Original article

External Ventricular Drainage Infections: Experience from a Tertiary Care Center in Nepal

Pradhanang AB[1], Sharma MR[3], Sedain G[2], Shilpakar SK[3]

[1]MCh Resident, [2]Assistant Professor, [3]Professor

Neurosurgery Unit, Department of Surgery, Tribhuvan University Teaching Hospital, Maharajgunj, Nepal

Correspondence: Dr. Amit B Pradhanang

Email: amitpradhanang@hotmail.com

Abstract

Introduction: External Ventricular Drainage (EVD) is one of the most commonly performed procedures in neurosurgical practice. EVD related infection is among the most dreaded complications encountered after the procedure with added morbidity and mortality.

Objectives: The primary objective of this study was to assess the incidence of EVD infections in this hospital. In addition, the researchers have made an attempt to evaluate the indication for EVD placement, influence of total drainage time on the risk of catheter infection, the most common bacterial spectra in cerebrospinal fluid (CSF) culture, their antibiotic sensitivity pattern, and the association of CSF cell count with bacterial growth.

Methods: This is a retrospective study of all patients who underwent EVD placement over a period of two years. Those patients who had bacterial growth in their initial samples were excluded from the study.

Results: Out of 62 patients, 54 met the inclusion criteria for analysis. The ventricular catheters were in place from 1 to 23 days. Overall shunt infection rate was 37%. CSF cell count was significantly associated with the occurrence of a positive CSF culture (Fisher's Exact Test, $p<0.01$). The most common bacterial species isolated were Acinetobacter baumannii and Burkholderia cepacia.

Conclusion: Despite many advances in care, there is still a significantly high incidence of EVD related infections. Contrary to earlier reports, the most common bacteria grown in the study were quite different and their antibiotic sensitivity varied accordingly.

Key words: External Ventriculostomy Drainage infection, hydrocephalus, antibiotics in external ventriculostomy drainage

Introduction

External ventricular drainage (EVD) is one of the most commonly performed procedures in neurosurgical practice. The common indications include acute hydrocephalus due to intraventricular hemorrhage (IVH), meningitis and tumors with obstructive hydrocephalus as well as in patients with chronic hydrocephalus that are not fit for a procedure under general anesthesia. They are also used to monitor intracranial pressure in acute traumatic brain injuries, subarachnoid and intraparenchymal hemorrhages. The most dreaded complication arising from EVD placement is infection, with resultant ventriculitis, meningitis, brain abscess, or subdural empyema. Other complications include hemorrhage, misplacement, dislodgement, and blockage. EVD related infections significantly prolong hospital stay, increase costs and often negatively affect the overall prognosis. Reported rates of infections range from <5% up to 23%; most literature quoting close to 10%.[1,6] An increased risk of infection has been observed in patients with a) subarachnoid or intraventricular hemorrhage or with concurrent systemic infections b) longer duration of

catheterization c) CSF leakage d) frequent manipulation of the EVD system.[1,5]

Although the often quoted EVD infection rate is close to 10%, we feel that this incidence is somewhat higher at our center. In addition, bacterial growth also seemed to be different than that reported in the literature. This study is an attempt to clarify the situation in our setting.

Objectives

The primary objective of the present study is to assess the incidence of EVD infection rate in our center. Also we attempted to find out the most common bacteria retrieved from cultures, the antibiotic sensitivity patterns, the total drainage time related to the risk of a positive bacteriological CSF culture, and the association of CSF cell count with a bacteriological culture.

Methods

Ethical approval for retrieval of patient data was taken from the concerned departments. All patients that underwent EVD placement during a 48 months period (February 2013 to February 2015) at Neurosurgical Unit, Department of Surgery, Tribhuvan University Teaching Hospital, Kathmandu, Nepal were included for this study. The procedures were all performed in a standard fashion, in the operating theaters under aseptic precautions by neurosurgical team. All patients received antibiotic therapy, a third generation cephalosporin (Ceftriaxone) at a dose of 30mg/kg, just before catheter placement. For drainage, conventional (Surgiwear, non-medicated) catheters were used. The antibiotic was continued in all patients from the day of insertion until a change was required as shown by culture and sensitivity results to the day of removal. CSF samples were obtained every alternate day from the ventricular drain and examined for cell count, total protein and glucose concentration and bacteriological CSF cultures. CSF pleocytosis was defined as a white cell count above 50/mm^3.[9]

A total of 62 patients were evaluated for the study. The charts of all patients were retrospectively reviewed in detail. In addition, demographics and EVD-related data were documented.

Inclusion and Exclusion Criteria

All patients requiring EVD placement were included in the study. Those patients who had a preexisting or ongoing CSF infection prior to EVD insertion were excluded.

Definition of Infection

The EVD related infection has been variously described as either (1) positive CSF culture result plus clinical symptoms or CNS pleocytosis/ cell count increase, or (2) in the case of negative CSF culture, clinical symptoms, and CNS pleocytosis/ cell count increase.[11] However, in this study the researchers have only labeled those patients who have a positive CSF culture along with clinical symptoms. To be more specific, we have only taken into consideration the first criteria in defining EVD-related infection and have disregarded the second criteria.

Statistical Analysis

Coding and entry of collected data were done in Epidata 3.1. Analysis was done in Version 20 of SPSS software. Data analysis was done by frequency run and cross-tabulations. Categorical variables were presented in frequency and percentage whereas continuous variables were presented in mean and standard deviation. Bivariate analysis was done to find our association between outcome and explorative variables. In bivariate analysis, Fisher exact test was applied to test the significance of association between independent and dependent variables. Odds ratio with 95 percent confidence interval (CI) was used to test the strength of the association.

Results

Altogether 62 patients underwent EVD placement over a period of two years. Eight patients already had positive bacteriological growth at the time of catheter placement and were excluded. Thus, remaining 54 patients made the basis for this study.

The age of patients ranged from 3 months to 71 years (mean= 37.3, SD 26.29). There was a slight male predominance (59%). Their diagnoses are summarized in Table 1 below. On analysis, 20 patients out of 54 grew bacteria in CSF (37%).

Table 1 Clinical diagnosis of patients requiring EVD (n=54). EVD = external ventricular drainage.

Diagnosis	Patients (n)
Acute hydrocephalus due to:	32
Intraventricular hemorrhage	15
Tumor	9
Subarachnoid Hemorrhage	4
Trauma	2
Shunt Malfunction	2
Chronic Hydrocephalus (unfit for GA)	22
Total	**54**

As shown in the Table 1. the most common indication for EVD placement was chronic hydrocephalus due to tubercular meningitis, rendered unfit for a shunting procedure under general anesthesia, followed by IVH.

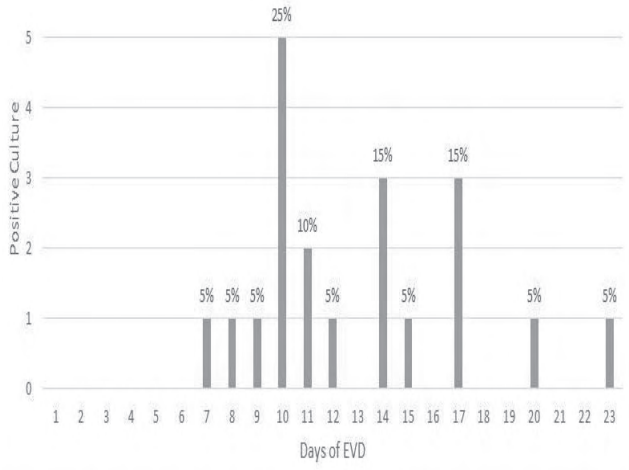


Figure 1 Positivity of bacterial growth in relation to duration of EVD placement (n=20).

As shown in Figure 1, bacteriological growth began from day 7 and was most common at day 10 of EVD placement. However the frequency showed a decreasing trend after day 10 with few spikes on day 14 and 17.

As depicted in Figure 2, the most common bacteria species isolated from CSF were Acenitobacter (n = 7) and Burkholderia (n = 7).

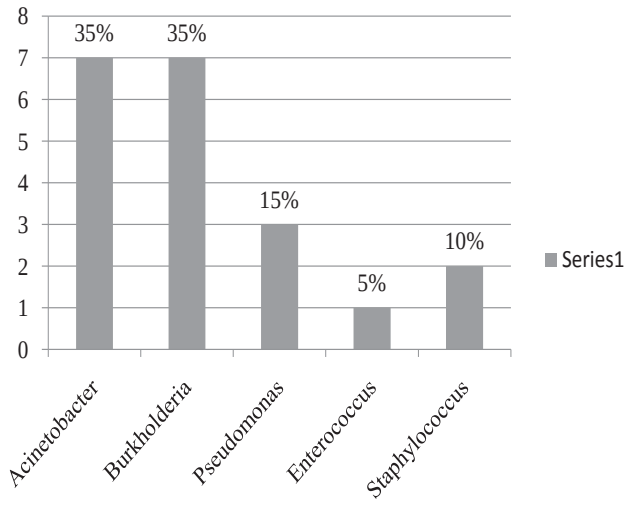
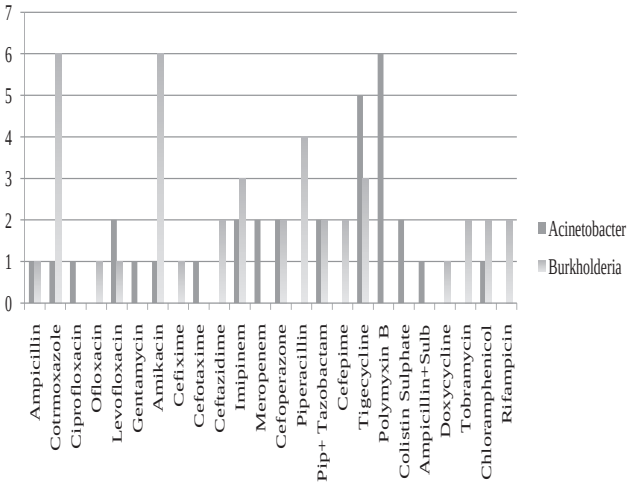


Figure 2 Distribution of Bacteria Isolated from CSF Analysis (n=20).



Among the most common two species of isolated bacteria, Acinetobacter was frequently sensitive to Tigecycline (n=5) and Polymyxin B (n=6), while Burkholderia was often sensitive to Cotrimoxazole (n=6) and Amikacin (n=6).

Figure 3 Antibiotic Sensitivity Pattern of the Two Most Common Isolated Bacteria Species (n = 14).

Further analysis of the association between CSF cell count and culture positivity was done (Table 2). Total count was found to be statistically significant with bacterial growth. Those patients with abnormal cell count in CSF analysis were 29 times more likely to have positive bacterial growth compared to those who have a normal cell count (OR=29.25, CI: 5.551-154.135).

Table 2 Association Between CSF Pleocytosis and Bacterial Growth. (n=54)

		Bacterial growth		p-value	OR (95 % CI)
		Yes	No		
Total Count	<50/ mm^3	2 (10.0%)	26 (76.5%)		Ref
	≥ 50/ mm^3	18 (90.0%)	8 (23.5%)	0.000*[1]	29.250 (5.551-154.135)

*Significant at p<0.001

[1]Fisher's Exact test

Ref= Reference category

Discussion

Catheter related infections are one of the most common complications in patients with an EVD. Once established, it necessitates aggressive treatment which includes intravenous and often intrathecal administration of potent antibiotics, removal or replacement of ventricular catheter in addition to other supportive measures. Despite these, many patients need long term critical care, and have increased morbidity and mortality. The health care cost in such patients often escalates, which is the most relevant factor in a country like Nepal. Therefore, prevention of catheter infection and its early diagnosis in these patients are of paramount importance.

Diagnosing EVD related infections on the basis of clinical features is sometimes notoriously difficult especially in ventilated ICU patients. Furthermore, patients with intracranial hemorrhage or severe head injury frequently show signs of aseptic meningitis, such as headache, nausea and neck stiffness. High fever with neurological deficits and an elevated leukocyte counts in the CSF favor an infection.[9] In most cases with an EVD, the diagnosis of CSF infection is based on laboratory findings. In this study, the CSF cell counts of the samples with positive bacteriological cultures were analyzed the same day. Those patients with CSF cell counts >50cells/mm^3 were 29 times more likely to have positive bacterial growth compared to those who have CSF cell counts <50cells/mm^3 (OR=29.25, CI: 5.551-154.135).(p<0.01). The analysis of CSF cell counts is therefore, a cheap, relatively easy and predictable investigation to diagnose an ongoing infection in a patient with EVD related infections. Our findings corroborates with the study by Pfisterer et al in this regard.[8]

The issue of whether or not to give prophylactic antibiotics in patients with EVDs is still controversial.[7] All patients in this study received intravenous, Ceftriaxone at the time of catheter insertion. Ceftriaxone was chosen as it was cheap, easily available and had good CSF penetration. Yet, a positive CSF culture was found in 37% patients as compared to 10% in the literature. The prophylactic use of 3rd generation cephalosporins until the arrival of bacteriological growth may not have any beneficial role, on the other hand it could promote growth of resistant strains. The possible factor for this significantly high incidence could be related to poor nutritional status, immunosupression due to tumor or post radiation status and the possible failure to adhere to a stringent protocol cannot be ruled out in this regard. Moreover the emergency nature of the procedure, and the lack of a dedicated neurosurgical operation theater could also contribute to the figure. Different measures have been taken to decrease infection rate like the use of antimicrobial impregnated shunts, routine change of catheters or the strict adherence to EVD bundle protocol while insertion of EVD.[2,13] This high incidence of CSF infections outlines the need for strict aseptic dressing and CSF collection techniques, prompt diagnosis to permit immediate specific treatment, such as the intraventricular administration of antibiotics, or the change of the ventricular catheter in severe infections.[10,12]

The most commonly isolated bacteria in the CSF samples in this study were Acinetobacter baumannii and Burkholderia cepacia species. The causative bacteria were isolated more than once with identical sensitivity and resistance pattern and biotype. In the study by Camacho et al in 2011, Acinetobacter contributed to majority (27.3%) of the infections of which 50% were carbapenem-resistant.[1] Pfisterer in 2003, noted that the majority of infections were caused by Staphylococcus epidermidis.[8] Rath et al in 2014, noted coagulase negative Staphylococci accounting for the majority (62%) of the infections.[10] Similarly, Hagel et al in 2014 found the majority of infections due to coagulase-negative Staphylococcos.[3] In a meta analysis of 35 studies conducted by Ramanan et al in 2014, majority of infections were caused by gram positive bacteria, predominantly coagulase-negative staphylococci (39%, including S. epidermidis) and S. aureus (15%).[9]

In our study, Acinetobacter baumanni was most commonly sensitive to Tigicycline and Polymixin B and resistant to carbapenems and other beta-lactam antibiotics, while Burkholderia cepacia was commonly sensitive to Cotrimoxazole and Amikacin.

Current recommendations from the Infectious Diseases Society of America (IDSA) regarding empirical antimicrobial therapy for postneurosurgical meningitis, are intravenous Vancomycin plus either Cefepime, Ceftazidime, or Meropenem.[12] However multidrug resistant Acinetobacter meningitis is becoming an increasingly

common entity especially in neurosurgical patients. In these situations intravenous Polymixin B or Colistin and an intraventricular aminoglycoside is recommended.[4]

Limitations of the Study

One major limitation of this study is that we analyzed only the patients with CSF samples which grew bacteria in them. Many patients could still have EVD related infections despite a negative bacteriological growth. Moreover our hospital lacked anaerobic culture facility, at the time of the study period. These factors could have further increased the actual incidence of EVD related infections. On the other hand, the researchers had to exclude significant number of cases with positive initial CSF analysis. This could have skewed the patient distribution. Further, it was a single center retrospective study.

Conclusion

EVD related infections are a potentially preventable cause of morbidity and mortality in neurosurgical patients, the incidence of which is quite high. The majority of the patients have growth of multidrug resistant bacteria. They were mainly Acinetobacter and Burkholderia species.

Recommendation

In view of the emergence of multidrug resistant bacteria in patients with EVD, consideration should be given to specific antibiotics use guided by the sensitivity pattern. Further multicenter prospective studies are recommended to analyze the true scenario of EVD-related infections.

Acknowledgments

Special thanks to the Department of Microbiology, Tribhuvan University Teaching Hospital, Kathmandu, Nepal.

Conflict of interest: None declared.

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