

Clinical and microbiological spectrum of external ventricular drain related infections (EVDRI) from a tertiary care center

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ABSTRACT

Background and Objectives: Insertion of an External Ventricular Drain (EVD) is a common and important lifesaving procedure that can lead to morbidity and mortality. This study was conducted to assess the infection rate, risk factors, causative organisms, and outcome of EVDs.

Materials and Methods: A prospective study was undertaken in a tertiary care centre from August 1st to October 30th, 2020. Over 192 patients had undergone insertion of EVDs in the neurosurgical intensive care unit. CSF samples were collected in sterile containers and transported to the laboratory.

Results: A total of 214 EVDs were inserted in 192 patients for 691 days. The median duration for EVD in situ and the mean time between catheter insertion and onset of infection were 14.5 days and 8 days. EVD related infection rate was 19.4 for 1000 EVD days. The most common risk factor for EVD insertion were tumors (55%) followed by hydrocephalus (40%). We identified 25 patients out of 192 (12%) who had clinical signs and symptoms with deranged CSF counts. A total of 13/25 (52%) specimens were culture positives out of which 10 (76.9%) were Gram negative pathogens and 3 (23%) were Gram positive pathogens and 3/10 (30%) Gram negative pathogens were Multidrug resistant organisms (MDROs).

Conclusion: It was observed that longer duration of catheter in situ was an important risk factor for EVD-related infections (ERIs) and also higher frequency of CSF sampling. A proper EVD infection prevention and control protocol must be followed in the form of a checklist at the time of EVD insertion.

Keywords: Cerebral ventriculitis; Infection control; Hydrocephalus; Intracranial pressure; Brain neoplasms

INTRODUCTION

Ventriculostomy catheters, also known as external ventricular drains (EVDs), are frequently used in neurosurgery to monitor and relief intracranial pressure (1). Insertion of an EVD is a lifesaving procedure carried out in various types of acquired brain injury, such as intracranial haemorrhage with intraventricular extension, subarachnoid haemorrhage,

traumatic brain injury, and bacterial meningitis, may benefit from EVD insertion. Many of these conditions are associated with raised intracranial pressure (ICP) above 20 mmHg due to obstruction of cerebrospinal fluid (CSF) outflow (2). EVD also provides a means of monitoring and controlling elevated intracranial pressure (ICP), especially in head trauma. In fact, EVD is the gold standard for ICP monitoring. Insertion of an EVD is perhaps one of the most com-

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mon neurosurgical procedures performed worldwide. However, patients with these surgically implanted foreign bodies are at risk of developing drain-related infections such as ventriculitis and meningitis, which may result in significant morbidity and even mortality if not treated appropriately (3).

EVDs are associated with very high rates of infection, with estimates of the incidence of EVD infection typically ranging from about 5% to 20% (4). EVD-related infection (ERI) is a significant complication that can lead to increased morbidity prolonged stay, increased healthcare costs. Risk factors that have been associated with EVD infection includes duration of EVD placement, cerebrospinal fluid (CSF) leak, frequency of CSF sampling and underlying systemic infection. Efforts to reduce ERI risk have included the introduction of EVD care bundles, the use of perioperative or continuous prophylactic antibiotics and the development of antimicrobial-impregnated catheters (5).

The present study was undertaken to assess the rate of infection, risk factors, observe the trend of acquisition of pathogenic organisms and study the outcome of EVD-related infections.

MATERIALS AND METHODS

In this prospective study we included all patients having a positive CSF culture while the EVD was in place or an abnormal CSF analysis result or positive blood cultures in the presence of neurological symptoms that were admitted under the neuro surgery department with a diagnosis of intracranial infection over a period of 15 months (August 1st 2019 to Oct 31st 2020).

We considered only tests that were performed while EVD was in place and up to three days after removal. Patients who had infection prior to EVD placement or a permanent ventriculoperitoneal (VP) shunt were excluded.

All catheters were inserted under sterile conditions in the operating theatre using a tunnelled procedure technique and a closed system for drainage. There was no policy of routine CSF sampling during the study period; CSF samples were sent for culture and sensitivity only if there were signs and symptoms of infection.

Data was obtained by direct interview and observation of the patient, review of the medical case sheets

and electronic medical records. CSF cultures were repeated if the initial results were positive, so as to rule out the possibility of contamination.

Microbiological workup. CSF samples were sent to the microbiology laboratory for direct examination, Gram stain, and culture. Culture was performed on blood agar and chrome agar (Biomérieux, France) and were incubated at 37°C for 18-24 hours. Identification and susceptibility testing was done by using Automated Vitek 2 compact system. Gram negative pathogens were identified using ID GN and AST N281 panel whereas Gram positive pathogens were identified using ID GP and P628 panel.

We defined Ventriculostomy related infection based on CDC-NHSN definition.

Meningitis or ventriculitis must meet at least one of the following criteria:

1. Patient has organism (s) identified from cerebrospinal fluid (CSF) by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment for example, not Active Surveillance Culture/Testing (ASC/AST).

2. Patient has at least two of the following:

- Fever (>38.0°C) or headache
- Meningeal sign(s)
- Cranial nerve sign(s)

And at least one of the following:

• Increased white cells, elevated protein, and decreased glucose in CSF (per reporting laboratory's reference range).

• Organism(s) seen on Gram stain of CSF.

• Organism(s) identified from blood by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment.

• Diagnostic single antibody titre (IgM) or 4-fold increase in paired sera (IgG) for organism.

In Statistical analysis continuous variables were described with medians. Categorical variables were described as percentages. Incidence rate of EVD-related Infection (ERI) was calculated.

RESULTS

A total of 207 CSF samples were received from the neurosurgical department during the period of study, 192/207 had undergone EVD insertion, out of which

25 (12%) had clinical signs and symptoms of infection post EVD insertion. A total of 13/25 (52%) specimens were CSF culture positives out of which 10 (76.9%) were Gram negative pathogens and 3 (23%) were Gram positive pathogens and 3/10 (30%) (Table 1), Gram negative pathogens were Multidrug resistant organisms (MDROs). 12/25 (48%) were sterile. CSF protein, glucose and WBC counts were analyzed for those showing clinical infection. Other samples sent for culture and sensitivity such as blood, urine, EVD tip, Tracheal aspirate, pus were also observed for any bacteriological growth.

Regarding the demographic data, out of the total 192 patients who underwent EVD insertion, 94 (49%) were males and 98 (51%) were females and among the total 25 patients who had clinical signs and symptoms, 14 (56%) were females and 11 (44%) were males. The median age was 22.5 years for the patients with EVD.

214 EVDs remained in situ for a total of 691 days (Table 2). For the 25 patients, external drainage was continued in median for 14.5 days. Meantime between catheter insertion and onset of infection by Gram negative bacteria was 8 days. The most common indication for EVD insertion was Tumours (55%) followed by Hydrocephalus (40%) and post traumatic sub-arachnoid haemorrhage (5%).

Table 1. Microorganism culture results of episodes of EVD infection.

Cultured Organisms	No. of cultures	Day of CSF sampling
<i>Klebsiella pneumoniae</i>	2	Day 20, Day 15
<i>Acinetobacter baumannii</i>	2	Day 7, Day 3
<i>Pseudomonas aeruginosa</i>	2	Day 6, Day 7
<i>Escherichia coli</i>	1	Day 6
<i>Morganella morganii</i>	1	Day 5
<i>Enterobacter cloacae</i>	1	Day 5
<i>Coagulase negative Staphylococcus</i>	1	Day 2
<i>Enterococcus species.</i>	1	Day 8

Table 2. Number of EVD Days.

EVD	EVD Catheter Days
1 st EVD	521
2 nd EVD	89
3 rd EVD	56
4 th EVD	25

Among the tumours, most common cause was Pituitary adenoma accounting to about 32% of the cases (n=8), followed by pineal gland tumours (n=5), gliomas (n=3), vestibular schwannomas (n=3), Rhabdomyosarcoma (n=1) and a postoperative case of atypical meningioma with pseudomeningocele (n=1) (Table 3).

Length of stay in the hospital among infected patients ranged from 11-50 days with median of 20 days. The most common clinical signs and symptoms observed were fever (n=6/25), headache (n=11/25), vomiting (n=11/25), blurring of vision (n=11/25) and altered sensorium (n=1/25), The most common comorbidity observed in the patients was seizures (7,28%), followed by diabetes (6, 24%) and VSD (1, 4%). The remaining patients did not have any comorbidities (11, 44%). 2/12 (8%) patients had CSF leak.

CSF counts were done, 18 (72%) of 25 had raised levels of protein (>15-45 mg/100 mL). 2 showed low levels of CSF glucose while 10 had higher levels of glucose in CSF.

36% (n=9) of the patients were given antibiotic prophylaxis and all of them were given an antibiotic cover of Injection Magnex forte (Cefoperazone-sulbactam) 1.5 g twice and injection amikacin 750mg twice intravenously before the procedure. Antibiotic prophylaxis was continued post EVD insertion with the same antibiotics for 3 weeks. The most common organism isolated was *Klebsiella pneumoniae* (n=3), followed by, *Pseudomonas aeruginosa* (n=2), *Acinetobacter baumannii* (n=2), *Escherichia coli* ESBL producer (n=1), *Morganella morganii* (n=1), *Enterobacter cloacae* (n=1), coagulase negative *Staphylococcus* (n=2) and *Enterococcus* species (n=1). Three of the patients had the same growth of *Klebsiella pneumoniae* in other samples including EVD tip and blood. Another patient had same growth of *Acinetobacter baumannii* in tracheal aspirate. Three of the thirteen isolates were multidrug resistant organisms (MDROs) (2 *Klebsiella pneumoniae* and 1 *Acinetobacter baumannii*) (Table 1).

Other samples of patients, showing clinical signs and symptoms of infection with sterile CSF cultures, were tested. 6 patients (24%) had sterile CSF cultures, but microbes grew in other samples of the patients. Tracheal aspirate in one patient with sterile CSF culture grew *Acinetobacter baumannii*. Blood cultures of two patients with sterile CSF culture were positive with *Acinetobacter baumannii*, and *Elizabethkingia meningoseptica*. Urine cultures of two patients with sterile CSF cultures showed growth of *Candida non*

Table 3. Neurosurgical procedures done

Type of Tumour	Neurosurgical procedure
Pituitary	
Adenoma (n=8)	Trans sphenoidal craniotomy and excision
Pineal gland tumour (n=5)	Occipital trans tentorial Craniotomy and excision
Gliomas (n=3)	Parasagittal craniotomy and subtotal excision
Vestibular Schwannomas (n=3)	Sub occipital Craniotomy and gross total resection
Rhabdomyosarcoma (n=1)	Frontotemporal craniotomy with subtotal resection
Postoperative case of Atypical meningioma with pseudomeningocele (n=1)	Removal of infected bone flap

albicans. One of the patients' pus sample from craniotomy site grew methicillin resistant *Staphylococcus aureus* (MRSA).

Among the 25 patients, 5 patients expired of whom three were CSF culture positives (two with *Klebsiella pneumoniae* and one with *Acinetobacter baumannii*), one was CSF sterile and blood culture positive (*Elizabethkingia meningoseptica*). One of the patients was epileptic and died due to cardiac arrest within 11 days of admission. Mortality rate was 25%.

A total of 214 EVDs were inserted in 192 patients for a period of 691 days. The EVD- related infection rate (ERI) was calculated as 19.4 per 1000 EVD days.

DISCUSSION

Intraventricular catheters (IVCs) are vital neurosurgical diagnostic and therapeutic tools that provide for continuous intracranial pressure monitoring and external CSF drainage. The incidence of EVD-related infection in the present study (per patient) was 13% which was 18.3% in a study by Camacho et al. (6) and 8.3% in a study by Hagel et al. (1). The device-associated infection rate observed in this study was 19.4 per 1000 EVD days which is higher than rate reported by Hagel et al. (10.4 per 1000 EVD-days), Scheithauer et al. (6.3 per 1000) and similar to 17 ERIs per 1000 catheter days observed by Ramanan and colleagues and 22.4 per 1,000 catheter-days in a study by Camacho et al. (6, 7).

The current notion is that EVD-related infections result from either inoculation of pathogens during EVD placement and/or contamination and colonization of the EVD system during the postoperative period. Postoperative colonization can either arise from endogenous organisms present on the skin, which spread along the intracutaneous tract or by exogenous organisms introduced into the EVD system

during manipulation at the EVD system by health-care workers.

Endogenous infections might be prevented by using antimicrobial coated EVD catheters which may decrease bacterial colonization and thus prevent infection (1). In the present study only plane catheters were used.

In our study, 76.9% of the infections were caused by Gram-negative bacteria; this was similar to a study by Camacho et al. where 77% of infections and Lyke et al. where 82% of infections were caused by Gram negative microbes (7, 8). Camacho et al. (7) showed that mean time between catheter insertion and onset of infection by Gram negative bacteria was 9 days. In the present study the mean time between catheter insertion and onset of infection was 8 days. The most common microorganism identified was *Klebsiella pneumoniae* similar to a study by Lyke et al. while coagulase negative staphylococci were the most common bacteria identified by Jamjoom et al. (34.5%) and Hagel et al. (62%). We hypothesize that Gram negative bacterial infection could be due to prolonged hospitalisation. Two of the thirteen EVD-related early infections were caused by coagulase-negative staphylococci (CONS) which may have arisen as direct inoculation during manipulation of the EVD by Healthcare workers.

In a study by Lyke et al. 3 of 12 patients had CSF leaks which resulted in cerebral ventriculitis (8). This is because of breaks in the integrity of the closed catheter system increased rate of infection. In the present study 2 of 25 patients had CSF leak where no ventriculitis was documented.

Several studies examined the relationship between concurrent systemic infections and EVD-related infection, showing that concurrent systemic infections are a risk factor for EVD-related infection (9). Some of the studies have observed that infection in other sites can increase the risk of central nervous system

infection (10).

Three of the 25 patients (12%) had concomitant systemic infection, where the same organism was observed in other samples of the patients. One of the 25 patients with ventriculitis had Ventilator associated pneumonia (VAP) which was observed probably due to translocation or dissemination of infection into lungs. In a study by Kim et al. concomitant systemic infection existed in 4.7% of patients with ventriculitis (11).

It has been estimated that if the patients present with pulmonary infection during EVD catheter placement, the pathogens are probably translocated to the surrounding environment through endotracheal intubation, which might contaminate the EVD system during drain insertion and manipulation, thereby leading to ventriculitis. Moreover, concomitant infection in other sites probably reduces immunity and resistance of the patients thereby increasing the potential risk of infection to these patients (12).

The duration of EVD in situ was identified as a risk factor for EVD-related infection by multiple studies. We found that patients developed infection after a mean duration of 8 days after EVD insertion. This was similar to study by Jamjoom et al. (8 days), Lyke et al. (6 days) and Mayhall et al. (5 days) (5, 8). In earlier studies, routine collection of cerebrospinal fluid specimen was shown to be not associated with the risk of EVD-related infection (13). EVD should be replaced if the patient develops infections, when inserted more than 10 days (12). Other scholars have suggested that the duration of EVD catheter retention is not correlated with the risk of EVD-related infection (14). Repeated catheter insertion to decrease the drainage time can increase the risk of infection instead was suggested by some authors (15, 16). It has been observed in previous studies that patients age, gender and primary diseases are not associated with the risk of EVD-related infection (17).

For all patients requiring EVD, preventive antibiotics were not routinely used, only 36% were given pre procedural antibiotics. If the patients were diagnosed with ventriculitis, EVD insertion combined with intravenous administration of antibiotics can yield high clinical efficacy (18). In the present study few patients were treated with perioperative antibiotics such as Injection Magnex forte 1.5gms Intravenously and Injection Amikacin 750gms OD intravenously.

To decrease EVD related infections, intravenous

antibiotics are administered commonly to cover normal skin flora (19). However, some authors suggest antibiotic prophylaxis may be a reason for development of resistant organisms, or much more morbid Gram-negative ventriculitis (20). Hence, perioperative use of antibiotics at and for short duration after EVD insertion, or continuation for the duration of drainage was followed (19). In our study, all plain EVDs were used, none were coated with antimicrobials so we could not compare the and antibiotic cover was given only to 6 of the 25 patients as five of them presented with post craniotomy infection and one had Subarachnoid haemorrhage, among whom only one showed growth in EVD CSF culture when sampling was done on postoperative day 9, with growth of *Klebsiella pneumoniae* multidrug resistant isolate (MDRO) in both EVD CSF and Blood. So patient was treated with colistin via Intraventricular route with a dose of 1,25,000 IU (10mg) but the patient could not be revived and eventually died. Thus, selective administration of antibiotics may predispose some of the sick patients to nosocomial ventriculitis. This was similar to findings by Murphy et al. where they showed that prolonged systemic antibiotic administration is associated with a statistically significant increase in the rate of systemic nosocomial infections like VAP and BSI (21).

The clinical outcome showed significant mortality; 20% (n=6) of the patients with clinical signs and symptoms expired which could be a result of both nosocomial ERI and underlying neurologic etiology. This was similar to a study by Jamjoom et al. (25.2%).

Probably high frequency of CSF sampling and longer duration of EVD in situ were associated with the EVD infections in the present study. Henceforth routine testing of samples from other sites is also necessary to rule out the concurrent systemic infection.

CONCLUSION

ERIs remains a serious complication of EVD use in neurosurgical units. Patients with an EVD left in situ for ≥ 8 days and who underwent more frequent sampling had a higher risk of infection. Antimicrobial coated EVD catheters may decrease bacterial colonization and thus prevent infection. EVD catheter should be electively changed whenever a longer duration of CSF drainage is required.

There is an urgent need to introduce EVD bundle care approach such as proper hand washing, use of full body drape sterile gloves, gown, cap, mask, chlorhexidine skin preparation during EVD insertion procedure to reduce the risk of EVD infections. Strict asepsis is advised during insertion and handling of EVD and exchange of EVDs to be done to prevent infections also proper wound care need to be given by adhering to Infection control practices Therefore it is suggested that prophylactic measures against drain related infections should be developed and implemented at the earlier onset. Maintenance, troubleshooting, and monitoring for EVD associated complications has essentially become a critical responsibility to prevent untoward events.

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