The Organisms and Factors Affecting Outcomes of External Ventricular Drainage Catheter-Related Ventriculitis: A Penang Experience

Abstract

Introduction: Ventriculostomy-related infection (VRI) from external ventricular drain (EVD) insertion is a common complication and carries a high mortality rate. Choice of empiric antibiotics depends on the institutions common causative organisms and their susceptibility. We determined risk factors for mortality in patients with VRI, the common organisms causing VRI, and the rate of EVD-related VRI at our institution. Methods: Medical records and operative data of patients with cerebrospinal fluid positive cultures with an EVD inserted from 2012 to 2015 were traced. Forty-five patients with EVD-related VRI were included in the study. Results: The overall rate of VRI was 6.3%, and the overall mortality rate due to VRI was 48.9%. Acinetobacter baumannii was the most common organism causing VRI (14 patients, 29.2%) with a mortality rate of 64.3%. Only 14.3% of A. baumannii are sensitive to meropenem and imipenem. We found that patients that had a decompressive craniectomy (DC) had a lower mortality rate (P = 0.042) and patients with a longer duration of the EVD being in place before the diagnosis of VRI had poor outcome (P = 0.040). Multivariate logistic regression was performed and we found that the use of steroid (P = 0.014), Pseudomonas aeruginosa infection (P = 0.010), multiple organism infection (P = 0.017), lower Glasgow Coma Scale (P = 0.043), and a longer duration the EVD was in place before the diagnosis of VRI (P = 0.008) were related with higher mortality. Conclusion: VRI mortality rate is high with an alarming resistance pattern seen in Acinetobacter VRI. EVDs should be removed as soon as feasible, and DC may be offered to patients with severe ventriculitis or meningitis.

Keywords: Acinetobacter, decompressive craniectomy, fatal outcome, nosocomial meningitis, risk factors, ventriculitis

Introduction

An external ventricular drain (EVD) is a temporary system for drainage of cerebrospinal fluid (CSF) and a conduit for intracranial pressure (ICP) monitoring. Ventriculitis, however, is a common but serious complication associated with ventricular catheters. Reported rates of EVD-related ventriculitis or ventriculostomy-related infection (VRI) range from 0% to 32.2%.[1-3] Mortality is as high as 10.3%–40.8%.[4,6] A good choice of perioperative prophylactic antibiotics and empiric antibiotics for ventriculitis while waiting for the culture report and sensitivity requires a sound knowledge of the institutions common causative organisms and their susceptibility. There is an alarming increase in resistance to antibiotics among the Gram-negative organisms.[1,7] Acinetobacter has been increasingly found to be the causative organism, and the greater fear lies in the fact that multidrug-resistant Acinetobacter baumannii (MRAB) infections are getting common.[5,8] Meropenem has been the drug of choice for nosocomial meningitis and ventriculitis to cover Gram-negative bacilli, including A. baumannii. However, polymyxin is frequently the only available therapeutic option with the emergence of carbapenem-resistant A. baumannii. Since the rates of EVD-related ventriculitis can be high, and mortality is not trivial, modifiable factors affecting the outcome of these patients negatively need to be recognized. In this article, we will determine the risk factors for poor prognosis of VRI, outline the common organisms causing VRI with special attention to Acinetobacter VRI, and the rate of EVD-related VRI at our institution.

Methods

This was a retrospective observational study conducted at Penang General Hospital, a...
Results

The age ranged from 12 to 75 years (mean, 50.62 years). The main two underlying diagnoses leading to insertion of EVD were spontaneous intracranial bleed 75.6% and traumatic intracranial bleed 15.6%. Slightly more than half of the patients had intraventricular hemorrhage (55.6%). Decompressive craniectomy (DC) was performed on 17 (37.8%) of the patients. Only three patients were on steroids, and 12 (26.7%) patients had diabetes mellitus. Bacteremia with the same organism as that cultured in the CSF was seen in 10 (22.2%) of the patients. Out of the 45 patients, 32 (71.1%) of them still required the EVD even when ventriculitis was diagnosed. In our center, 34 (75.6%) of the patients suffered Gram-negative ventriculitis. Only three (6.7%) patients had endured recurrent infection. Discordan empirical antibiotics were given to 35 (77.8%) patients. The mortality rate from VRI for this study was 48.9%. The time from EVD insertion till confirmation of ventriculitis ranged from 2 to 21 days with a mean of 8.73 days. The mean GCS score before operation or endotracheal intubation was 7.93 with a range of 3–15 [Table 1].

During the 4-year study period of 2012–2015, a total of 796 EVDs were inserted, but 77 of them had preexisting CNS infections. The overall rate over the 4 years was 6.3% [Table 2]. This is in keeping with the published rates of 0%–32.2%.[1-3] There is a slow rise in the rate of VRI in our center, and future studies need to be taken to identify the root causes before it escalates further.

Three patients had recurrent infection, and so the total number of mono-organisms cultured was 48. A. baumannii and Pseudomonas aeruginosa together make up 50% of the causative organisms. Seven (14.6%) patients contracted coagulase negative Staphylococcus (CONS), and only 3 (6.2%) patients were infected with Staphylococcus aureus [Table 3]. Most of the Acinetobacter are resistant to carabapenems and only sensitive to polymyxin [Table 4]. Only 14.3% of Acinetobacter are sensitive to meropenem and imipenem. Ceftriaxone sensitivity is 0%, and resistance is 64.3%. As a whole, a higher proportion of A. baumannii is resistant with very few being sensitive to the common antibiotics. Out of the 14 patients with A. baumannii infection, 12 of them received discordant empirical antibiotics.

From our group of 45 patients, six of them died before specific antibiotics based on the organism susceptibility reports could be started [Table 5]. Five of the patients did not receive empiric antibiotics presumably due to a missed diagnosis initially, or the patient died before CSF analysis results could be acted on.

Discussion

Common nosocomial organisms causing infection after neurosurgical procedures include CONS, S. aureus,
Although Gram-positive pathogens were the main organisms isolated in some studies, there is increasing Gram-negative pathogens being responsible for ventriculitis. This is consistent with our study, which showed higher incidence of Gram-negative infections. A. baumannii and P. aeruginosa constituted almost half of the total organisms associated with ventriculitis in our cohort.

The name, Acinetobacter, comes from the Latin word for “motionless” because they lack cilia or flagella with which to move. The respiratory system is the most common site for Acinetobacter infection because of its transient pharyngeal colonization of healthy persons and a high rate of tracheotomy colonization, which is a common occurrence in neurosurgical patients. Most of the A. baumannii isolated in our study was resistant to all cephalosporins and carbapenems, but only sensitive to polymyxin. This observation raises major concern as the occurrence of these multi-resistant Gram-negative bacteria results in a significant reduction of therapeutic options for the treatment of these infections. MRAB is an emerging problem in VRI due to its ability to tolerate desiccation and to accumulate diverse mechanisms of resistance. Polymyxin is frequently the only available therapeutic option for MRAB but has poor CNS penetration. A recent study showed that only the combination of parenteral with intrathecal or intraventricular administration of polymyxin has the potential to achieve therapeutic concentrations and eradicate MRAB from the CNS.

The empirical antibiotics used in our cohort consisted predominantly ceftriaxone, meropenem, and cefoperazone/sulbactam, which covered most of the Gram-negative bacteria but not MRAB [Table 5]. However, we do not advocate the use of polymyxin as first-line empirical therapy for EVD-related ventriculitis. This is because the indiscriminate use of polymyxin may contribute to the selection of further resistance and may also expose patients to unnecessary renal toxicity. Furthermore, polymyxin has weak activity against P. aeruginosa and other common bacteria. Therefore, careful selection of patients who should receive polymyxin as empirical therapy covering MRAB is essential. Previous colonization with A. baumannii resistant to carbapenems is a variable independently associated with the development of an infection caused by MRAB. New ventriculitis occurring during an outbreak or in a previously colonized patient, and unresolved infections despite treatment with broad-spectrum antibiotics are the most compelling reasons for MRAB empirical coverage with polymyxin. It is important to note that A. baumannii transmission in neurosurgical patients is mainly due to interactions between health-care workers, patients, and contaminated fomites in the ward environment, equipment, and EVD. Infection

### Table 1: Characteristics of patients with external ventricular drain ventriculitis

| Characteristics                        | n (%)          |
|----------------------------------------|----------------|
| Sex                                    |                |
| Male                                   | 28 (62.2)      |
| Female                                 | 17 (37.8)      |
| Diagnosis                              |                |
| Spontaneous intracranial bleed         | 33 (75.6)      |
| Traumatic intracranial bleed           | 7 (15.6)       |
| Brain tumor                            | 2 (4.4)        |
| Brain infarction                       | 1 (2.2)        |
| Pneumoventricle                       | 1 (2.2)        |
| Indication of EVD                      |                |
| ICP monitoring                         | 2 (4.4)        |
| CSF drainage                           | 43 (95.6)      |
| Cranectomy                             |                |
| Yes                                    | 25 (55.6)      |
| No                                     | 20 (44.4)      |
| Steroid use                            |                |
| Yes                                    | 3 (6.7)        |
| No                                     | 42 (93.3)      |
| Diabetes mellitus                      |                |
| Yes                                    | 12 (26.7)      |
| No                                     | 33 (73.3)      |
| Bacteremia                             |                |
| Yes                                    | 10 (22.2)      |
| No                                     | 35 (77.8)      |
| Persistent EVD                         |                |
| Yes                                    | 32 (71.1)      |
| No                                     | 13 (28.9)      |
| CSF gram stain                         |                |
| Positive                               | 10 (22.2)      |
| Negative                               | 34 (75.6)      |
| Both                                   | 1 (2.2)        |
| Recurrent infection                    |                |
| Yes                                    | 3 (6.7)        |
| No                                     | 42 (93.3)      |
| Discordant antibiotics                 |                |
| Yes                                    | 35 (77.8)      |
| No                                     | 10 (22.2)      |
| Multiple organisms                     |                |
| Yes                                    | 5 (11.1)       |
| No                                     | 40 (88.9)      |
| Multi-resistant organisms              |                |
| Yes                                    | 21 (46.7)      |
| No                                     | 24 (53.3)      |
| Outcome                                |                |
| Alive                                  | 23 (51.1)      |
| Dead                                   | 22 (48.9)      |
| Total                                  | 45 (100)       |

EVD – External ventricular drain; CSF – Cerebrospinal fluid; IVH – Intraventricular hemorrhage; ICP – Intracranial pressure

Enterobacteriaceae, P. aeruginosa, and A. baumannii. 

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Ventriculitis caused by Acinetobacter baumannii was strongly associated with the development of VRI. Our analysis showed that the duration of the EVD being in place was significant in determining the outcome of patients with VRI. Colony of the drain at the insertion site, and (4) hematogenous seeding. The study suggests that VRI is chiefly caused by pathogens colonizing the drain insertion site and hence, there are four main postulated mechanisms of VRI by Mounier et al.: (1) during insertion, (2) during disconnection or manipulation of the EVD system, (3) colonization of the drain at the insertion site, and (4) hematogenous seeding. The study suggests that VRI is chiefly caused by pathogens colonizing the drain insertion site and hence, the higher number of CONS VRI. Looking at the trend of organisms at our center, it is highly likely that Gram-negative infections did not occur during the insertion of EVDs. Colonization of the drain or hematogenous seeding may be a possibility since 22.2% of our patients had the same organism both in blood cultures and CSF. There are four main postulated mechanisms of VRI by Mounier et al.: (1) during insertion, (2) during disconnection or manipulation of the EVD system, (3) colonization of the drain at the insertion site, and (4) hematogenous seeding. The study suggests that VRI is chiefly caused by pathogens colonizing the drain insertion site and hence, the higher number of CONS VRI. Looking at the trend of organisms at our center, it is highly likely that Gram-negative infections did not occur during the insertion of EVDs. Colonization of the drain or hematogenous seeding may be a possibility since 22.2% of our patients had the same organism both in blood cultures and CSF cultures, but it could also be hematogenous dissemination of the VRI instead.

We believe our findings will create awareness among other hospitals about the rising trend of MRAB ventriculitis, which was also highlighted in other reports. The level of discordance in empiric antibiotics at our center is very high (77.8%), but was statistically insignificant in terms of mortality with our small sample size (\(P = 0.170, \text{odds ratio} = 2.77\)). By knowing our center’s organisms, it is our hope that there will be less wastage of antibiotics, prolongation of hospital stay, or even morbidity due to discordant antibiotics. Since there is a high rate of nosocomial MRAB ventriculitis, we will have to consider giving our patients polymyxin when they are not responding to a course of empirical antibiotics. Based on our experience, we strongly encourage every neurosurgical center to conduct a similar study to identify common causative organisms in their own ventriculitis cohort.

Various regimes of surgical prophylactic antibiotics have been tested, including cefepime, cephalothin, ampicillin/sulbactam, aztreonam, ceftaroline, trimethoprim-sulfamethoxazole, and cefuroxime. Cefuroxime is the main surgical prophylactic antibiotic used at our center. Although there is evidence that antibiotic prophylaxis may reduce VRI, the data available are still of suboptimal quality. It is postulated that the use of cephalosporins, especially aminothiazolyl cephalosporins such as cefuroxime and ceftriaxone are associated with promoting resistance due to their broad spectrum cover. In view of these, it may be reasonable to use single-dose cefazolin for patients undergoing clean neurosurgical procedures, CSF-shunting procedures, or intrathecal pump placement to prevent the increase in number of resistant organisms at our center as recommended by the American Society of Health-System Pharmacists report in 2013. A dosage of 1 g of cefazolin just before skin incision translates to a CSF concentration above the minimal inhibitory concentration level for approximately 5 h.

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Our analysis showed that the duration of the EVD being in place before the diagnosis of VRI was made is statistically significant in determining the outcome of patients with VRI [Table 6]. The results indicated that there is a significant association between the duration of EVD being in place before the diagnosis of VRI was made and the outcome of patients with VRI (\(P = 0.040\)). It has been shown that EVD colonization was strongly associated with the development of VRI. It is possible that colonization or VRI precedes detectable signs and symptoms, and therefore, the longer the EVD is within the ventricles, the higher the bacteria...
burden is and hence more difficult to cure. On top of that, prolonged indwelling catheters may promote the selection of resistant strains. Although a persistent EVD state was not associated with a higher mortality rate in our study, it was significant in another study.[32] Yet, another paper recommends the removal of infected EVDs to improve cure rate.[32] All these information supports the early removal of EVDs if possible even if clinical VRI is not present yet. Not only does prolonged duration of EVD increase the risk of contracting VRI but it also increases the mortality rate if VRI does occur.[33]

Those who underwent a DC in our cohort of patients had a lower proportion of mortality ($P = 0.042$) [Table 7]. The mortality rate among those that had a DC was 29.4% as compared to 60.7% in those that did not have a DC. Our findings support the anecdotal evidence that DC may be beneficial in patients with bacterial meningitis with high refractory ICP.[34,35] It must be clarified that all patients in this study had the DC done for other reasons such as intracranial bleeds and not for VRI and therefore the DC was done before VRI was diagnosed. Although just a postulation, brain edema causing raised, ICP may be a cause of reduced cerebral perfusion and thus reduced antibiotic delivery and impaired transport of immune cells and factors to combat the infection. This is further supported by the fact that ICP-targeted treatment has also been recommended for bacterial meningitis.[36] In neurosurgical patients with reduced GCS and ventriculitis, it would be ideal for these patients to have their ICP monitored so that DC may be carried out if other treatment measures fail to reduce the ICP.

Multivariate logistic regression was performed, and we found that the use of steroid, $P. aeruginosa$ infection, multiple organism infection, lower GCS, and a longer duration the EVD was in place before the diagnosis of VRI were related with higher mortality [Table 8]. There are various other factors that have been identified to be risk factors for poor outcome in ventriculitis. In one study, mortality was strongly related to age, white cell counts, and removal of EVD.[32] Another study showed that shock, C-reactive

| Table 4: *Acinetobacter baumannii* antibiotic susceptibility from 14 mono-organism cerebrospinal fluid cultures |
|----------------------------------|--------------|--------------|--------------|--------------|
| Antibiotic                        | Sensitive, $n$ (%) | Intermediate, $n$ (%) | Resistant, $n$ (%) | Unknown, $n$ (%) |
| Ampicillin/sulbactam              | 5 (35.7)     | 0            | 9 (64.3)      | 0            |
| Amoxycillin/clavulanic acid       | 1 (7.1)      | 1 (7.1)      | 10 (71.5)     | 2 (14.3)     |
| Trimethoprim/sulfamethoxazole     | 4 (28.6)     | 1 (7.1)      | 7 (50.0)      | 2 (14.3)     |
| Gentamicin                        | 6 (42.9)     | 0            | 8 (57.1)      | 0            |
| Amikacin                          | 7 (50.0)     | 0            | 7 (50.0)      | 0            |
| Cefuroxime                        | 0            | 0            | 9 (64.3)      | 5 (35.7)     |
| Ceftazidime                       | 2 (14.3)     | 0            | 11 (78.6)     | 1 (7.1)      |
| Ceftriazone                       | 0            | 0            | 9 (64.3)      | 5 (35.7)     |
| Cefepime                          | 1 (7.1)      | 0            | 13 (92.9)     | 0            |
| Ciprofloxacin                     | 6 (42.9)     | 0            | 7 (50.0)      | 1 (7.1)      |
| Imipenem                          | 2 (14.3)     | 0            | 11 (78.6)     | 1 (7.1)      |
| Meropenem                         | 2 (14.3)     | 0            | 11 (78.6)     | 1 (7.1)      |
| Doripenem                         | 1 (7.1)      | 0            | 4 (28.6)      | 9 (64.3)     |
| Cefoperazone/sulbactam            | 3 (21.4)     | 4 (28.6)     | 6 (42.9)      | 1 (7.1)      |
| Piperacillin/tazobactam           | 1 (7.1)      | 0            | 12 (85.7)     | 1 (7.1)      |
| Polymyxin B                       | 13 (92.9)    | 0            | 0             | 1 (7.1)      |
| Cefoperazone/sulbactam            | 2 (14.3)     | 0            | 11 (78.6)     | 1 (7.1)      |
| Tigecycline                       | 1 (7.1)      | 2 (14.3)     | 2 (14.3)      | 9 (64.3)     |

| Table 5: Empiric antibiotics |
|-----------------------------|-----------|
| Antibiotics                | $n$ (%)   |
| Ceftriazone                | 10 (22.2) |
| Meropenem                  | 8 (17.8)  |
| Cefoperazone/sulbactam     | 7 (15.6)  |
| Cefuroxime                 | 3 (6.7)   |
| Piperacillin/tazobactam    | 3 (6.7)   |
| Cefepime                   | 2 (4.4)   |
| Ampicillin/sulbactam       | 2 (4.4)   |
| Imipenem                   | 1 (2.2)   |
| Vancomycin                 | 1 (2.2)   |
| Ciprofloxacin              | 1 (2.2)   |
| Amoxicillin/clavulanate    | 1 (2.2)   |
| Colistin and cefoperazone/sulbactam | 1 (2.2) |
| No empiric antibiotics     | 5 (11.1)  |
| Total                      | 45 (100)  |

| Table 6: Statistical analysis of univariate continuous variables in association with outcome |
|-----------------------------------------------|--------|--------|
| Characteristics                         | Alive | Dead   |
|------------------------------------------|-------|--------|
| Duration of EVD (number of days)         | 23    | 22     |
| Age (years)                              | 23    | 22     |
| GCS                                       | 23    | 22     |
| $n$ Mean (SD)                             |       |        |
| $P$                                        |       |        |
| **0.040**                                 |       |        |
| **0.370**                                 |       |        |
| **0.605**                                 |       |        |

*Mann-Whitney test applied, presented as median (IQR); Independent t-test applied. GCS – Glasgow Coma Scale; SD – Standard deviation; EVD – External ventricular drain; IQR – Interquartile range
Table 7: Statistical analysis of univariate categorical variables in association with outcome

| Characteristics                      | Outcome, n (%)         | P     | OR   | 95% CI          |
|--------------------------------------|------------------------|-------|------|-----------------|
|                                      | Alive                  | Dead  |      |                 |
| Craniectomy                          |                        |       |      |                 |
| Yes                                  | 12 (70.6)              | 5 (29.4) | 0.042 | 0.27 | 0.07 | 0.98 |
| No                                   | 11 (39.3)              | 17 (60.7) |       |       |      |      |
| Gender                               |                        |       |      |                 |
| Male                                 | 15 (53.6)              | 13 (46.4) | 0.672 | 0.77 | 0.23 | 2.58 |
| Female                               | 8 (47.1)               | 9 (52.9)  |       |       |      |      |
| IVH                                  |                        |       |      |                 |
| Yes                                  | 11 (44.0)              | 14 (56.0) | 0.286 | 1.91 | 0.58 | 6.30 |
| No                                   | 12 (60.0)              | 8 (40.0)  |       |       |      |      |
| Indication of EVD                    |                        |       |      |                 |
| ICP monitoring                       | 1 (50.0)               | 1 (50.0)  | 0.974 | 1.05 | 0.06 | 17.85 |
| CSF drainage                         | 22 (51.2)              | 21 (48.8) |       |       |      |      |
| Steroid                              |                        |       |      |                 |
| Yes                                  | 1 (33.3)               | 2 (66.7)   | 0.521 | 2.20 | 0.19 | 26.16 |
| No                                   | 22 (52.4)              | 20 (47.6)  |       |       |      |      |
| Diabetes                             |                        |       |      |                 |
| Yes                                  | 8 (66.7)               | 4 (33.3)   | 0.208 | 0.42 | 0.11 | 1.66 |
| No                                   | 15 (45.5)              | 18 (54.5)  |       |       |      |      |
| Bacteremia                           |                        |       |      |                 |
| Yes                                  | 5 (50.0)               | 5 (50.0)   | 0.936 | 1.06 | 0.26 | 4.32 |
| No                                   | 18 (51.4)              | 17 (48.6)  |       |       |      |      |
| Persistent EVD                       |                        |       |      |                 |
| Yes                                  | 15 (46.9)              | 17 (53.1)  | 0.372 | 1.81 | 0.49 | 6.76 |
| No                                   | 8 (61.5)               | 5 (38.5)   |       |       |      |      |
| Recurrent infection                  |                        |       |      |                 |
| Yes                                  | 1 (33.3)               | 2 (66.7)   | 0.521 | 2.20 | 0.19 | 26.16 |
| No                                   | 22 (52.4)              | 20 (47.6)  |       |       |      |      |
| Discordant antibiotics               |                        |       |      |                 |
| Yes                                  | 16 (45.7)              | 19 (54.3)  | 0.170 | 2.77 | 0.61 | 12.51 |
| No                                   | 7 (70.0)               | 3 (30.0)   |       |       |      |      |
| Multi-resistant organism             |                        |       |      |                 |
| Yes                                  | 8 (38.1)               | 13 (61.9)  | 0.102 | 2.71 | 0.81 | 9.06 |
| No                                   | 15 (62.5)              | 9 (37.5)   |       |       |      |      |
| Acinetobacter                       |                        |       |      |                 |
| Yes                                  | 5 (35.7)               | 9 (64.3)   | 0.165 | 2.49 | 0.68 | 9.19 |
| No                                   | 18 (58.1)              | 13 (41.9)  |       |       |      |      |
| Staphylococcus aureus                |                        |       |      |                 |
| Yes                                  | 3 (75.0)               | 1 (25.0)   | 0.306 | 0.32 | 0.03 | 3.31 |
| No                                   | 20 (48.8)              | 21 (51.2)  |       |       |      |      |
| Coagulase negative Staphylococcus    |                        |       |      |                 |
| Yes                                  | 4 (57.1)               | 3 (42.9)   | 0.728 | 0.75 | 0.15 | 3.81 |
| No                                   | 19 (50.0)              | 19 (50.0)  |       |       |      |      |
| Klebsiella                           |                        |       |      |                 |
| Yes                                  | 5 (55.6)               | 4 (44.4)   | 0.765 | 0.80 | 0.18 | 3.47 |
| No                                   | 18 (50.0)              | 18 (50.0)  |       |       |      |      |
| Pseudomonas                          |                        |       |      |                 |
| Yes                                  | 3 (27.3)               | 8 (72.7)   | 0.069 | 3.81 | 0.86 | 16.94 |
| No                                   | 20 (58.8)              | 14 (41.2)  |       |       |      |      |
| Multiple organisms                   |                        |       |      |                 |
| Yes                                  | 1 (20.0)               | 4 (80.0)   | 0.129 | 4.89 | 0.50 | 47.71 |
| No                                   | 22 (55.0)              | 18 (45.0)  |       |       |      |      |

Contd...
protein ≥10 mg/dL, and persistent EVD state was associated with higher mortality rates.\(^5\) Gram-negative infection, CSF glucose <30 mg/dL, CSF protein >200 mg/dL, concurrent nosocomial infection, and GCS score <10 were associated with higher mortality in another study.\(^6\)

This study has its limitations. The sample size is small even with 4 years of data, and this is a retrospective study where there maybe information bias and missing data. The study was done in a single center, and generalization of its findings to other centers is limited. Performing a prospective study and expanding the scope to include other hospitals is a suitable aim.

### Conclusion

The rate of EVD-related ventriculitis in our center remains relatively low but increasing nonetheless. Worrying susceptibility patterns, especially those of *Acinetobacter* VRI needs special attention before it is too late. EVDs should be removed as soon as feasible to avoid VRI and higher mortality rates. In patients with ventriculitis/meningitis, DC maybe considered as a life-saving measure.

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### Conflicts of interest

There are no conflicts of interest.

### References

1. Lwin S, Low SW, Choy DK, Yeo TT, Chou N. External ventricular drain infections: Successful implementation of strategies to reduce infection rate. Singapore Med J 2012;53:255-9.
2. Schade RP, Schinkel J, Visser LG, Van Dijk JM, Voormolen JH, Kuijper EJ. Bacterial meningitis caused by the use of ventricular or lumbar cerebrospinal fluid catheters. J Neurosurg 2005;102:229-34.
3. Omar MA, Mohd Haspasi MS. The risk factors of external ventricular drainage-related infection at hospital Kuala Lumpur: An observational study. Malays J Med Sci 2010;17:48-54.
4. Do BH, Kim SW, Oh JT, Son JW, Ha SW, Lee EK, et al. The external ventricular drain-related ventriculitis: Organisms and appropriateness of empiric antibiotic therapy. Infect Chemother 2005;37:92-8.
5. Kim HI, Kim SW, Park GY, Kwon EG, Kim HH, Jeong JY, et al. The causes and treatment outcomes of 91 patients with adult nosocomial meningitis. Korean J Intern Med 2012;27:171-9.
6. Erdem I, Hakan T, Ceran N, Metin F, Akcay SS, Kucukercan M, et al. Clinical features, laboratory data, management and the risk factors that affect the mortality in patients with postoperative meningitis. Neurol India 2008;56:433-7.
7. O’Neill E, Humphreys H, Phillips J, Smyth EG. Third-generation cephalosporin resistance among Gram-negative bacilli causing meningitis in neurological patients: Significant challenges in ensuring effective antibiotic therapy. J Antimicrob Chemother 2006;57:356-9.
8. Yadegarynia D, Gachkar L, Fatemi A, Zali A, Nobari N, Asoodeh M, et al. Changing pattern of infectious agents in postneurosurgical meningitis. Caspian J Intern Med 2014;5:170-5.
9. Ramanan M, Lipman J, Shorr A, Shankar A. A meta-analysis of ventriculostomy-associated cerebrospinal fluid infections. BMC Infect Dis 2015;15:3.
10. Logigan C, Mihalache D, Turcu T. Clinical study of 57 cases of nosocomial meningitis. J Prev Med 2008;16:59-68.
11. Streharova A, Benca J, Holeckova K, Balik J, Sula I, Lesnakova A, et al. Comparison of postsurgical and community acquired bacterial meningitis – Analysis of 372 cases within a nationwide survey. Neuro Endocrinol Lett 2007;28 Suppl 3:7-9.
12. Wcislo M, van de Beek D, Spanjaard L, de Gans J. Nosocomial bacterial meningitis in adults: A prospective series of 50 cases. J Hosp Infect 2007;66:71-8.
13. Wang KW, Chang WN, Huang CR, Tsai NW, Tsiu HW, Wang HC, et al. Post-neurosurgical nosocomial bacterial meningitis. J Hosp Infect 2012;80:51-4.

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**Table 7: Contd...**

| Characteristics | Outcome, n (%) | \( P \) | OR | 95% CI | \( \text{Lower limit} \) | \( \text{Upper limit} \) |
|-----------------|---------------|---------|-----|--------|----------------|----------------|
| Alive | Dead |
| Yes | 8 (72.7) | 3 (27.3) | 0.099\(^a\) | 0.30 | 0.07 | 1.31 |
| No | 15 (44.1) | 19 (55.9) |

Gram-negative

| Characteristics | Outcome, n (%) | \( P \) | OR | 95% CI | \( \text{Lower limit} \) | \( \text{Upper limit} \) |
|-----------------|---------------|---------|-----|--------|----------------|----------------|
| Yes | 16 (45.7) | 19 (54.3) | 0.170\(^b\) | 2.77 | 0.61 | 12.51 |
| No | 7 (70.0) | 3 (30.0) |

\(^a\)Pearson Chi-square test applied, \(^b\)Fisher’s exact test applied. OR – Odds ratio; CI – Confidence interval; EVD – External ventricular drain; IVH – Intraventricular hemorrhage; ICP – Intracranial pressure; CSF – Cerebrospinal fluid

**Table 8: Multivariate logistic regression test (using enter method)**

| Characteristics | \( P \) | OR | 95% CI | \( \text{Lower limit} \) | \( \text{Upper limit} \) |
|-----------------|---------|-----|--------|----------------|----------------|
| Steroid | 0.014 | 121.420 | 2.646 | 5572.509 |
| *Pseudomonas* | 0.010 | 16.822 | 1.978 | 143.096 |
| Multiple organism | 0.017 | 86.766 | 2.211 | 3404.349 |
| GCS | 0.043 | 0.722 | 0.527 | 0.990 |
| Duration of EVD | 0.008 | 1.212 | 1.096 | 1.854 |

OR – Odds ratio; CI – Confidence interval; GCS – Glasgow Coma Scale; EVD – External ventricular drain

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Nil.
meningitis in adults: Microbiology, clinical features, and outcomes. J Clin Neurosci 2005;12:647-50.
14. van de Beek D, Drake JM, Tunkel AR. Nosocomial bacterial meningitis. N Engl J Med 2010;362:146-54.
15. McClelland S 3rd, Hall WA. Postoperative central nervous system infection: Incidence and associated factors in 2111 neurosurgical procedures. Clin Infect Dis 2007;45:55-9.
16. Ziaka M, Markantonis SL, Foustri M, Zygoulis P, Panidis D, Karvouniari M, et al. Combined intravenous and intraventricular administration of colistin methanesulfonate in critically ill patients with central nervous system infection. Antimicrob Agents Chemother 2013;57:1938-40.
17. Corbella X, Montero A, Pujol M, Domínguez MA, Ayats J, Argerich MJ, et al. Emergence and rapid spread of carbapenem resistance during a large and sustained hospital outbreak of multiresistant Acinetobacter baumannii. J Clin Microbiol 2000;38:4086-95.
18. Fierobe L, Lucet JC, Decré D, Muller-Serieys C, Deleuze A, Joly-Guillou ML, et al. An outbreak of imipenem-resistant Acinetobacter baumannii in critically ill surgical patients. Infect Control Hosp Epidemiol 2001;22:35-40.
19. Rodríguez Guardado A, Blanco A, Asensi V, Pérez F, Rial JC, Pintado V, et al. Multidrug-resistant Acinetobacter meningitis in neurological patients with intraventricular catheters: Assessment of different treatments. J Antimicrob Chemother 2008;61:908-13.
20. Khan FY, Abukhattab M, Baager K. Nosocomial postneurosurgical Acinetobacter baumannii meningitis: A retrospective study of six cases admitted to Hamad General Hospital, Qatar. J Hosp Infect 2012;80:176-9.
21. Stein GE, Yasin F, Smith C, Scharmen A, Havlichek D, Bill C. A pharmacokinetic/pharmacodynamic analysis of ceftriaxone prophylaxis in patients with external ventricular drains. Surg Infect (Larchmt) 2015;16:169-73.
22. Wong GK, Poon WS, Lyon D, Wai S, Cefepime vs. ampicillin/sulbactam and aztreonam as antibiotic prophylaxis in neurological patients with external ventricular drain: Result of a prospective randomized controlled clinical trial. J Clin Pharm Ther 2006;31:231-5.
23. Blomstedt GC. Results of trimethoprim-sulfamethoxazole prophylaxis in ventriculostomy and shunting procedures. A double-blind randomized trial. J Neurosurg 1985;62:694-7.
24. Lucey MA, Myburgh JA. Antibiotic prophylaxis for external ventricular drains in neurosurgical patients: An audit of compliance with a clinical management protocol. Crit Care Resusc 2003;5:182-5.
25. Alleyne CH Jr., Hassan M, Zabramski JM. The efficacy and cost of prophylactic and perioperative antibiotics in patients with external ventricular drains. Neurosurgery 2000;47:1124-7.
26. Sonabend AM, Korenfeld Y, Crisman C, Bajjatia N, Mayer SA, Connolly ES Jr. Prevention of ventriculostomy-related infections with prophylactic antibiotics and antibiotic-coated external ventricular drains: A systematic review. Neurosurgery 2011;68:996-1005.
27. Dancer S. The problem with cephalosporins. J Antimicrob Chemother 2001;48:463-78.
28. Bratza DW, Dellingler EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Surg Infect (Larchmt) 2013;14:73-156.
29. Klekner A, Ga’spa’r A, Kardos S, Szabó J, Cse’csei G. Cefazolin prophylaxis in neurosurgery monitored by capillary electrophoresis. J Neurosurg Anesthesiol 2003;15:249-54.
30. Mounier R, Lobo D, Cook F, Martin M, Attias A, Alí-Mamar B, et al. From the skin to the brain: Pathophysiology of colonization and infection of external ventricular drain, a prospective observational study. PLoS One 2015;10:e0142320.
31. Hetem DJ, Woerdeman PA, Bonten MJ, Ekkelenkamp MB. Relationship between bacterial colonization of external cerebrospinal fluid drains and secondary meningitis: A retrospective analysis of an 8-year period. J Neurosurg 2010;113:1309-13.
32. Kim BN, Peleg AY, Lipman J, Li J, Nation R, et al. Management of meningitis due to antibiotic-resistant Acinetobacter species. Lancet Infect Dis 2009;9:245-55.
33. Holloway KL, Barnes T, Choi S, Bullock R, Marshall LF, Eisenberg HM, et al. Ventriculostomy infections: The effect of monitoring duration and catheter exchange in 584 patients. J Neurosurg 1996;85:419-24.
34. Hoehe J, Friedrich M, Brawanski A, Melter M, Schebesch KM. Decompressive craniectomy and early cranioplasty in a 15-year-old boy with N. meningitidis meningitis. Surg Neurol Int 2015;6:58.
35. Di Rienzo A, Iacoangeli M, Rychlicki F, Veccia S, Scerrati M. Decompressive craniectomy for medically refractory intracranial hypertension due to meningocencephalitis: Report of three patients. Acta Neurochir (Wien) 2008;150:1057-65.
36. Glimáker M, Johansson B, Halldorsdottir H, Wanecek M, Elmi-Terander A, Karvouniaris M, et al. Neuro-intensive treatment targeting intracranial hypertension improves outcome in severe bacterial meningitis: An intervention-control study. PLoS One 2014;9:e91976.