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Original Article

Assessment of risk factors for external ventricular drainage-induced infections in the neurosurgery department

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Abstract: Objective: External ventricular drainage (EVD) is frequently used in neurosurgery for cerebrospinal fluid (CSF) drainage. The purpose of this retrospective single center study was to assess the prevalence and potential risk factors of EVD-related infections. Methods: Clinical data of 58 patients undergoing EVD in the Intensive Care Unit (ICU), Neurosurgery Department of Xuanwu Hospital of Capital Medical University between January 1 and December 31, 2015 were collected. The incidence of ventricular infection, use of antibiotics, concurrent infection, pathogenic bacteria, duration of catheter drainage, and CSF sampling frequency were retrospectively analyzed. Forty-eight patients were diagnosed with subarachnoid hemorrhage/intracranial hemorrhage, 7 with intracranial tumors, and 3 cases were diagnosed with alternative diseases. Twenty-five patients were administered with antibiotics to prevent the risk of infections. Results: Fifty-eight patients received EVD for 456 days. The infection rate was calculated as 8.6% (10.9/1000 EVD days). The duration of EVD (≥11 d, Wals=4.8, RR=17.3, 95% CI: 1.4-218.3, P=0.028), CSF sampling frequency (≤2 d, Wals=5.3, RR=15.3, 95% CI: 1.5-243.7, P=0.022), and concomitant pulmonary infection (RR=7.8, 95% CI: 0.8-74.8, *P*=0.04) were risk factors of EVD-related infections. Conclusion: Multivariate analysis has demonstrated that long duration of catheter drainage, CSF sampling frequency, and concomitant pulmonary infection are risk factors of EVD-induced infections. Widespread attention should be diverted to these factors to reduce the incidence of EVD-related infections in the clinical setting.

Keywords: Infection, external ventricular drainage, cerebrospinal fluid, risk factor

Introduction

External ventricular drainage (EVD) is commonly applied in the treatment of acute severe hydrocephalus in clinical practice. In the intensive care unit of the Neurosurgery Department, the incidence of subarachnoid hemorrhage (SAH) or intracranial hemorrhage (ICH) complicated with hydrocephalus is alarmingly high. These patients have to undergo EVD intervention.

The purpose of EVD is to divert fluid from the ventricles of the brain and allow for dynamic monitoring of intracranial pressure. Nevertheless, EVD placement is an invasive procedure, which is associated with several potential complications. For instance, bleeding can occur along the EVD insertion tract or in the several layers of the meninges that prevent the passage into the brain. Mechanical complications from EVD placement, include malplacement, obstruction, and migration of the EVD device. Futthermore, the EVD device is a foreign body inserted into the brain, and it represents a potential portal for severe infection. Occasionally, neurological deficits from passing the EVD catheter across the brain might occur in certain cases. All these complications are likely to prolong the length of hospital stay, increase hospitalization expense, and enhance the mortality rate [1, 2]. Previous investigations have reported the risk of cerebral infection induced by EVD is approximately 2%-24% [3-6]. Effective measures should be implemented to reduce the risk of EVD-related brain infection, shorten the length of hospital stay and lower the hospitalization expense.

Table 1. Analysis of risk factors of EVD-related infection

Baseline data	Non-infection group (n=53)	Infection group (n=5)	Statistical value	*RR (95% CI)*	*P value*
Age ($\bar{x}$±s, year)	56.2±17.9	63.2±9.0	T=0.86	-	0.390
Gender (male/female, n)	32/26	3/2	X^2=0.052	1.2 (0.19-8.0)	0.820
Primary diseases [n (%)]					
SAH/ICH	44 (75.9%)	4 (6.9%)	X^2=0.029	0.82 (0.082-8.2)	0.860
Intracranial tumors	6 (10.3%)	1 (1.7%)	χ^2=0.320	2.0 (0.19-21.0)	0.570
Others	3 (5.2%)	0 (0.0%)	χ^2=0.300	1.1 (1.0-1.2)	0.590
Use of preventive antibiotics [n (%)]	22 (37.9%)	3 (5.2%)	χ^2=0.640	2.1 (0.3-13.7)	0.430
Retention time of drainage tube ($\bar{x}$±s, d)	7.3±3.9	15.2±7.3	t=3.600	-	0.001
Interval time of cerebrospinal fluid sampling collection ($\bar{x}$±s, d)	3.8±2.2	1.7±0.37	t=-2.0	-	0.045

Note: "-" represents RR value is not calculated.

In this study, clinical data of 58 patients admitted to the Neurosurgery Department undergoing EVD were retrospectively analyzed. The use of an EVD device, the incidence of EVD-related infection, and risk factors were comprehensively evaluated.

Material and methods

Baseline data

Clinical data of 58 patients admitted to the neurosurgery department of Xuanwu Hospital undergoing EVD between January and December 2015 were retrospectively analyzed. Inclusion criteria: patients admitted to the intensive care unit of the Neurosurgery Department; those undergoing EVD and those receiving extubation after hospital dischage. Exclusion criteria: patients with open cranial bone fracture, cerebrospinal fluid leakeage, congenital hydrocephalus, central nervous system infection upon EVD placement and those transferred to other departments throughout the treatment process were excluded from subsequent analysis.

EVD procedures

A closed drainage system was adopted in which the drainage tube was placed via percutaneous route. Dressing change was delivered every 2 days. Several patients had received antibiotics prior to catheter insertion due to loss of consciousness, pulmonary infection on radiography or positive outcomes for sputum culture. The remaining cases had no medical history of intake of preventive antibiotics.

Cerebrospinal fluid sampling

The cerebrospinal fluid specimen was collected at 5 days after catheter insertion. Triplicate samples were retained weekly. The cerebrospinal fluid specimen was immediately obtained when the patients presented with fever, consciousness changes, and increased white blood cell count. After collection of cerebrospinal fluid specimen, the samples were immersed into the disinfection solution and packaged under sterile conditions. The retention time of drainage tube was determined according to the requirement of clinical treatment. The time of drainage did not exceed 14 days.

Diagnostic criteria of EVD-related infection

Positive outcomes for cerebrospinal fluid bacterial culture included: clinical manifestations of central nervous system infection including fever, intracranial hypertension, meningeal irritation, consciousness changes and leukocytosis in the peripheral blood, and/or increased white blood cell count in the cerebrospinal fluid >300×10^9/L; the percentage of multinuclear cells higher than that of mononuclear cells [3, 4].

Statistical analysis

SPSS 19.0 software was utilized for statistical analysis (SPSS Inc., Chicago, IL). Age, duration of catheter drainage and the time interval of cerebrospinal fluid specimen collection were normally-distributed. Measurement data were expressed as $\bar{x}$±s. The risk factors were subject to univariate logistic regression analysis. Comparison between two groups was per-

formed by using a *t*-test. Enumeration data were analyzed by X^2 test. A value of $P<0.05$ was considered as statistically significant.

Results

Baseline data

In this study, 58 patients were recruited with a mean age of (56.8±17.4) years (5-82 years). In the infection group (n=5), patients were aged (56.2±17.9) years on average and (63.2±9.0) years for their counterparts in the non-infection group (n=53). In the infection group, 3 patients were male and 2 female. Among them, 4 cases underwent EVD due to SAH or ICH and 1 patient was diagnosed with cerebral tumors. In the non-infection group, 29 patients were male and 24 female. Forty-four cases underwent EVD due to SAH or ICH, 6 with brain tumors and 3 due to alternative reasons. No statistical significance was observed between two groups in terms of age, gender and primary diseases, *etc*., as illustrated in **Table 1**.

Comparison of EVD-related infection between two groups

A total of 58 patients underwent 456 cycles of EVD. The mean duration of catheter drainage was calculated as 7.9 days. The cerebrospinal fluid specimen was collected every 3.4 days. Among them, 5 patients were diagnosed with central nervous system infection with an infection rate of 8.6%. The catheter-related infection rate was calculated as 10.9/1000. In the infection group, the mean duration of catheter drainage was (15.2±7.3) days. The cerebrospinal fluid specimen was collected at a mean time interval of (1.7±0.37) days. In the non-infection group, the mean duration of catheter drainage was (7.3±3.9) days. The cerebrospinal fluid specimen was obtained at a mean time interval of (3.8±2.2) days. The duration of catheter drainage and time interval of cerebrospinal fluid specimen collection significantly differed between the infection and non-infection groups (both $P>0.05$), as illustrated in **Table 1**.

Analysis of risk factors

Univariate regression analysis demonstrated that the risk of EVD-related infection was significantly increased along with the duration of catheter drainage (≥11 d, *Wals*=4.8, *RR*=17.3, 95% *CI*: 1.4-218.3, $P=0.028$), and the shorter time interval of cerebrospinal fluid specimen collection (≤2 d, *Wals*=5.3, *RR*=15.3, 95% *CI*: 1.5-243.7, $P=0.022$). Patients without cerebrospinal fluid specimen collection during EVD did not present with infection ($\chi^2=38.4$, *RR*=0.12, 95% *CI*: 0.051-0.270, $P=0.001$).

Pathogen detection outcomes

In the infection group, 4 patients were positive for cerebrospinal fluid culture including *Acinetobacter baumannii* in 1, Burkholderia cepacia in 1, *Staphylococcus warneri* in 1 and *Staphylococcus aureus* in 1. The remaining 1 case obtained negative results, whereas the clinical symptoms were consistent with the signs of central nervous system infection. The white blood cell count in the cerebrospinal fluid was detected >300. The proportion of multinuclear cells was higher than that of mononuclear cells. Usage of preventive antibiotics and the incidence of pulmonary infection prior to catheter placement were correlated with the risk of EVD-related infection. Whether use of preventive antibiotics was not associated with the incidence of EVD-related infection (*RR*=2.1; 95% *CI*: 0.3-13.7, $P=0.425$). The incidence of pulmonary infection prior to catheter placement could increase the risk of EVD-related infection (RR=7.8, 95% *CI*: 0.8-74.8, $P=0.04$). The outcomes of cerebrospinal fluid and sputum culture were identical in patients infected with *Acinetobacter baumannii* and *Staphylococcus aureus*.

Discussion

In this investigation, the EVD-related infection rate in the intensive care unit of neurosurgery department was calculated as 8.6%, which was almost consistent with previous findings (2%-24%) [1, 3-6]. Previous studies have demonstrated that patients' age, gender and primary diseases are not correlated with the risk of EVD-related infection [6, 7]. Alternative research has indicated that ICH invading into the brain can cause the obstruction of cerebrospinal fluid drainage and probably require lavage intervention, thereby increasing the risk of EVD-induced infection [3, 8].

In this clinical trial, prolongation of the duration of catheter drainage could significantly elevate the risk of EVD-related infection, which is

consistent with previous findings [2-8]. Moreover, the risk of infection was considerably enhanced in patients receiving catheter drainage for ≥11 days. Other scholars suggest that the duration of EVD catheter retention is not correlated with the risk of EVD-related infection. Repeated catheter insertion to shorten the drainage time can increase the risk of infection instead [9]. Additionally, the longer the duration of drainage and the higher frequency of cerebrospinal fluid specimen retention, the risk of EVD-related infection was higher. Therefore, balancing the time of EVD catheter retention and the frequency of catheter insertion remains controversial among scholars and will need to be elucidated by more prospective studies [3, 5, 9, 10]. The EVD catheter should be immediately replaced if patients receiving EVD for >10 days present with EVD-related infection. Furthermore, thorough drainage and administration of antibacterial medication are highly recommended to prevent and treat the bacterial infection.

In this study, the cerebrospinal fluid specimen was collected at 5 days after catheter placement, and three times every week thereafter. The cerebrospinal fluid specimen was also collected when the patients suffered from fever, consciousness changes, elevated percentage of white blood cell count, *etc*. The cerebrospinal fluid specimen was collected during the catheter insertion in a majority of patients, whereas it was not performed in those receiving catheter insertion for <5 days. In this study, patients whose cerebrospinal fluid specimen was not collected during EVD did not present with central nervous system infection. Previous studies have suggested that routine collection of cerebrospinal fluid specimen is not associated with the risk of EVD-related infection [11]. Other researchers have considered that the collection of cerebrospinal fluid specimen does not increase the risk of EVD-related infection if the procedures are performed strictly according to standard requirement by an experienced practitioner [12]. According to the results of this investigation, increasing the frequency of cerebrospinal fluid specimen collection indeed elevated the exposure of the drainage system and the risk of infection, which was an independent risk factor of EVD-related infection, which was consistent with previous findings [8, 13, 14]. EVD system is a closed and sterile device. Any open system operation can cause external contamination and enhance the risk of infection. Consequently, effective measures should be taken to reduce the unnecessary cerebrospinal fluid specimen collection. However, cerebrospinal fluid specimen collection should be immediately performed when the patients present with clinical symptoms related to central nervous system infection, such as fever, intracranial hypertension, meningeal irritation, consciousness changes, and leukocytosis in the peripheral blood.

Patients diagnosed with severe central nervous system disease constantly suffer from vomiting, respiratory system impairment, and pulmonary infection. Previous studies have demonstrated that complicated with infection in other sites can increase the risk of central nervous system infection [9, 15]. Kim et al. [5] have demonstrated no significant correlation between the infection in alternative sites and EVD-related infection, whereas they have found that 50% of the pathogens in the cerebrospinal fluid are identical to those in the other infection sites. Staphylococcus has been considered as pathogenic bacterion [5, 15-18]. Mounier et al. [19] have demonstrated that bacterial infection via biopsy puncture is a main pathogenic bacterium for EVD-related infection, especially if the puncture tract infection and cerebrospinal fluid leakage are complicated. In this study, four patients were positive for cerebrospinal fluid culture including 2 infected with positive bacteria and the remaining 2 with negative bacteria. The outcomes of the cerebrospinal fluid and sputum culture were consistent in 2 patients infected with *Acinetobacter baumannii* and *Staphylococcus aureus.* It has been extrapolated that if the patients are complicated with pulmonary infection during EVD catheter placement and drainage procedures, the pathogens are probably transmitted to the surrounding environment through endotracheal intubation, which might contaminate the EVD drainage system during EVD catheter insertion and other procedures, thereby leading to central nervous system infection. Moreover, contaminant infection in other sites probably reduces immunity and resistance of the patients and increases the potential risk of infection to these patients. Therefore, explicit and comprehensive evaluation of the EVD indications should be performed for patients who are diagnosed with pulmonary

infection. All surgical procedures should be delivered under sterile conditions.

For all patients undergoing EVD, routine use of preventive antibiotics was not delivered. In this retrospective analysis, the usage of preventive antibiotics failed to reduce the risk of EVD-related infection in patients admitted to the intensive care unit of the Neurosurgery Department. If the patients were diagnosed with central nervous system infection, brain drainage, lavage combined with intravenous administration of antibiotics can yield high clinical efficacy [20]. The categories of antibiotics should be selected based upon the clinical experience and drug sensitivity test results.

To conclude, standard EVD catheter placement, shorter time of drainage tube retention (<10 d), lower frequency of cerebrospinal fluid specimen collection and intimate monitoring and nursing care and absolutely sterile operation can collectively contribute to reduce the risk of EVD-related infection.

Disclosure of conflict of interest

None.

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References

[1] Lwin S, Low SW, Choy DKS, Yeo TT, Chou N. External ventricular drain infections: successful implementation of strategies to reduce infection rate. Singapore Med J 2012; 53: 255-259.

[2] Williams TA, Leslie GD, Dobb GJ, Roberts B, van Heerden PV. Decrease in proven ventriculitis by reducing the frequency of cerebrospinal fluid sampling from extraventricular drains. J Neurosurg 2011; 115: 1040-1046.

[3] Mayhall CG, Archer NH, Lamb VA, Spadora AC, Baggett JW, Ward JD, Narayan RK. Ventriculostomy-related infections. A prospective epidemiologic study. N Engl J Med 1984; 310: 553-559.

[4] Lozier AP, Sciacca RR, Romagnoli MF, Connolly ES Jr. Ventriculostomy-related infections: a critical review of the literature. Neurosurgery 2002; 51: 170-181.

[5] Kim JH, Desai NS, Ricci J, Stieg PE, Rosengart AJ, Härtl R, Fraser JF. Factors contributing to ventriculostomy infection. World Neurosurg 2012; 77: 135-140.

[6] Camacho EF, Boszczowski I, Basso M, Jeng BC, Freire MP, Guimarães T, Teixeira MJ, Costa SF. Infection rate and risk factors associated with infections related to external ventricular drain. Infection 2011; 39: 47-51.

[7] Hoefnagel D, Dammers R, Ter Laak-Poort MP, Avezaat CJ. Risk factors for infections related to external ventricular drainage. Acta Neurochir 2008; 150: 209-214.

[8] Holloway KL, Barnes T, Choi S, Bullock R, Marshall LF, Eisenberg HM, Jane JA, Ward JD, Young HF, Marmarou A. Ventriculostomy infections: the effect of monitoring duration and catheter exchange in 584 patients. J Neurosurg 1996; 85: 419-424.

[9] Lo CH, Spelman D, Bailey M, Cooper DJ, Rosenfeld JV, Brecknell JE. External ventricular drain infections are independent of drain duration: an argument against elective revision. J Neurosurg 2007; 106: 378-383.

[10] Wong GK, Poon WS, Wai S, Yu LM, Lyon D, Lam JM. Failure of regular external ventricular drain exchange to reduce cerebrospinal fluid infection: result of a randomised controlled trial. J Neurol Neurosurg Psychiatry 2002; 73: 759-761.

[11] Schade RP, Schinkel J, Roelandse FW, Geskus RB, Visser LG, van Dijk JM, Voormolen JH, Van Pelt H, Kuijper EJ. Lack of value of routine analysis of cerebrospinal fluid for prediction and diagnosis of external drainage-related bacterial meningitis. J Neurosurg 2006; 104: 101-108.

[12] Kitchen WJ, Singh N, Hulme S, Galea J, Patel HC, King AT. External ventricular drain infection: improved technique can reduce infection rates. Br J Neurosurg 2011; 25: 632-635.

[13] Korinek AM, Reina M, Boch AL, Rivera AO, De Bels D, Puybasset L. Prevention of external ventricular drain--related ventriculitis. Acta Neurochir 2005; 147: 39-45.

[14] Williamson RA, Phillips-Bute BG, McDonagh DL, Gray MC, Zomorodi AR, Olson DM, Britz GW, Laskowitz DT, James ML. Predictors of extraventricular drain-associated bacterial ventriculitis. J Crit Care 2014; 29: 77-82.

[15] Clark WC, Muhlbauer MS, Lowrey R, Hartman M, Ray MW, Watridge CB. Complications of intracranial pressure monitoring in trauma patients. Neurosurgery 1989; 25: 20-24.

[16] Rafiq MF, Ahmed N, Aii S, Khan MN, Khaleeq-uz-Zaman. Culture and sensitivity pattern in patients with external ventricular drain infection. J Ayub Med Coll Abbottabad 2011; 23: 118-120.

[17] Beer R, Lackner P, Pfausler B, Schmutzhard E. Nosocomial ventriculitis and meningitis in neu-

rocritical care patients. J Neurol 2008; 255: 1617-1624.
[18] Tong SY, Davis JS, Eichenberger E, Holland TL, Fowler VG Jr. Staphylococcus aureus infections: epidemiology, pathophysiology, clinical manifestations, and management. Clin Microbiol Rev 2015; 28: 603-661.
[19] Mounier R, Lobo D, Cook F, Martin M, Attias A, Aït-Mamar B, Gabriel I, Bekaert O, Bardon J, Nebbad B, Plaud B, Dhonneur G. From the skin to the brain: pathophysiology of colonization and infection of external ventricular drain, a prospective observational study. PLoS One 2015; 10: e0142320.
[20] Gozal YM, Farley CW, Hanseman DJ, Harwell D, Magner M, Andaluz N, Shutter L. Ventriculostomy-associated infection: a new, standardized reporting definition and institutional experience. Neurocrit care 2014; 21: 147-151.