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Clinical Study

Efficacy of antibiotic-impregnated external ventricular drains in reducing ventriculostomy-associated infections

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ABSTRACT

Use of an external ventricular drain (EVD) is essential for managing patients with hydrocephalus or intracranial hypertension. While this procedure is safe and efficacious, ventriculostomy-associated infections (VAI) continue to cause significant morbidity. In this study, we evaluated the efficacy of antibiotic-coated EVD (AC-EVD) in reducing the occurrence of VAI. Between July 2007 and July 2009, 203 patients underwent placement of an EVD. A total of 145 of these patients met the inclusion criteria, with 76 patients (52.4%) receiving AC-EVD and 69 patients (47.6%) receiving uncoated EVD. Ten patients (6.9%) developed VAI, of whom three were in the AC-EVD group and seven were in the uncoated EVD group ($p = 0.19$). The mean duration between catheter insertion and positive cerebrospinal fluid culture was significantly greater in the AC-EVD group *versus* the uncoated EVD group (15 ± 4 days *versus* 4 ± 2 days, respectively; $p = 0.001$). In the uncoated EVD group, 17 of 69 patients (24.6%) were dead at 3 years *versus* 12 of 76 (15.8%) patients in the AC-EVD group ($p = 0.21$). The overall VAI rate was 6.9% with a trend toward lower infection rates in the AC-EVD group compared to the uncoated EVD group (3.9% *versus* 10.1%, respectively; $p > 0.05$).

1. Introduction

External ventricular drains (EVD) allow for diagnosis and treatment of intracranial hypertension. While their use is essential in neurocritical care, ventriculostomy-associated infections (VAI) and secondary ventriculitis lead to significant morbidity and costs. Previous clinical series have reported a 3–19% occurrence of VAI, leading to longer stays in the intensive care unit (ICU) as well as increased morbidity [1–3]. A retrospective analysis performed at the University of Michigan, USA showed that the infection rate in patients with EVD for longer than 10 days was approximately 8.6% [4]. Antibiotic-coated EVD (AC-EVD), as well as prophylactic antibiotics, are frequently used in an attempt to reduce the incidence of VAI. Poon et al. showed that antibiotic prophylaxis continued for the duration of EVD placement reduces the rate of VAI from 11% to 3% ($p = 0.01$) [5]. In addition, the advent of AC-EVD may have reduced the occurrence of VAI to less than 3% [6,7]. Following a review of the literature, the University of Michigan protocol was modified in July 2008 to require placement of the Bactiseal AC-EVD (DePuy, Raynham, MA, USA) in all patients requiring an EVD. Our objective was to perform a retrospective analysis of the impact of the use of AC-EVD on the incidence of VAI at our institution.

2. Methods

2.1. Study design

This retrospective study evaluating the incidence of VAI was approved by the University of Michigan Institutional Review Board. All patients requiring EVD placement between July 2007 and July 2009 were eligible for inclusion in the study. Exclusion criteria consisted of known or suspected infection of cerebrospinal fluid (CSF), placement of more than one EVD, replacement of the EVD within a 30 day period, and/or EVD removal less than 24 hours after insertion.

2.2. Insertion and maintenance of EVD

All EVD insertions were performed using standard sterile precautions in the operating room, angiography suite, emergency department, or neurosurgical/trauma-burn ICU. Uncoated EVD were employed prior to implementation of the July 2008 protocol. Thereafter, Bactiseal EVD impregnated with 0.15% clindamycin and 0.054% rifampicin were employed as the standard catheter. The EVD was introduced at a location approximately 1 cm anterior to

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the coronal suture in the midpupillary line. All patients received antibiotic prophylaxis with intravenous cefazolin until the EVD was removed unless the patient had a penicillin allergy, in which case intravenous vancomycin was utilized. When a pre-existing infection was being treated with a broad-spectrum antibiotic, this agent was considered to function as prophylactic coverage for the EVD. Identical insertion and maintenance protocols were used for both coated and uncoated catheter types. EVD were inspected daily by the neurosurgical team for evidence of CSF leak and infection at the insertion site. Sampling and analysis of CSF was performed only when clinical suspicion of infection existed. Such analysis included cell count with differential, glucose, protein, Gram stain, and culture.

2.3. Data collection

Inpatient progress notes, operative notes, outpatient notes, laboratory data, and radiological images were evaluated for each patient. We collected the following data points: catheter type used (coated *versus* uncoated), age, sex, diagnosis with reason for EVD implantation, performance of craniotomy, presence of subarachnoid or intraventricular hemorrhage, location of insertion, duration the EVD remained in place, history of diabetes, history of cardiovascular conditions including hypertension, antibiotic administered, use of steroids, complications associated with EVD insertion, number of insertion attempts, presence or absence of a CSF leak, presence of concomitant lumbar or subdural drain, volume of CSF drained per day, presenting Glasgow Coma Scale (GCS) score, and presence of stapled gauze *versus* adhesive transparent film dressing.

The primary endpoint of this analysis was to evaluate the incidence of VAI as defined by the occurrence of positive CSF cultures. A positive CSF culture within 1 week of removal of the EVD with clinical evidence of ventriculitis was treated with a full course of antibiotics and was also considered to represent a VAI. Secondary outcome measures included mean number of days between EVD insertion and positive CSF culture, median change in GCS score between admission and removal of EVD, need for new CSF diverting shunt placement, length of stay within the ICU following placement of EVD, and 3 year mortality. Cases of eosinophilic meningitis associated with AC-EVD were also recorded.

2.4. Statistical analysis

All continuous variables were subjected to the D'Agostino–Pearson test for normal distribution. Mean and standard deviation with range was calculated for variables with normal distribution. For variables without normal distribution, the median with interquartile range (IQR) was calculated. Univariate assessment of categorical variables with outcomes of interest was accomplished using chi-squared or Fisher exact test as appropriate. Univariate assessment of normally distributed continuous variables was performed using Student's *t*-test and non-normally distributed variables with the Mann–Whitney *U* test. The threshold for statistical significance was $p < 0.05$. All univariate associations that attained $p < 0.2$ were included, along with the exploratory variable (use of AC-EVD) in multivariate logistic regression models.

3. Results

Between July 2007 and July 2009, 203 patients had EVD placed at the University of Michigan. Fifty-eight patients were excluded from study for the following reasons: EVD replacement within a 30 day period, EVD placed secondary to ventriculitis or meningitis, bilateral ventriculostomies, or unknown EVD type.

Of the 145 patients evaluated in the final analysis, 76 (52.4%) patients received AC-EVD catheters, while 69 (47.6%) patients received uncoated EVD. Overall there were 10 positive CSF cultures (6.9%), of which nine patients had CSF drawn while the EVD was in place and one was drawn 6 days following removal of the EVD. This last patient was re-admitted with headache and neck stiffness leading to a lumbar puncture and positive CSF cultures. The distribution of variables in patients with and without VAI is shown in Table 1. Only the median volume of CSF drained attained statistical significance ($p < 0.05$) in univariate analysis with the primary outcome (VAI).

Seventy-three of 135 patients (54.1%) without VAI and three of 10 patients (30.0%) with VAI received an AC-EVD ($p = 0.19$).

Table 1
Distribution of variables in patients with and without ventriculostomy-associated infection after external ventricular drain placement

Variable	VAI absent (n = 135)	VAI present (n = 10)	*p* Value
Mean age (years) ± SD	54 ± 17	54 ± 14	0.96
Female (%)	80 (59)	7 (70)	0.96
Antibiotic-coated catheter used (%)	73 (54)	3 (30)	0.19
Diagnosis (n)			0.85
Hydrocephalus	4	0	
Intracerebral hemorrhage	20	2	
CSF leak	3	0	
SAH	65	7	
Ischemic stroke	4	0	
Traumatic brain injury	9	0	
Tumor	24	1	
Unruptured vascular malformation	6	0	
Craniotomy (%)	85 (63)	5 (50)	0.50
SAH/IVH present (%)	76 (56)	8 (80)	0.19
Diabetes (%)	19 (14)	0 (0)	0.36
Cardiovascular comorbidity (%)	61 (45)	6 (60)	0.51
Steroid use (%)	7 (5)	1 (10)	0.48
Median initial GCS score (IQR)	15 (9–15)	15 (10–15)	0.85
Total duration of EVD use, days (IQR)	7 (3–13)	11 (8–15)	0.06
Multiple passes required during EVD placement (%)	8 (6)	1 (10)	0.48
Site of EVD insertion (n)			0.87
Angiography suite	5	0	
Emergency room	35	2	
Neurological ICU	29	3	