control group received intravenous cephalosporin alone. Treatment allocation was based on documented clinical practice and was not determined by the investigators.

Intraventricular Vancomycin Group (Group A, n=45): Patients received intraventricular vancomycin 10 mg immediately following EVD placement, then 10 mg daily for 7 days. The EVD was temporarily clamped for 30 minutes after each intraventricular dose to allow adequate drug distribution. In addition, all patients received standard intravenous prophylaxis with ceftriaxone 2 g daily (or ceftazidime 2 g daily in cases of suspected meningitis).

Control Group (Group B, n=45): Patients received intravenous cephalosporin prophylaxis alone (ceftriaxone 2 g daily or ceftazidime 2 g daily) without intraventricular antibiotics. All patients received the same standardized EVD care bundle, which included: non-antimicrobial silicone catheters (standard, non-impregnated), subcutaneous tunnelling of at least 5 cm, sterile dressing changes at the catheter site every 72 hours and cerebrospinal fluid sampling only when clinically indicated. EVDs were discontinued when no longer clinically required and weaned according to a standardized institutional protocol.

Outcomes

Primary Outcome: Occurrence of study-defined ERI within 30 days of EVD placement.

Secondary Outcomes

- ICU length of stay (days)
- Hospital length of stay (days)
- Glasgow Coma Scale (GCS) at ICU discharge and hospital discharge
- Microbial profile of ERI cases (organism identification and gram stain category)
- EVD duration (days)
- EVD replacement rates and indications
- In-hospital mortality
- Adverse events related to intraventricular vancomycin administration

Infection Definition

ERI was defined using pre-established CDC/NHSN-based criteria. Definite ERI required a positive CSF culture with compatible clinical signs. Probable ERI required clinical suspicion with at least two compatible symptoms/signs and one supportive laboratory finding, including abnormal CSF parameters, organisms on Gram stain, or a positive blood culture without another source.

CSF was collected aseptically through the EVD after discarding the first 1–2 mL and analyzed for cell count, glucose, protein, Gram stain, and aerobic culture. Positive cultures were reviewed to differentiate true infection from contamination. A single positive culture for skin commensals, such as coagulase-negative staphylococci, was considered infection only when accompanied by compatible clinical and CSF findings.

CSF Sampling and Surveillance: Routine CSF samples were obtained on days 3 and 7 of EVD placement, as well as when clinically indicated (fever $>38^{\circ}\text{C}$, new neurological deterioration, or abnormalities on visual inspection of CSF). All samples were immediately transported to the microbiology laboratory and processed within 30 minutes.

Data Collection: Demographic, clinical, microbiological, treatment, and outcome data were retrospectively extracted from electronic medical records. Variables included age, sex, comorbidities, indication for EVD, admission GCS, dates of EVD insertion and removal, reasons for EVD replacement, CSF parameters when sampled, CSF culture results, antimicrobial administration details, ICU and hospital discharge dates, discharge GCS, and adverse events. Adverse events were recorded daily by the study team and reviewed weekly by the data and safety monitoring board. Chemical ventriculitis was defined as CSF pleocytosis (>10 WBC/mm³) with negative cultures following

vancomycin administration, in the absence of clinical signs of infection.

Statistical Analysis: The students' t-test or Mann-Whitney U test were used to compare continuous variables that were summarised as mean $\pm$ standard deviation or median (interquartile range). The chi-square test or Fisher's exact test, depending on the situation, were used to compare categorical variables.

Given the small number of events, a two-sided Fisher's exact test was used to compare the primary outcome (ERI rate). 95% confidence intervals are shown for effect estimates. Both the absolute risk difference and the relative risk are presented for the main binary outcome. 1/absolute risk reduction was used to determine the number needed to treat (NNT).

Statistical significance was defined as a two-sided p-value of less than 0.05. These analyses should be regarded as exploratory since secondary outcomes were not adjusted for multiple comparisons. R version 4.2.0 and SPSS version 26.0 were used for statistical analysis.

Results

Participant Flow and Baseline Characteristics: Between January 2023 and December 2025, 102 patients undergoing EVD placement were assessed for eligibility from institutional records. Twelve patients were excluded according to the predefined eligibility criteria, leaving 90 patients in the final retrospective cohort. Patients were classified according to the prophylactic antimicrobial therapy documented in their medical records: 45 patients received intraventricular vancomycin plus intravenous cephalosporin prophylaxis, and 45 received intravenous cephalosporin prophylaxis alone. Baseline demographic and clinical characteristics were similar between the two groups (Table 1).

Table 1: Baseline Patient Demographics and Clinical Characteristics

Characteristic	Group A: Intraventricular Vancomycin + IV Cephalosporin (n=45)	Group B: IV Cephalosporin Alone (n=45)	P-value
Age, years, mean $\pm$ SD	54.5 $\pm$ 17.0	53.9 $\pm$ 17.5	0.87
Male sex, n (%)	26 (57.8)	24 (53.3)	0.83
Admission GCS, mean $\pm$ SD	9.3 $\pm$ 3.8	9.5 $\pm$ 3.6	0.80
Indication for EVD, n (%)			
Subarachnoid haemorrhage	18 (40.0)	19 (42.2)	0.83
Traumatic brain injury	12 (26.7)	11 (24.4)	0.81
Intraventricular haemorrhage	8 (17.8)	7 (15.6)	0.78
Tumor/hydrocephalus	5 (11.1)	6 (13.3)	0.75
Other	2 (4.4)	2 (4.4)	1.00
Comorbidities, n (%)			
Diabetes mellitus	7 (15.6)	8 (17.8)	0.78
Hypertension	19 (42.2)	18 (40.0)	0.83
Immunosuppression	3 (6.7)	2 (4.4)	0.65

GCS, Glasgow Coma Scale; IV, intravenous; EVD, external ventricular drain. P-values from t-test for continuous variables and chi-square test for categorical variables.

EVD Characteristics: Mean EVD duration was 8.1 ± 4.5 days in the intraventricular vancomycin group and 8.9 ± 4.9 days in the control group ($p=0.42$). EVD replacement was required in 7 patients (15.6%) in the intraventricular vancomycin

group and 8 patients (17.8%) in the control group ($p=0.78$).

The most common reason for replacement was catheter occlusion in both groups, followed by infection and haemorrhage (Table 2).

Table 2: EVD Characteristics and Outcomes

Parameter	Group A (n=45)	Group B (n=45)	P-value
EVD duration, days, mean $\pm$ SD	8.1 ± 4.5	8.9 ± 4.9	0.42
EVD replacement, n (%)	7 (15.6)	8 (17.8)	0.78
Reasons for replacement, n (% of replacements)			
Occlusion	4 (57.1)	5 (62.5)	0.84
Haemorrhage	1 (14.3)	1 (12.5)	0.92
Infection	1 (14.3)	2 (25.0)	0.61
Other	1 (14.3)	0 (0)	0.49

Primary Outcome: Twelve out of forty-five patients (26.7%) in the control group and three out of forty-five patients (6.7%) in the intraventricular vancomycin group experienced ERI. The relative risk was 0.25 (95% CI: 0.08 to 0.81), and the

absolute risk reduction was 20.0 percentage points (95% CI: 5.2% to 34.8%).

The result of Fisher's exact test was $p=0.02$. Five (95% CI: 3 to 19) was the number needed to treat (NNT). Table 3 provides a summary of these results.

Table 3: Primary Outcome - ERI Rates

Outcome	Group A (n=45)	Group B (n=45)	Effect Estimate (95% CI)	P-value
ERI, n (%)	3 (6.7)	12 (26.7)	ARR: 20.0% (5.2% to 34.8%); RR: 0.25 (0.08 to 0.81)	0.02

*ARR, absolute risk reduction; RR, relative risk; CI, confidence interval. Fisher's exact test (two-sided).

Microbial Profile: All 3 infections in the intraventricular vancomycin group (100%) were caused by gram-negative organisms, compared with only 2 of 12 infections (16.7%) in the control group. This difference in microbial distribution was statistically significant by Fisher's exact test ($p=0.02$), although the small number of ERI events

makes this finding hypothesis-generating rather than definitive.

The specific organisms identified are detailed in Table 4. No vancomycin-resistant infections were reported in either group.

Table 4: Microbial Profile of ERI Cases

Microbial Category	Group A (n=3 infections)	Group B (n=12 infections)	P-value
Gram-positive, n (%)	0 (0)	10 (83.3)	0.02
Gram-negative, n (%)	3 (100)	2 (16.7)	
Specific organisms			
Staphylococcus epidermidis	0	4 (33.3)	
Staphylococcus aureus	0	3 (25.0)	
Enterococcus faecalis	0	2 (16.7)	
Other gram-positive	0	1 (8.3)	
Escherichia coli	1 (33.3)	1 (8.3)	
Klebsiella pneumoniae	1 (33.3)	0	
Enterobacter cloacae	1 (33.3)	0	
Acinetobacter baumannii	0	1 (8.3)	

Note: Given the small number of events, the microbial findings should be interpreted as hypothesis-generating rather than definitive evidence of antimicrobial selection pressure. The 95% confidence intervals around these proportions are wide; for example, the observed 3/3 gram-negative proportion in the intraventricular vancomycin group has a 95% CI of 29% to 100%.

Secondary Outcomes: The intraventricular vancomycin group had a substantially lower overall hospital stay (16.8 ± 7.2 vs. 24.3 ± 8.9 days; mean difference, -7.5 days; 95% CI, -11.0 to -4.0 ; $p=0.01$). Additionally, the ICU stay was considerably shorter (10.5 ± 5.9 vs. 15.7 ± 6.8

days; mean difference, -5.2 days; 95% CI, -7.9 to -2.5 ; $p=0.03$).

Both groups' GCS at ICU and hospital discharge were comparable. The results are given in Table 5.

Table 5: Secondary Outcomes

Outcome	Group A (n=45)	Group B (n=45)	Mean Difference (95% CI)	P-value
ICU stay, days, mean $\pm$ SD	10.5 ± 5.9	15.7 ± 6.8	-5.2 days (-7.9 to -2.5)	0.03
Hospital stay, days, mean $\pm$ SD	16.8 ± 7.2	24.3 ± 8.9	-7.5 days (-11.0 to -4.0)	0.01
GCS at ICU discharge, mean $\pm$ SD	11.9 ± 3.2	11.3 ± 3.5	$+0.6$ (-0.8 to 2.0)	0.40
GCS at hospital discharge, mean $\pm$ SD	12.6 ± 3.0	12.0 ± 3.3	$+0.6$ (-0.7 to 1.9)	0.37
In-hospital mortality, n (%)	5 (11.1)	12 (26.7)	RD: -15.6% (-31.7% to 0.5%)	0.10

ICU, intensive care unit; GCS, Glasgow Coma Scale; SD, standard deviation; CI, confidence interval; RD, risk difference. Mean differences are calculated as intraventricular vancomycin exposure minus control.

Adverse Events: Two patients (4.4%) in the intraventricular vancomycin group developed transient chemical ventriculitis, defined as CSF pleocytosis (>10 WBC/mm³) with negative cultures following vancomycin administration. These episodes were self-limited, resolved without specific treatment and had no sequelae. No seizures or systemic vancomycin toxicity were observed. No serious adverse events related to intraventricular vancomycin administration occurred during the study period.

Discussion

In this retrospective cohort study, adjunctive intraventricular vancomycin was associated with a statistically significant lower ERI rates compared with intravenous cephalosporin prophylaxis alone (6.7% vs 26.7%; absolute risk reduction, 20.0 percentage points; 95% CI, 5.2% to 34.8%; $p=0.02$).

The relative risk reduction of 75% and the number needed to treat of 5 patients represent a clinically meaningful potential benefit, although these estimates should be interpreted with caution given the pilot nature and small sample size of the study.

Comparison with Previous Studies: The ERI rate in the control group (26.7%) was higher than the 8–10% rates reported in most systematic reviews. This elevated baseline infection rate may reflect the severity of illness in our patient population, prolonged ICU stays, differences in infection surveillance practices, or local epidemiological factors. Importantly, the intraventricular vancomycin exposure remained associated with lower rates even in this high-risk population, suggesting that intraventricular vancomycin may be particularly beneficial in settings with elevated baseline infection rates.[3]

Our results are comparable to the retrospective data of Fu et al. (2017), who showed a significant

reduction in ERI with pre-emptive intrathecal vancomycin (2.7% vs 11.9%, $p<0.01$).[1] However, our findings are inconsistent with the prospective study by Tartara et al. (2022), who reported non-significant ERI rates of 4.8% in the intrathecal vancomycin group compared to 9.3% in the control group ($p=0.34$).[2] This difference may be attributed to the variation of sample size, baseline infection rates, infection definitions and patient populations. The much higher infection rate in the control group in our study (26.7%) might have contributed to the observed between-group difference, but the small sample size limits the precision and generalisability of this estimate. A systematic review and meta-analysis by Karvouniaris et al. (2018) demonstrated that intraventricular antibiotics, particularly in combination with systemic therapy, improve microbiological eradication and reduce mortality in gram-negative ventriculitis,[11] supporting the biological plausibility of our findings.

Microbial Profile and Ecological Considerations

An important and concerning finding was the significant shift in microbial distribution. All 3 infections in the intraventricular vancomycin group were gram-negative, whereas 83.3% of control group infections were gram-positive ($p=0.02$). This is biologically plausible: vancomycin selectively suppresses gram-positive flora, creating an ecological niche favouring overgrowth of gram-negative organisms.[1,2] This phenomenon was also noted by Tartara et al. (2022), who found that all ERI cases in their vancomycin group were due to gram-negative organisms, compared with predominantly gram-positive infections in the control group. This pattern is concerning given the high mortality associated with gram-negative ventriculitis, which has been reported as high as 47.6% in some series.[4,8] Furthermore, gram-negative infections,

especially those due to carbapenem-resistant organisms, generally have a longer EVD duration before infection and higher mortality than gram-positive ERI.[11]

The emergence of gram-negative infections in the vancomycin group raises important questions about the optimal prophylactic regimen. Combination therapy with an agent active against gram-negative organisms (eg, gentamicin or other ceftazidime) may provide broader coverage and potentially prevent this microbial shift. The potential for selecting multidrug-resistant organisms, however, must be carefully weighed against the benefits. Consider increased microbiological surveillance and empiric antibiotic protocols covering gram-negative organisms in patients on vancomycin prophylaxis and suspected ERI.

Clinical Outcomes: There was a significant difference between the intraventricular vancomycin group and the control group with a shorter stay in the ICU (10.5 days vs 15.7 days; $p=0.03$) and hospital (16.8 days vs 24.3 days; $p=0.01$). The differences are clinically and economically significant. The posted reduction of 7.5 days of hospital stay could result in significant cost savings in health systems where the daily cost of a hospital bed is high.

This benefit is probably not only the direct one of not having ERI, but also the one of having a longer period of rehabilitation, weaning from mechanical ventilation and transfer to step down units without the presence of ERI. The difference in in-hospital mortality was not significant (11.1% vs 26.7%) nor was it statistically significant. This could be related to the multi-factorial aspect of mortality in this critically ill population where underlying pathology (subarachnoid haemorrhage, traumatic brain injury etc.) may play a more important role than infection alone.[4,8]

Safety Profile: No serious drug-related adverse events were reported and intraventricular vancomycin was well-tolerated. The rate of transient chemical ventriculitis (4.4%) was comparable with that reported in the literature. This was a non-specific complication and did not require any specific treatment. No seizures or systemic vancomycin toxicity could be seen, as described previously.[12,13]

Strengths

- Comparable group sizes and standardized EVD care protocols.
- Use of CDC/NHSN-based infection definitions.
- Evaluation of both ERI incidence and microbial profile.

- Assessment of EVD-related and clinical outcomes, including ICU and hospital stay, mortality, and adverse events.
- Reporting of effect estimates with confidence intervals.

Limitations

The study has a number of limitations, including a single-center retrospective design that may limit generalizability and introduce the possibility of selection bias, information bias, and confounding; a relatively small sample size and a limited number of ERI events ($n=15$); a higher-than-expected ERI rate in the control group, which may have influenced the observed association and limited its applicability to centers with lower baseline infection rates; a 30-day follow-up period; and the lack of CSF vancomycin levels to measure drug exposure.

Clinical Implications: The results imply that in patients with EVD placement, intraventricular vancomycin prophylaxis may be linked to decreased ERI rates and shorter ICU and hospital stays. However, the vancomycin group's prevalence of gram-negative infections necessitates close microbiological monitoring and takes local pathogen and resistance patterns into account. Regular intraventricular vancomycin prophylaxis is not supported by these results. Before recommending changes in clinical practice, larger, sufficiently powered multicenter investigations are required to validate the reported connection and assess potential microbiological effects.[5]

Conclusion

In this retrospective cohort analysis, intraventricular vancomycin prophylaxis was linked to shorter ICU and hospital stays as well as a considerably decreased rate of EVD-related infection (6.7% vs. 26.7%; $p=0.02$) when compared to intravenous cephalosporin prophylaxis alone. However, the vancomycin group's prevalence of gram-negative infections raises questions about possible shifts in the distribution of pathogens. These results should be regarded as preliminary and hypothesis-generating due to the retrospective, single-center design and limited sample size. These results do not support the use of routine intraventricular vancomycin prophylaxis. To validate the connection and further assess its advantages, hazards, and microbiological ramifications, larger multicenter investigations are required.

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