Pediatr Drugs (2015) 17:239–244
DOI 10.1007/s40272-015-0127-3

SHORT COMMUNICATION

Antimicrobial Prophylaxis for External Ventricular Drains in Pediatric Neurosurgical Patients

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Published online: 20 March 2015

Abstract

Background Our goal was to describe the use of antibiotics for surgical prophylaxis of external ventricular drains (EVDs) in a pediatric neurosurgical population and determine the incidence of EVD-related infections among different antimicrobial prophylaxis strategies.

Main Outcome Measures This retrospective chart review included patients up to 18 years old who underwent EVD insertion at either of two tertiary care academic hospitals in the same health system between August 1, 2008, and July 31, 2012. Patients were included if they received at least one dose of antibiotics before EVD insertion. Patients who received only perioperative antibiotics were compared with those who also received antibiotics after this period. The primary endpoint was incidence of EVD-related infection. Descriptive statistics were used to summarize baseline characteristics and compare antibiotic regimens between groups. Pearson's chi square and Mann Whitney *U* tests compared nonparametric data.

Results A total of 182 EVD insertions were documented, and 88 included in the study. Of these 88, 27 were associated only with perioperative doses of antibiotics, and 61 with prolonged antibiotic use. Baseline characteristics and antibiotic choices were similar between the groups. At least 55 (63 %) catheters were antibiotic-impregnated, but types of catheters couldn't be compared between groups due to insufficient data. No central nervous system infections were identified in either group, so the primary objective could not be evaluated statistically.

Conclusion No infections were identified in any study subjects during EVD treatment. An adequately powered, multi-center prospective study should be performed to determine if prolonged use of antibiotics beyond the perioperative period is of benefit.

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Key Points

External ventricular drains (EVDs) are useful in the care of neurosurgical patients, but expose patients to the risk of infection.

It is unknown whether providing antimicrobial prophylaxis for the duration of EVD placement in neurosurgical patients decreases the risk of infection.

In this study of 88 patients, no patient experienced a new cerebrospinal fluid infection while an EVD was present, although some patients received extended prophylaxis and some did not.

1 Introduction

External ventricular drains (EVDs) are commonly used to remove excessive cerebrospinal fluid (CSF), permitting measurement and control of intracranial pressure, drainage of ventricular blood, and management of hydrocephalus [1]. Although EVDs provide many advantages in the care of neurosurgical patients, they also expose patients to risks and complications such as infection [2].

Previously reported rates of EVD-related infections range from 0 to 27 % [2]. Precautions employed to minimize the risk of EVD-related infections include skin preparation, aseptic insertion in an operating room, optimal wound care, catheter tunneling, use of a closed drainage and monitoring system, minimization of EVD interruptions, use of antibiotic-impregnated catheters, and administration of systemic antibiotics [1]. Prophylactic antibiotic administration, including choice, dose, and duration, is often based on prescriber experience because published data are lacking. Few studies exist for adult patients, and pediatric data are limited to only one retrospective study published several decades ago [2–5]. Data obtained from adults might be of limited use in pediatrics due to several differences, including disparity in infection rates.

Additionally, the prophylactic antibiotic selection has changed over time, limiting the relevance of previous data. Although ampicillin and trimethoprim-sulfamethoxazole were previously used, first- and second-generation cephalosporins, namely cefazolin and cefuroxime, are more commonly used today [2, 4]. The data that do exist are conflicting, hindering evidence-based practice. Thus, standardization, even within a single institution, may be rare.

McCarthy et al. [6] surveyed members of the Neurocritical Care Society regarding prophylactic antibiotic strategies employed in the placement of EVDs in adult patients. Of the nearly 600 neurosurgeons who responded, 73.5 % reported that they do use prophylactic antibiotics with EVDs, whereas 26.5 % reported no use of prophylactic antibiotics. Among patients receiving prophylactic antibiotics, administration of antibiotics for the entire duration of EVD placement was the antibiotic prophylaxis method most commonly used (56.3 %). Other methods included administration of one dose of antibiotics within an hour before EVD insertion (29.6 %), administration of antibiotics for the 24-h period immediately following EVD placement (5.7 %), administration of antibiotics for the first 3 days immediately following EVD placement (3.4 %), and other methods (5 %) [6].

The importance of preventing surgical site infections via evidence-based practices has continued to gain attention from national organizations, healthcare accrediting agencies, and payers. A decrease in the incidence of surgical site infections is a quality and safety goal that will be tied to hospital reimbursement. Thus, obtaining evidence to guide practice is increasingly important. Clinical practice guidelines regarding prevention of surgical site infections with antimicrobial prophylaxis were recently updated; but best practice in certain circumstances remains unclear [7]. For example, the authors of the guidelines did not recommend for or against the use of continued prophylactic antibiotics in conjunction with EVDs, but they did recommend that a single dose of antibiotics be used with shunting procedures. EVD-related infections are associated with increased length of stay in the intensive care unit, which increases the overall cost of hospitalization along with morbidity and mortality [1]. A recently published retrospective observational study in pediatric patients showed that increased EVD duration is associated with EVD-related infection [8]. However, prolonged antibiotic prophylaxis also poses risks, including increasing antimicrobial resistance and *Clostridium difficile* colitis [9]. We undertook this study to determine the incidence of EVD-related infections in pediatric neurosurgical patients who have no additional risk factors for infection and to determine if the use of prophylactic antibiotics beyond the perioperative period leads to a difference in the incidence of infection or in the resistance patterns of causative organisms.

2 Methods

We performed a retrospective chart review of pediatric patients who underwent EVD insertion at Riley Hospital for Children or at Methodist Hospital, between August 1, 2008, and July 31, 2012. Riley Hospital for Children and Methodist Hospital are both tertiary teaching hospitals within the academic campus of Indiana University Health, in the US. Patients were identified using current procedural terminology (CPT) codes (61107 and 61210). Since the CPT codes for EVD placement are the same as CPT codes

for other neurosurgery procedures, a chart review was subsequently conducted to identify patients who underwent EVD insertion.

Patients were included in the *perioperative prophylaxis group* if they received a dose of prophylactic antibiotics within 1 h before EVD placement and *all* subsequent antibiotic doses within 24 h after the initial antibiotic dose. Patients were included in the *prolonged prophylaxis group* if they received a dose of prophylactic antibiotic within 1 h before EVD placement, but continued antibiotics past the 24-h period.

Patients were included in the study if they were 18 years old or younger at the time of EVD insertion and had received at least one dose of perioperative antibiotics, as defined above, for EVD placement. Patients were excluded from the study if they had a known CSF or shunt infection at the time of EVD placement or were at increased risk for a central nervous system (CNS) infection at the time of EVD placement. Patients were considered to have an increased risk of CNS infection if CSF leakage was noted, if they had presented with a depressed skull fracture, sinus fracture, or basilar skull fracture, or if they were immunocompromised.

An EVD-related infection was defined as the presence of at least one positive CSF culture from either the EVD or lumbar puncture obtained after the EVD insertion but while the EVD was still in place. Cultures were obtained at the discretion of the treating physician as needed for clinical care; surveillance cultures were not routinely collected. Patient demographics, EVD indication, EVD type and duration, perioperative antibiotic regimen, and presence of a prolonged antibiotic regimen were collected. Data collection for each patient ended at the time of EVD removal. The primary outcome of interest was the difference in incidence of EVD-related infection between patients who received only perioperative antibiotic doses and patients who also received prolonged antibiotic doses. The secondary goal of this investigation was to describe the patients and prophylactic antibiotic regimens utilized in patients with EVDs. This study was approved by the Indiana University Institutional Review Board.

Descriptive statistics were used to summarize baseline characteristics and to compare antibiotic regimens between the two groups. Pearson's chi squared and Mann Whitney *U* tests were performed to compare nonparametric data.

3 Results

During the study period, 182 EVD insertions were performed. Of these insertions, 94 were excluded based on pre-defined exclusion criteria (Fig. 1). Of the 88 included EVD insertions, 27 patients (30.7 %) received only perioperative antibiotics and 61 patients (69.3 %) received perioperative antibiotics plus prolonged antibiotics. Baseline characteristics between the two groups were similar (Table 1).

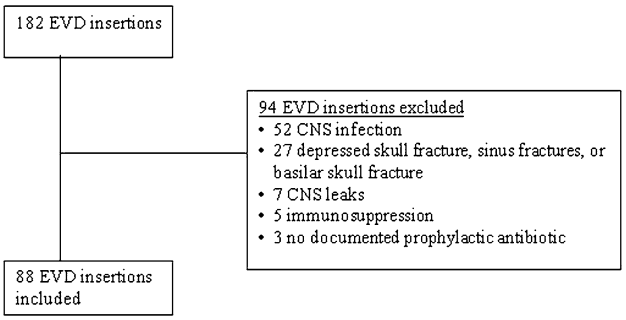

Fig. 1 Flow diagram describing inclusion and exclusion of study sample. *CNS* central nervous system, *EVD* external ventricular drain

The reasons for EVD insertion also were similar between the two groups; brain tumor, most commonly an undifferentiated posterior fossa tumor, was the most frequent indication for EVD insertion.

The majority of patients in both groups received EVDs impregnated with rifampin and clindamycin (Table 2). Nearly all patients in both groups were given cefazolin for perioperative and prolonged prophylaxis, and all patients received at least one dose of antibiotics before EVD placement. Two patients in the prolonged antibiotics group and one patient in the perioperative group received piperacillin/tazobactam because of the need for an empiric broad-spectrum antibiotic in response to positive blood cultures at the time of EVD placement.

We were not able to determine the EVD type in this retrospective review of documentation for 21 patients (24 % of the subjects). Though it is known that an antibiotic-impregnated EVD was used in at least 68.9 % of patients in the prolonged group and in at least 48.2 % of patients in the perioperative-only group, we were unable to make comparisons due to the missing data. Patients in the perioperative-only group had a shorter median EVD duration compared with patients in the prolonged group (6 vs 8 days, $p = 0.0096$). At least one culture was obtained from the majority of patients (59 of 88, 67 %). The median ($\pm$standard deviation) number of CSF cultures drawn per patient was 1.0 ± 1.25. No CNS infections were identified in either group, so the incidence of EVD infections could not be statistically compared between groups.

4 Discussion

The purpose of this study was to determine the incidence of EVD-related infections and determine if the use of prophylactic antibiotics outside the perioperative period leads

Table 1 Baseline demographic characteristics

Variable	Perioperative group ($n = 27$)	Prolonged group ($n = 61$)	p value
Age (years)			
Median (IQR)	6.6 (3.8–10.7)	6.4 (2.9–12)	0.560
Gender			
Male	16 (59.3 %)	34 (55.7 %)	0.758
EVD indication			
Posterior fossa tumor	13 (48.2 %)	30 (49.2 %)	
Other types of tumors	8 (29.6 %)	13 (21.3 %)	
Hemorrhage[a]	3 (11.1 %)	10 (16.4 %)	0.634
CSF shunt malfunction[a]	1 (3.7 %)	7 (11.5 %)	
Other[a]	2 (7.4 %)	1 (1.6 %)	

CSF cerebrospinal fluid, *EVD* external ventricular drain, *IQR* interquartile range

[a] Considered as one group for significance testing

Table 2 Characteristics of EVD insertion

Variable	Perioperative group ($n = 27$)	Prolonged group ($n = 61$)	p value
EVD type			
Antibiotic impregnated	13 (48.2 %)	42 (68.9 %)	
Nonantibiotic impregnated	1 (3.7 %)	11 (18.0 %)	
Unknown	13 (48.2 %)	8 (13.1 %)	
Perioperative antibiotic			
Cefazolin	26 (96.3 %)	59 (96.7 %)	0.998
Piperacillin/tazobactam	1 (3.7 %)	2 (3.3 %)	
EVD duration (days)			
Median (IQR)	6 (3.5–8)	8 (6–10)	0.010
Antibiotic duration (days)			
Median (IQR)	1	7 (5–9)	0.000
CNS infection			
Total	0 (0 %)	0 (0 %)	NS

CNS central nervous system, *EVD* external ventricular drain, *IQR* interquartile range, *NS* not significant

to a difference in the incidence of infection or in the resistance patterns of causative organisms in pediatric patients. Many organisms can cause infections in patients with EVDs. Normal skin flora, such as *Staphylococcus epidermidis* and *Staphylococcus aureus* (including methicillin-resistant strains), are frequently implicated in EVD-related infections. Gram-negative organisms, most commonly *Escherichia coli* and *Klebsiella pneumoniae*, also contribute to EVD-related infections [1]. Since there were no EVD-related infections identified in either group in this study, we were not able to evaluate the primary endpoint (the rate of EVD-related infection).

In a 1972 retrospective single-center study of 70 patients (mean age 7.2 years) with EVD placement, those receiving no prophylactic antibiotics ($n = 26$) were compared with patients receiving antibiotics on the day of EVD placement ($n = 44$) [5]. The infection rate for patients who did not receive prophylactic antibiotics was 27 %, significantly higher than an infection rate of 9 % in those who did receive prophylactic antibiotics. A higher infection rate was associated with longer EVD duration in both groups, which led the authors to conclude that prophylactic antibiotics should be used for the duration of EVD placement in patients in whom the anticipated EVD duration is 3 or more days.

A retrospective single-center study examined EVD infection rates in 308 adult patients who had an EVD for 3 or more days [2]. Patients received either periprocedural cefuroxime 1.5 g every 8 h for three doses or fewer ($n = 99$) or they received the same antibiotic dose and frequency for the duration of their EVD ($n = 209$). Because the rates of infection did not differ between the groups (3.8 vs 4.0 %), the authors concluded that the use of continuous prophylactic antibiotics may not offer a benefit over periprocedural dosing in adult patients with EVDs. The present study provides more recent evidence to support the performance of prospective trials regarding the duration of antibiotic prophylaxis in EVD procedures. Such studies, including

pediatric studies, are needed to further answer points of uncertainty in the current practice guidelines [7].

There have been many interventions aimed at decreasing the rate of EVD-related infections reported in the literature. Efficacy of antibiotic-impregnated EVD catheters was demonstrated in adults in a 2003 prospective randomized clinical trial [10]. It can be difficult to determine the impact of one intervention when multiple interventions have been instituted, but a bundle approach with various interventions including use of antibiotic-impregnated catheters decreased the incidence of EVD-related infections from 9.2 % to nearly 0 [11]. Findings of another study that evaluated over 300 adults and children indicate that antibiotic-impregnated catheters are cost effective in decreasing incidence of EVD-related infection [12]. It is our impression that antibiotic-impregnated catheters are commonly used in children with EVDs, which again raises the question of need for prolonged systemic antibiotics.

There were several limitations in the present study, many related to its retrospective nature. Documentation procedures were not uniform during the study period; rather, they improved throughout the study period as new functionality of patients' electronic medical records allowed for standardized processes for recording data. Although we suspect that a large majority of catheters were antibiotic-impregnated due to recent purchasing information, the type of catheter was not documented in many cases. We did not evaluate the physical location of the EVD placement procedure, so we cannot compare those placed in an operating room with those placed at the bedside. Furthermore, the frequency of EVD manipulation was not documented, which would have been valuable to quantify since minimizing EVD manipulation has been associated with lower infection rates. This study included two sites, but differences in practice at other sites may limit the external validity of these results. Although this study included several years of data, the small sample size may have limited the ability to assess the primary endpoint. Patients with previous CSF infection or at high risk of CSF infection were excluded as a means of controlling for additional factors beyond the antibiotic prophylaxis, but this decreased the number of evaluable patients and hinders broader application of results. This study only examined EVD-related infections during the period of CSF drainage. Definition of CSF infection was limited to positive CSF cultures, so patients with elevated CSF white blood cells and clinical signs of infection with negative cultures would have been missed. Though not systematically evaluated, progress notes plus systemic temperatures were reviewed in the course of data extraction and no clinical infections were noted. Results of CSF cultures obtained after EVD removal were not examined, preventing identification of infections after EVD removal and outcomes such as readmissions due to late infection. It is possible that longer follow-up would have led to identification of additional infections. Additionally, 31 % of the patients initially identified as possible study patients were excluded because of the presence of additional neurosurgical risk factors for infection. Although this exclusion was done to limit the risk for infection to the presence of the EVD alone, it does prevent extrapolation of these results to a considerable percentage of patients who require EVD placement.

5 Conclusion

Regardless of the antimicrobial prophylaxis strategy used, no EVD-related infections were noted in this sample of pediatric patients who did not have additional risk factors for CNS infections and who predominately received antibiotic-impregnated EVDs. This study includes preliminary data to suggest that prolonged antibiotic duration may not provide a benefit in a similarly 'low-risk' pediatric population. It would be reasonable and desirable to conduct prospective research in a population of pediatric patients without additional infection risk factors to assess the safety and efficacy of perioperative-only antibiotic dosing for EVD prophylaxis.

Acknowledgments The authors report no conflicts of interest concerning the materials or methods used in this study or the findings specified in this paper. This study was not funded. All ethical standards were strictly followed.

Portions of this study were presented as a platform presentation at the 28th Annual Great Lakes Pharmacy Resident Conference, Purdue University, West Lafayette, Indiana, USA, April 25, 2013.

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