ORIGINAL ARTICLE

Development of an Evidence-based Care Bundle for Prevention of External Ventricular Drain-related Infection: Results of a Single-center Prospective Cohort Study and Literature Review

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Abstract

Background: External ventricular drain (EVD)-related infection (ERI) is a common complication in cranial neurosurgery practice with high mortality. The risk factors associated with ERI are not well studied in low- and middle-income countries (LMIC) like India. Identifying the risk variables is a necessity to design robust evidence-based care bundles for ERI prevention.

Materials and methods: This is a single-center prospective cohort study. Patients with and without ERI during the 2-year study period were analyzed along with literature review to identify the risk variables associated with ERI. The Institute for Healthcare Improvement (IHI) comprehensive flowchart was used to develop the concept care bundle for ERI prevention.

Results: A total of 211 EVD were inserted during the study period. 15 ERI (7.1%) were identified based on IDSA criteria, with an average infection rate of 11.12 per 1000 EVD days. *Gram negative bacteria* (GNB) were the predominant pathogen (12/15, 80%), with *Klebsiella pneumoniae* (6/15, 40%) being the most common bacteria isolated. In multivariate analysis, the risk variables associated with ERI were use of broad spectrum pre-surgical antimicrobial prophylaxis for long duration, choice of posterior craniometric points for EVD insertion, EVD duration >7 days, EVD leak and surveillance cerebrospinal fluid (CSF) sampling at periodic intervals. Based on the risk variables identified in this study and literature review, a consensus decision on the care elements for the insertion and maintenance phases was chosen for the concept care bundle for ERI prevention.

Conclusion: An evidence-based concept care bundle for ERI prevention is proposed for further multicentric evaluation and validation.

Keywords: Care bundles, Cerebrospinal fluid drainage, External ventricular drain, Meningitis, Ventriculitis.

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Highlights

This manuscript highlights the risk factors identified in our single-center 2-year prospective cohort study for external ventricular drain (EVD)-related infections (ERI), along with literature review to identify the modifiable risk factors for designing an evidence-based care bundle for prevention of ERI, which is not yet reported from India.

Introduction

External ventricular drain insertion is a commonly employed cranial neurosurgery technique widely used for intracranial pressure monitoring and ventricular decompression. This technique can be lifesaving in conditions of raised intracranial pressure like hydrocephalus, subarachnoid hemorrhage, ventricular hemorrhage and intraparenchymal hemorrhage. Although a lifesaving intervention, EVD insertion can lead to complications like malposition, intracranial hemorrhage and ERI like meningitis or ventriculitis. External ventricular drain-related infections rate can range between 1 and 45% depending on the case definitions and the nature of neurosurgery cases (elective vs emergency proportion) handled by individual neurosurgery centers. External ventricular drain-related infections are associated with increased healthcare costs, longer ICU and hospital stay and increased mortality.[1,2] External ventricular drain-related infections can occur due to various risk factors during the insertion process, or due to colonization or contamination of the device during the maintenance phase in the postoperative period. These identified risk factors can be further classified as non-modifiable and

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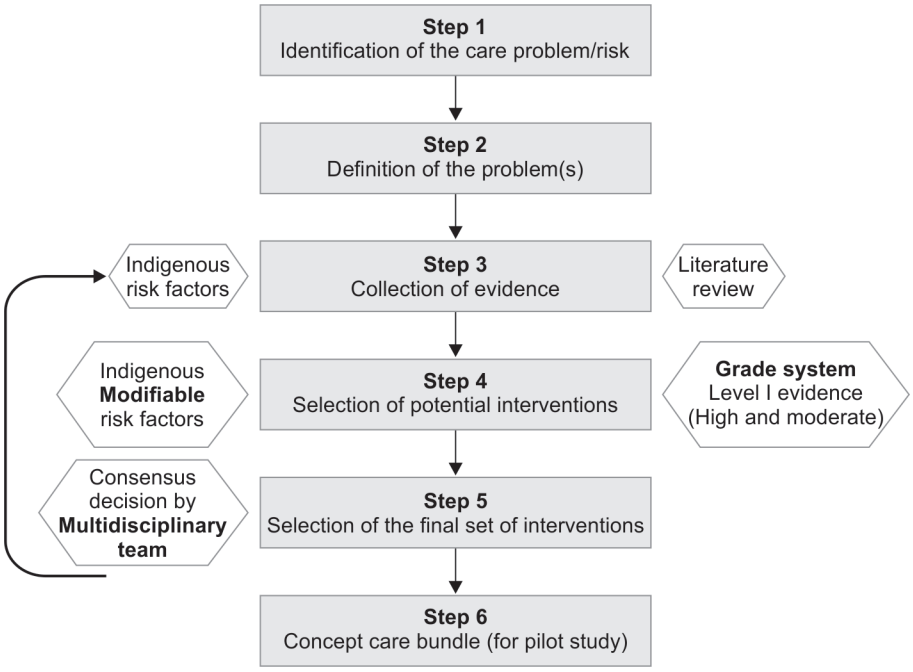

Fig. 1: Comprehensive flowchart for designing care bundle for prevention of EVD-ERI

Source: Adapted from Institute for Healthcare Improvement

modifiable risk factors to identify the core preventive interventions. The Institute for Healthcare Improvement (IHI) introduced the care bundle concept in 2001, where a set of evidence-based preventive interventions targeted against modifiable risk factors, labeled as "care elements", are bundled and implemented to enhance the quality of patient care, thereby improving clinical outcomes.[3] The effectiveness of these care bundles, (e.g., central line bundle, ventilator bundle, sepsis bundle, etc.) in prevention of common healthcare associated infections has led to the utilization of this concept in designing care bundles for the prevention of life-threatening CNS infections due to the use of newer life-sustaining devices like EVD which are increasingly used in the current neurosurgery practice.

Materials and Methods

Aim

Identify risk-reduction strategies to develop evidence-based best practice concept care bundle for ERI prevention.

Study Design

This was a 2-year single-center, prospective, observational, cohort study.

Study Setting

The study was conducted at the Sree Chitra Tirunal Institute for Medical Sciences and Technology (SCTIMST), a 253-bedded quaternary referral center for Cardiac and Neurological Disorders in Thiruvananthapuram, Kerala, India.

Study Approval

The study was approved by the Institute' Technical Advisory Committee (TAC) (SCT/S/2019/990 dated 04.11.2019) and Institute Ethics Committee (IEC) (SCT/IEC/1497/December-2019 dated 05.02.2020). The study period was from October 2020 to September 2022 (2 years).

Materials and Methods

The Institute for Healthcare Improvement (IHI) comprehensive flowchart was used to develop the care bundle for the prevention of ERI (Fig. 1).[3]

The steps included in the flowchart are:

Step 1: Identification of care problem/risk

Step 2: Definition of the problems

Step 3: Collection of evidence

Step 4: Selection of potential interventions

Step 5: Selection of the final set of interventions

Step 6: Concept care bundle

Step 1: Identification of the Care Problem/Risk

The problem statement was structured and analyzed in population/problem statement (P), intervention (I), comparison (C), and outcome (O) (PICO) format.

Population (P)

Patients included in the study were recruited from the inpatient wards/ICU of the Department of Neurosurgery, SCTIMST, Thiruvananthapuram, Kerala, India.

All patients who had undergone EVD insertion at our hospital during the study period were included. EVD insertions performed on a patient with a documented pre-existing CNS infection were excluded.

Problem statement (P): Patients with indwelling EVD are at increased risk of developing meningitis/ventriculitis (ERI).

Intervention

Estimate the prevalence and risk factors of ERI.

Comparison

Comparison of risk factors between patients who had and had not developed ERI.

Outcome

Evidence-based care bundle based on identified risk factors to prevent ERI.

The surveillance of ERI (expressed as rate per 1000 EVD days) was calculated from the Hospital information system (HIS).

ERI rate = Number of patients with EVD-related infection/ Number of EVD days (ERI rate expressed as per 1000 EVD days).

Step 2: Definition of the Problems

The case definition was adapted from the 2017 Infectious Diseases Society of America's (IDSA) clinical practice guidelines for healthcare-associated ventriculitis and meningitis.[4]

Contamination

An isolated positive cerebrospinal fluid (CSF) culture or gram stain, with normal CSF cell count and glucose and protein concentrations, and with a lack of clinical symptoms suspicious for ventriculitis or meningitis.

Colonization

Multiple positive CSF cultures or Gram stain, with normal CSF cell count and glucose and protein concentrations, and with a lack of clinical symptoms suspicious for ventriculitis or meningitis.

Infection

Single or multiple positive CSF cultures with CSF pleocytosis and/ or hypoglycorrhachia, or an increasing cell count, and clinical symptoms suspicious for ventriculitis or meningitis.

Step 3: Collection of Evidence

The indigenous risk factors for developing ERI were identified by comparing the infected vs non-infected groups as per the case definition, using a data collection tool.

Review of the published literature was undertaken to identify the reported modifiable risk variables associated with ERI.

- Is there increased infection risk in patients undergoing EVD insertion outside operation theatre?
- Does surgical site hair removal, such as clipping rather than shaving, reduce infection risk?
- Does use of prophylactic antibiotic reduce the risk?
- Is there increased risk based on the surgeon's experience?
- Does point of insertion of EVD associated with an increased infection risk?
- Does increase in tunelling distance reduce infection risk?
- Does use of antimicrobial-impregnated drains reduce infection risk?
- Does the skin preparation and postoperative dressing method reduce the risk of infection?
- Does closed drainage system reduce infection risk as compared to routine daily/weekly CSF sampling protocols or a change of catheter?
- Is there an increased risk of infection if the duration of drain placement increases?

Step 4: Selection of Potential Interventions

The indigenous modifiable risk variables identified in our 2-year prospective cohort study along with the risk variables identified in literature review, high and moderate level of evidence were used to design the concept care bundle.[5]

Step 5: Selection of the Final Set of Interventions

Based on the risk factors identified, a consensus decision on the potential care elements was arrived with the multidisciplinary team involving the neurosurgeons, clinical microbiologists, infection control nurse and neurointensive care team.

Step 6: Concept Care Bundle

The Institute for Healthcare Improvement (IHI) criteria for designing the care bundle was used, which includes, constitution of 3–6 descriptive evidence-based final interventions as care elements with each element being relatively independent with compliance assessable as all or none approach (Yes or No).

Results

During the 2-year prospective study period, a total of 211 EVD were inserted. The commonest surgical indication for EVD insertion was tumor excision (58.2%). The mean age of the patient population for EVD insertion was 32.3 years. A total of 15 ERI (15/211, 7.1%) events occurred, and the average ERI rate was 11.12 per 1,000 EVD days during the study period. *Gram negative bacteria* (GNB) was the causative agent in 12 patients (80%). The most common causative organism for ERI was *Klebsiella pneumoniae* (6/15, 40%), followed by *Acinetobacter baumannii* complex (4/15, 27%) and *Pseudomonas aeruginosa* (2/15, 13%).

The indigenous risk factors for ERI identified in this prospective cohort study are summarized in Table 1. Drain insertion had a 11.7 times higher risk of infection when compared to the insertion of a permanent CSF diversion procedure (shunt). In univariate analysis, the significant risk variables identified were use of broad spectrum pre-surgical antimicrobial prophylaxis for long duration (3 days) (HR - 3.61, 95% CI: –1.486 to 5.017, p - 0.001) choice of posterior craniometric point (Dandy's) for EVD insertion (HR - 15.66, 95% CI: 1.601–153.34, p - 0.018), EVD duration >7 days (HR - 1.065, 95% CI: 1.022–1.110, p - 0.003), CSF leak during postoperative period (HR - 8.621, 95% CI: 3.144–23.641, $p < 0.0001$), CSF sampling at regular intervals (daily/weekly) (HR - 0.169, 95% CI: 0.033–0.857, p - 0.032), EVD leak (compromised closed drainage) (HR - 9.986, 95% CI: 2.481–40.191, p - 0.01), tumor being the indication for surgery (HR - 0.058, 95% CI: 0.003–0.978, p - 0.048), associated scalp infection (HR - 6.973, 95% CI: 2.764–17.592, $p < 0.0001$) and systemic infection (HR - 8.617, 95% CI: 3.333–22.277, $p < 0.0001$). In multivariate analysis, use of broad spectrum presurgical antimicrobial prophylaxis for long duration (3 days) (HR - 1.824, 95% CI: –1.424–7.861, p - 0.041), choice of posterior craniometric point (Dandy's) for EVD insertion (HR - 16.31, 95% CI: 2.085–127.61, p - 0.008), EVD duration >7 days (HR - 0.994, 95% CI: 0.988–1.001, p - 0.011), EVD leak (compromised closed drainage) (HR - 6.096, 95% CI: 1.689–22.005, p - 0.006) and CSF sampling at regular intervals (daily/weekly) (HR - 0.175, 95% CI: 0.00–0.755, p - 0.019) were the statistically significant risk variables identified for ERI. The modifiable risk factors, identified by a review of published literature, are summarized in Table 2. Based on the evidence from our prospective cohort study and review of the published

Table 1: List of indigenous ERI risk variables evaluated in this prospective cohort study

	Univariate analysis			*Multivariate analysis*		
Parameter	*Hazard ratio*	*95% CI*	*p-value*	*Hazard ratio*	*95% CI*	*p-value*
Age	1.001	0.984–1.019	0.872	1.002	0.978–1.028	0.843
Sex	1.341	0.863–1.521	0.171	2.137	0.897–5.091	0.086
CSF leak	1.626	0.724–3.652	0.268	1.168	0.426–3.210	0.762
Presurgical prophylactic antibiotic choice						
Amikacin + Ceftriaxone	Reference			Reference		
Amikacin + Meropenem	2.175	0.646–7.322	0.210	0.943	0.073–12.179	0.964
Cefuroxime	3.61	–1.486–5.017	0.001*	1.824	–1.424–7.861	0.041*
Pre-OP ASA	1.432	0.757–2.711	0.270	0.872	0.459–1.657	0.677
Elective vs Emergency	1.339	0.654–2.740	0.438	0.554	0.213–1.440	0.226
Duration of surgery >4 hours	1.000	0.998–1.002	0.937	0.999	0.997–1.002	0.767
Operating surgeon experience						
<5 years	Reference			Reference		
5–10 years	0.674	0.209–2.171	0.508	0.532	0.184–2.075	
>10 years	1.052	0.335–3.302	0.931	0.987	0.297–3.963	0.642
Diversion device						
Shunt	Reference					
Drain	1.174	0.547–2.521	0.684	11.738	3.536–38.963	<0.0001*
Insertion point						
Kocher's point	Reference					
Frazier's point	1.205	0.306–4.747	0.790	1.959	0.409–9.387	0.400
Keene's point	2.765	0.508–15.039	0.239	2.295	0.535–14.231	0.271
Dandy's point	15.667	1.601–153.34	0.018*	16.311	2.085–127.614	0.008*
Trigone point	3.133	0.272–36.084	0.360	13.607	1.110–166.864	0.241
Drain duration >7 days	1.065	1.022–1.110	0.003*	0.994	0.988–1.001	0.011*
Post-op CSF leak	8.621	3.144–23.641	<0.0001*	2.569	0.751–8.786	0.132
Associated scalp skin and soft tissue infection	6.973	2.764–17.592	<0.0001*	2.770	0.924–8.304	0.069
Associated systemic infection	8.617	3.333–22.277	<0.0001*	0.901	0.220–3.693	0.885
EVD leak	9.986	2.481–40.191	0.01*	6.096	1.689–22.005	0.006*
CSF sampling frequency						
1–Daily	Reference			Reference		
2–Once a week	3.000	0.443–20.315	0.260	1.721	0.323–9.162	0.524
3–Only when clinically indicated	0.169	0.033–0.857	0.032*	0.175	0.000–0.755	0.019*
Indication for surgery						
CSF rhinorrhea	0.036	0.001–1.086	0.056	0.193	0.012–3.198	0.251
Aneurysm	0.091	0.003–2.852	0.173	0.224	0.011–4.474	0.328
Hydrocephalus	0.065	0.004–1.108	0.059	0.087	0.000–0.900	0.356
Tumor	0.058	0.003–0.978	0.048*	0.307	0.032–2.949	0.307
Intracranial pressure (>250 mm H_2O)	0.352	0.000–0.999	0.998	6.666	0.000–0.999	0.997

*Statistically significant ($p < 0.05$) risk variables; CSF, cerebrospinal fluid

literature, a consensus decision on the care elements were chosen for the insertion and maintenance phases of EVD (concept care bundle), for the prevention of ERI (Table 3).

Discussion

There are various risk factors for ERI reported in the literature. These can be further classified as modifiable and non-modifiable risk factors. The care bundles for prevention of device-associated infections are evidence-based interventions identified based on high-quality evidence on the modifiable risk factors published in the literature. Based on the risk factor evaluation model suggested by Sorinola et al. our prospective study design had evaluated risk factors for ERI.[6] Studies evaluating the association of the site of drain placement were mostly retrospective studies. In a retrospective study, point source contamination of the operating room (OR) by a single healthcare worker led to *P. aeruginosa* ERI outbreak.[7] Although few retrospective studies report a significant risk of ERI in patients undergoing drain placement outside OR, prospective observational studies and meta-analyses report no significant risk with drain placement outside the OR.[2,8–15] In our prospective study, there was no increased risk for drain-associated infection in patients undergoing device placement outside OR. In cranial neurosurgery, surgical site infections (SSI) increase the propensity for progression to ventriculitis, with or without any CSF diversion devices *in-situ*. World Health Organization (WHO) global guidelines for the prevention of SSI recommend that hair not being removed or, if necessary, only to be removed by clipping rather than shaving.[16]

Table 2: Literature review of hypothesis statements on modifiable ERI risk variables

Risk factor	*Study reference*	*Study design*	*Odds ratio (OR)*	*95% CI*	*p-value*
Is there increased infection risk in patients undergoing EVD/ LD insertion outside operation theatre?	Trick et al.[7]	Retrospective	–	–	0.004*
	Schödel et al.[8]	Retrospective	–	–	0.034*
	Arabi et al.[9]	Retrospective	3.21	0.92–11.28	0.058
	Foreman et al.[10]	Retrospective	3.66	1.01–13.18	0.303
	Omar et al.[11]	Prospective	0.67	0.58–0.78	1.000
	Berger Estilita et al.[12]	Prospective	0.52	0.24–1.13	0.242
	Hussein et al.[13]	Prospective	1.60	0.16–15.84	0.103
	Sweid et al.[14]	Retrospective	0.72	0.19–2.74	0.631
	Dorresteijn et al.[15]	Meta-analysis	6.00	1.79–20.19	0.543
	Zhou et al.[2]	Meta-analysis	1.11	0.60–2.07	0.736
	Fried et al.[17]	Consensus statement	No convincing evidence of increased risk	–	–
Does surgical site hair removal, clipping rather than shaving reduce infection risk?	Bekar et al.[18]	Prospective	–	–	>0.05
	Kose et al.[19]	RCT	–	–	<0.001*
	Shi et al.[20]	Meta-analysis	0.32	0.03–3.19	0.33
	Tanner et al.[21]	Meta-analysis	0.43	0.18–1.02	0.06
	Lefebvre et al.[22]	Meta-analysis	0.57	0.40–0.82	<0.05*
	WHO 2018[16]	Guideline	Strong recommendation for non-hair removal or clipping than shaving		
Does use of prophylactic antibiotic reduce risk?	Alleyne et al.[23]	Retrospective	0.95	0.28–3.22	>0.05
	Hoefnagel et al.[24]	Retrospective	1.71	0.92–3.21	0.11
	Camacho et al.[25]	Prospective	1.18	0.93–1.49	0.08
	Hussein et al.[13]	Prospective	1.17	0.25–5.53	0.47
	Fried et al.[17]	Consensus statement	Single dose	–	–
	Dorresteijn et al.[15]	Meta-analysis	prophylaxis	0.30–1.33	>0.05
	Zhou et al.[2]	Meta-analysis	0.64	0.66–1.14	0.308
			0.87		
Is there increased risk based on surgeon's experience?	Omar et al.[11]	Prospective	2.49	0.67–9.33	0.21
	Kohli et al.[26]	Retrospective	–	–	0.114
	Yuen et al.[27]	Retrospective	–	–	0.180
	Khalaveh et al.[28]	Retrospective	–	–	>0.05
	Walek et al.[29]	Retrospective	–	–	>0.05
Does point of insertion of EVD associated with increased infection risk?	Walek et al.[29]	Retrospective	–	–	>0.05
Does increasing tunnelling distance reduce infection risk?	Omar et al.[11]	Prospective	0.184	0.083–0.406	<0.001*
	Zhou et al.[30]	RCT	–	–	0.034*
	Jamjoom et al.[31]	Prospective	0.75	0.36–1.55	0.44
	Garg et al.[32]	Meta-analysis	0.027	0.0003–2.5	<0.05*
	Rojas-Lora et al.[33]	Prospective	–	–	<0.001*
Does use of antimicrobial-impregnated drains reduce infection risk?	Zabramski et al.[34]	RCT	0.13	0.03–0.60	<0.001*
	Gutiérrez-González et al.[35]	Retrospective	0.59	0.20–1.67	0.310
	Muttaiyah et al.[36]	Prospective	0.44	0.15–1.28	0.06
	Pople et al.[37]	RCT	0.78	0.46–1.32	0.504
	Lemcke et al.[38]	Retrospective	0.37	0.07–2.08	>0.05
	Wang et al.[39]	Meta-analysis	0.25	0.12–0.52	<0.05*
	Mikhaylov et al.[40]	Retrospective	0.36	0.09–1.47	0.19
	Jamjoom et al.[31]	Prospective	0.87	0.37–2.03	0.75
	Zhou et al.[2]	Meta-analysis	0.60	0.41–0.88	0.009*
Does the skin preparation and postoperative dressing method reduce the risk of drain-associated infection?	Flint et al.[41]	Retrospective	0.04	0.003–0.494	0.012*

(Contd...)

Table 2: *(Contd...)*

Risk factor	*Study reference*	*Study design*	*Odds ratio (OR)*	*95% CI*	*p-value*
Does closed drainage system reduce infection risk as compared to routine daily/weekly CSF sampling protocols or change of catheter?	Korinek et al.[42]	Retrospective	–	–	<0.0001*
	Hoefnagel et al.[24]	Retrospective	0.15	0.04–0.51	0.003*
	Williams et al.[43]	Prospective	0.44	0.22–0.88	0.02*
	Jamjoom et al.[31]	Prospective	4.73	1.28–17.42	0.02*
	Lu et al.[44]	Retrospective	0.024	0.005–0.122	0.000*
	Khalaveh et al.[28]	Retrospective	12.91	–	<0.001*
	Walek et al.[45]	Retrospective	–	–	0.011*
	Hoefnagel et al.[46]	Prospective	1.55	1.28–1.88	<0.0001*
	Zhou et al.[2]	Meta-analysis	5.05	3.67–6.96	<0.001*
Is there increased risk of infection if the duration of drain placement increases?	Korinek et al.[42]	Retrospective	–	–	>0.05*
	Hoefnagel et al.[24]	Retrospective	4.1	1.8–9.2	0.001*
	Williams et al.[43]	Prospective	1.22	1.10–1.34	<0.001*
	Jamjoom et al.[31]	Prospective	2.47	1.12–5.45	0.03*
	Lu et al.[44]	Retrospective	0.749	0.602–0.933	0.01*
	Walek et al.[29]	Retrospective	0.62	0.07–5.45	0.669
	Zhou et al.[2]	Meta-analysis	4.62	2.26–9.43	<0.001*
	Huang et al.[47]	Retrospective	–	–	<0.001*

*Statistically significant ($p < 0.05$) risk variables; CSF, cerebrospinal fluid

Table 3: Insertion and maintenance phase care elements of ERI prevention concept care bundle

Phase	*No.*	*Evidence-based care element*
Insertion phase	1.	Site preparation: Complete or Wide clipping (NOT shaving) of scalp hair (to fit a medium-sized sterile, transparent semipermeable dressing) with cleansing of the site with an aqueous antiseptic/soap solution.
	2.	Prophylactic antibiotic: A single dose of a narrow spectrum prophylactic antibiotic (cefuroxime) administered within 30–60 minutes prior to the incision.
	3.	Surgical hand preparation: Hand jewelry, nail polish, wristwatches and artificial nails are removed. The surgical team decontaminates their hands initially using aqueous antiseptic surgical scrub (10% povidone-iodine) solution, and further with 0.5–2% chlorhexidine-alcohol handrub preparation prior to the procedure.
	4.	Aseptic technique: Procedure performed with minimal personnel required and their restricted movement with strict aseptic precautions (full draping of patient exposing only surgical field with the surgeon donning gown, cap, mask and gloves).
	5.	Skin preparation: Surgical skin disinfection is performed using a 2–2.5% chlorhexidine gluconate-alcohol preparation and allowed to airdry.
	6.	Drain insertion and fixation: Drain (preferably silver/minocycline-rifampicin coated catheters) inserted in the first attempt, using anterior craniometric approach wherever possible, with a tunneling distance of atleast 5 cm with an exit-site chlorhexidine biopatch, the external portion of drain fixed with surgical staples and a transparent dressing, in a curved "S" or "question mark" pattern, with the transparent dressing borders secured using adhesive strips.
Maintenance phase	1.	Catheter indication assessment: The daily assessment for the need for the drain is clearly documented with a clear indication.
	2.	Entry site dressing: The status of the entry site transparent dressing is checked and documented DAILY; and changed only if the dressing is soiled or loose.
	3.	Positioning, levelling and securing: Zero leveling (Tragus), prescribed chamber pressure gauge level and closed drainage is checked and documented on HOURLY basis and when the patient is transported/moved.
	4.	CSF sampling and manipulation: Avoid unless indicated. If indicated, the indication is clearly documented, and the sampling port is handled using aseptic precautions.
	5.	Drain Maintenance: The 3-way taps are ensured to be open (unless the patient is moved/transported) with chamber volume documented on HOURLY basis, and drainage bag is changed when ¾ full using aseptic precautions. Hand hygiene is performed before and after handling the bag.

CSF, cerebrospinal fluid

A meta-analysis of 19 randomized controlled trials (RCT) showed a higher risk of SSI when the shaving method is used, with no difference observed between clipping and chemical depilation. Among the 19 RCTs, only 1 RCT had studied the risk of various hair removal, the techniques in cranial neurosurgery.[22] The timing of hair removal, immediate preoperative period, or day-before the procedure did not have statistical significance.[21] In a systematic review, evaluation of the role of preoperative hair removal by shaving with no-hair removal showed no supportive evidence for preoperative hair removal in prevention of surgical wound infections in neurosurgery. Future RCTs are required to evaluate the role of no-hair removal vs clipping in prevention of SSI and ERI.[48]

In a single-center quasi-experimental study, limited duration antibiotic prophylaxis had a reduced incidence of non-ERI infection, while ERI and *Clostridioides difficile* infection rates were similar.[49] In our study, reducing the duration of antibiotic prophylaxis from 3 days to a single dose as well as shifting from a broad-spectrum antibiotic (amikacin with ceftriaxone or meropenem) to a narrow spectrum antibiotic (cefuroxime) as part of the antimicrobial policy for cranial neurosurgery, showed significant reduction in ERI infection rates and drug resistance.[50,51] Literature review, including 2 meta-analyses showed no benefit of decreased ERI risk when the pre-surgical antibiotic prophylaxis is administered, while the consensus statement from the neurocritical care society suggests a single antimicrobial dose prior to EVD insertion.[2,13,15,17–25] Pre-surgical antibiotic prophylaxis policy of a single dose of a narrow spectrum antibiotic is still substantial in reducing emergence or reversal of multi-drug resistance in *gram negative bacilli*. Numerous studies evaluating the risk of ERI based on the operating surgeon's experience uniformly report no statistically significant association.[11,26,28] In 2 retrospective studies, various strata of experience of the surgeons were evaluated, and no significant association was found in ERI risk, similar to the findings of our study.[27,29]

Ventriculostomy can be achieved by access through various craniometric points, of which the Kocher's point, an anterior access point, is the most common point chosen for EVD insertion.[52] There are scarce reports on studying the choice of various craniometric points as a risk factor for ERI. In a recent retrospective study, the choice of the anatomic site of EVD insertion was not associated with increased ERI risk.[29] In contrast, our prospective study showed EVD insertion through posterior craniometric points (Dandy's) was associated with an increased risk of ERI. The EVD can be inserted in 2 ways: standard (non-tunneled) and tunneled. In standard EVD placement, the exit site of the catheter in the scalp is close to the entry puncture point to the lateral ventricles, leading to an increased chance of CSF leak and microbial contamination from the scalp along the catheter surface. In tunneled catheters, the drain is placed in the subcutaneous plane for a few centimeters before exiting the scalp tissue. This leads to a reduced risk of flow of CSF outside the catheter surface, thereby reducing the risk of microbial contamination. In a 7-year single center retrospective review, patients with CSF leaks had 15.1 times higher odds of developing ERI.[14] A tunnelling distance of >5 cm was associated with a reduced risk of ERI.[11,30–33] However, in a UK prospective multicentric study, the comparison of various tunneling distances stratified as <5 cm, 5–10 cm and >10 cm did not show a statistically significant reduction of ERI.[31] During our study period, all EVD were tunneled 3–5 cm and hence comparison could not be made on its role in ERI risk reduction. There are numerous studies comparing the utility of antimicrobial-impregnated catheters (AIC) with the use of standard catheters (SC) in ERI prevention. Most studies did not show any statistically significant reduction in infection risk, while a randomized controlled trial and 2 meta-analyses showed significant reduction in the risk of ERI when an antimicrobial-impregnated catheter is utilised.[2,31–39] In a meta-analysis, significant ERI risk reduction was observed for AIC (clindamycin/rifampicin and minocycline/rifampicin coated catheters) while not observed in silver-coated catheters.[39] The lower rates of infection were reported for *gram-positive* bacterial infections only. In India, *GNB* is the predominant pathogen causing ERI. A 3-year retrospective study from Northern India showed *GNB* as the commonest causative agent of ERI (76%) with *A. baumannii* (34%) as the commonest pathogen in contrast to *K. pneumoniae* (40%) at our centre.[53] Hence among the AIC, minocycline-coated catheters along with chlorhexidine biopatch at exit site could be a better option for adaptation in the Indian scenario since the antimicrobial spectrum of minocycline and chlorhexidine covers the common causative agents *Enterobacterales* and non-fermenting *GNB* as well as the uncommon *gram positive bacteria*. Further cost-benefit and number need to treat (NNT) analysis studies are required to evaluate the efficacy of various AIC's and exit biopatch interventions in cost-effective prevention of ERI. A recent meta-analysis report also found a significant reduction in ERI when silver-coated catheters were used (OR - 0.57 95% CI: 0.38–0.87, *p* - 0.008).[2] Although most studies didn't report a statistically significant reduction in ERI, the duration of time to suspected infection (8.8 ± 6 days for AIC vs 4.6 ± 4.2 days for SC, *p* - 0.002) and CSF positivity (15 ± 4 days for AIC vs 4 ± 2 days for SC, *p* - 0.001) were prolonged in patients with AIC.[37,40] In addition to wide hair clipping, preoperative aseptic technique with chlorhexidine-based skin disinfection and postoperative securement of the EVD in a 'question mark' or 'S' shape pattern with staples or sutures, chlorhexidine biopatch at the exit site with transparent dressing secured with adhesive strips introduced as components of the maintenance care bundle reduced CSF culture positivity and ventriculitis significantly.[41] Once the EVD collection system is set at a desired height, periodic monitoring of the EVD position is part of the neurocritical nursing care. The position of the EVD is adjusted to a level where the pressure transducer is at the level of the foramen of Monro (the External auditory meatus of the ear in the supine position and the mid-sagittal line between the eyebrows). This is termed as zero leveling and is achieved using a laser leveling device to ensure continuous drainage as per the set level, volume and time.[54]

Once the EVD is *in-situ*, sampling CSF on a daily or weekly basis to ensure culture negativity is a common surveillance strategy. Early studies evaluating the frequency of CSF sampling as a risk factor for ventriculitis found reduction of CSF sampling frequency to once every 3 days rather than on a daily basis reduced ERI rates significantly.[28,43,44] Recent multicentric prospective studies and meta-analyses report further reduction of ventriculitis risk when the sampling frequency is reduced from once every 3 days to only when clinically indicated.[2,24,31,46]

Similar to other devices, the duration of EVD placement increases the ERI risk significantly. An early retrospective study reported EVD duration having no effect on the increased incidence of ERI.[42] In subsequent studies, increased total duration of EVD placement was found to be associated with higher ventriculitis risk. Hoefnagel et al. reported EVD duration >11 days, while Huang et al. reported EVD duration >14 days, as a significant risk factor for ERI.[24,47] Most other recent studies, including multicentric prospective and meta-analyses, report increased risk of ERI when EVD is *in-situ* for >7 days, in concurrence with our study findings.[2,29,31,44] If intracranial pressure monitoring is the only indication, intraparenchymal pressure monitors are better alternatives to ventricular drains, since the rates of infections are low (0.6%).[55] In the recent meta-analysis by Zhou et al., the presence of bilateral EVD was also identified as a significant risk factor for ERI [OR - 2.25 (95% CI: 1.03–4.89), *p* - 0.041]. In addition to these, the surgical site preparation with chlorhexidine gluconate and aseptic precautions during the procedure as per the WHO global guidelines for the prevention of SSI were adapted for designing the care bundle recommendations. Due to the increased

utility of such temporary CSF diversion procedures for measuring and managing raised intracranial pressure, increasing incidence of ERI and ventriculitis are being observed depending on the nature of neurosurgical interventions undertaken in the healthcare setting. Identification of indigenous modifiable risk factors contributing to ERI risk along with literature review can help in designing evidence-based care bundles for prevention of these life-threatening device-associated CNS infections.

Conclusion

The ERI rate during the study period was 11.12 per 1000 EVD days. Use of broad spectrum pre-surgical antimicrobial prophylaxis for long duration, choice of posterior craniometric point for EVD insertion, EVD duration >7 days, EVD leak, and surveillance CSF sampling at periodic intervals were the indigenous risk variables identified. A concept care bundle is proposed based on the risk variables identified in our study and literature review for ERI prevention and further multicentric evaluation and validation.

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