Antibiotic Prophylaxis for External Ventricular Drains in Neurosurgical Patients: An Audit of Compliance with a Clinical Management Protocol

M. A. LUCEY, J. A. MYBURGH
Intensive Care Unit, The St. George Hospital, Sydney, NEW SOUTH WALES

ABSTRACT

Objective: *To examine the clinical impact of a management protocol for external ventricular drains (EVD).*

Patients and Methods: *All patients with EVDs over a six-month period were reviewed retrospectively. Data concerning the indications for EVD placement, antibiotics and cerebrospinal fluid (CSF) analyses were collected. A restrictive antibiotic protocol (e.g. intravenous cephalothin 1g 6-hourly for 24 hours, unless other antibiotics were prescribed for a documented pre-existing infection) was introduced for all patients requiring placement of an EVD during the following six months and all patients were observed prospectively. Daily CSF samples were collected under sterile conditions and examined for organisms, cells, glucose and protein and sent for microbiological culture. External ventricular drains were removed after five days and replaced if further monitoring or CSF drainage was required. Adherence to the protocol and the incidence of ventriculitis was determined.*

Results: *Twelve patients with EVDs were identified during the 6 month pre-protocol period and 15 patients with EVDs were identified during the 6 month post-protocol period. There was no significant difference between the total (72 vs 88 days) and mean (6 vs 5.9 days) drain placement times between the two groups. There was no significant difference between the mean numbers of CSF samples in the two groups. CSF aspirates were not analysed in 35/72 samples (49%) in the pre-protocol group compared with 45/88 (51%) samples in the post-protocol group.*

Positive CSF Gram-stains were found in 3/12 (25%) patients in the pre-protocol group and in 0/15(0%) in the post-protocol group. Positive CSF cultures decreased significantly in the post-protocol group (17 vs 5, p = 0.0009). Prophylactic antibiotics were prescribed in 5/12 (42%) patients in the pre-protocol group compared with 12/15 (80%) patients in the post-protocol group.

Conclusions: *The protocol was associated with a statistically significant improvement in compliance with antibiotic prescription and reduction in the incidence of positive CSF cultures.* (**Critical Care and Resuscitation 2003; 5: 182-185**)

Key words: External ventricular drain, ventriculitis, cerebrospinal fluid, antibiotics, prophylaxis

Perioperative antibiotics have an established role in the prevention of infection with guidelines for antibiotic prophylaxis directed at potential organisms for the period of infective risk. The awareness of antibiotic-associated complications, particularly the development of resistance and nosocomial sepsis, has resulted in shorter duration of prescription. Despite the promulgation of evidence-based guidelines, there are variable prescription practices and compliance with these guidelines.

Correspondence to: Associate Professor. J. A. Myburgh, Intensive Care Unit, The St. George Hospital, Kogarah, New South Wales 2217 (e-mail: j.myburgh@unsw.edu.au)

Patients undergoing insertion of an EVD for neuromonitoring or drainage of cerebrospinal fluid (CSF) are at risk of developing ventriculitis. A sterile technique, perioperative antibiotics and microbiological surveillance of the CSF are essential for the prevention of infection. In 1994, the Infection in Neurosurgery Working Party recommended that antibiotic prophylaxis for CSF shunt surgery be delegated to the attending surgeon.[1] Suggestions for prophylaxis included intraventricular vancomycin and gentamicin for internal infection and first- or second-generation cephalosporins for external infections. For sterile, non-implant surgery a single dose of a first- or second-generation cephalosporin was recommended, with a single dose of amoxicillin/clavulinic acid recommended for clean-contaminated procedures.

The ambiguity of these recommendations may have, in part, contributed to variable clinical practice. Additional standards for antimicrobial prophylaxis in surgical procedures published in 1994 did not conclusively address EVD prophylaxis.[2]

Following a perceived increased incidence of positive CSF cultures in a sequence of head injured patients monitored using EVDs in our intensive care unit, a retrospective audit of the management of these patients over a six month period was conducted. Following this review, an antibiotic prescription and drain management protocol was developed in accordance with current evidence. Subsequent practice was reviewed 6 months after the implementation of this protocol.

PATIENTS and METHODS

Institutional ethics committee approval was obtained to conduct this study. All patients admitted to the intensive care unit with an EVD were included. Intravenous cephalothin (1g 6-hourly for 24 hours) was the antibiotic of choice, unless other appropriate antibiotics were prescribed for a documented pre-existing infection. Daily CSF samples were collected under sterile conditions and examined for organisms, cells, glucose, and protein and sent for microbiological culture.

External ventricular drains were removed after five days and replaced if further monitoring or CSF drainage was required. External ventricular drains left in situ for longer than 5 days, due to technical reasons such as cerebral oedema making reinsertion difficult, were managed as above. Patients who required a second drain were counted as a separate patient and the protocol was restarted.

Ventriculitis was defined as the presence of pathogenic organisms in CSF on Gram-stain or a positive culture, and was treated with appropriate antibiotics until sterility of the CSF was achieved. The presence of CSF pleocytosis alone was not regarded as sufficient for a diagnosis of ventriculitis. Data collected included patient demographics, the indication for, and duration of, EVD, antibiotic prescription practice and CSF data.

Statistics

Values are presented as the mean ± SD (continuous variables) or as a percentage of the group from which they were derived (categorical variables). Differences within and between non-parametric groups were analysed using Fisher's Exact test using a two-tailed t-test. A p value < 0.05 was considered to indicate statistical significance.

RESULTS

Twelve patients with EVDs were identified in first 6 months and 15 patients with EVDs were identified in the 6 months following implementation of the protocol. Demographic data and diagnosis are shown in Table 1. There was no statistically significant difference between patient ages and APACHE II scores.

Table 1. Demographic data of patients with external ventricular drains in the pre-protocol and post-protocol groups

	Pre-protocol (n=12)	*Post-protocol (n=15)*
Male:Female	9:3	9:6
Age (years)	49.6 ± 20.5	40.6 ± 17.5
APACHE II (mean ± SD)	17.9 ± 4.7	19.8 ± 3.2
Diagnosis		
Head Injury	7	8
Subarachnoid haemorrhage	3	5
Hydrocephalus	2	2

APACHE II = acute physiology and chronic health evaluation score.

A summary of the management of the EVDs is shown in Table 2. There was no statistically significant difference between the total drain placement times between the two groups (72 vs 88 days). Despite the protocol's recommendation to review all drains for removal at, or before, day five, the mean duration of drain placement was similar in both groups (6 vs 5.9 days).

There was no statistically significant difference between the mean numbers of CSF samples in the two groups. Cerebrospinal fluid aspirates were not sent for analysis in 35 of a potential 72 samples (49%) in the

pre-protocol group compared with 45/88 (51%) samples in the post-protocol group. Of the omitted samples in the post-protocol group (n = 45), 16 (35%) were omitted due to inability to aspirate CSF (either due to raised intracranial pressure and/or compressed lateral ventricles), 12 (27%) because the drain had been inserted or removed on that day, 8 (18%) due to medical oversight, 6 (13%) for surgical reasons requiring the drain to remain closed and 3 (7%) in patients where treatment had been withdrawn.

Table 2. Summary of the management of external ventricular drains

	Pre- protocol (n=12)	*Post-protocol (n=15)*	*p*
Total drain placement time (days)	72	88	NS
Mean drain placement time (days)	6.0	5.9	NS
Drains removed at day 5 (%)	6/12 (50)	9/12 (60)	NS
Total CSF samples drawn	37	43	NS
CSF samples per patient	3.1	2.9	NS
Omitted CSF samples (%)	35/72 (48)	45 (51)	NS
Number of positive gram stain (%)	3/37 (8)	0/43 (0)	NS
Number of positive culture (%)	17/37 (45)	5/43 (12)	0.0009

CSF = cerebrospinal fluid.

In the pre-protocol group, positive Gram-stains were identified in 3/12 (25%) patients. A total of 17 positive CSF cultures were isolated from this group. Two patients had sequential positive cultures for *Staphylococcus aureus*, 1 patient developed a polymicrobial ventriculitis growing *Acinetobacter*, *Serratia* and *Enterococcus* spp., in sequential cultures. One patient grew a coagulase-negative *Staphylococcus* as a sole isolate. In the post-protocol group no positive Gram-stains were identified. A total of 5 CSF cultures were positive, which was significantly lower than the pre-protocol group (p = 0.0009). Two patients yielded separate positive cultures with different organisms: coagulase-negative *Staphylococcus* in one sample and *Pseudomonas* spp., in another; and Gram-negative bacilli in one sample and coagulase-negative *Staphylococcus* spp., in two others). No polymicrobial infections were identified in the post-protocol group.

A summary of the indications and duration of antibiotics is shown in Table 3. In the pre-protocol group, 5/12 (42%) patients received prophylactic antibiotics: these were discontinued at 24 hours in 1 patient; continued for a documented clinical indication in 1 patient and continued "prophylactically" without indication in 3 patients. Four patients did not receive any antibiotic prophylaxis and 4 patients had other indications for antibiotic therapy on admission.

Table 3. Summary of indications and duration of antibiotic prescription

	Pre-protocol	*Post-protocol*	*p*
Prophylaxis only (%)	5/12 (42)	12/15 (80)	NS
Ceased after 24 hr (%)	1/5 (20)	10/12 (83)	0.02
Continued for another reason (%)	1/5 (20)	0/12 (0)	NS
No reason for continuation (%)	3/5 (60)	2/12 (17)	NS
No antibiotics given (%)	4/12 (33)	2/15 (13)	NS

In the post-protocol group, 12/15 (80%) patients received prophylactic antibiotics. Of these, 10/12 (83%) were discontinued at 24 hours, which was significantly different form the pre-protocol group (p = 0.02), whilst 2 (17%) were continued without indication. Two (17%) patients did not receive any antibiotics and 1 (8%) had a separate indication for antibiotics on admission to the intensive care unit.

DISCUSSION

The aim of this study was to examine compliance with a protocol for the antibiotic management of EVDs in our intensive care unit and its impact on the incidence of associated ventriculitis.

There are various definitions for the diagnosis of CSF infection. These may be based solely on the identification of pathogenic organisms on culture,[3] and/or associated with increased cell counts and/or altered CSF biochemistry.[4] For the purposes of this study, we defined CSF infection as the presence of organisms in the CSF sample identified by Gram-stain or isolated by culture.

Peri-operative prophylaxis is the most common indication for antibiotic therapy in intensive care unit patients.[5] Despite national, international and institutional evidenced-based guidelines, compliance with recommended prescription practices is variable. The reasons for this are many and include clinician preference, failure to review medication on a daily basis and "omission" to discontinue antibiotics, lack of published protocols within individual units and a perceived,

yet unvalidated concern that "premature" cessation of antibiotics may be associated with an increased incidence of infection. The latter point has been identified in neurosurgical patients in a number of small case series where the morbidity and mortality of ventriculitis associated with EVDs are high.[1]

The complications of overuse of antibiotics are associated with an identifiable morbidity and mortality. These include the development of multiply resistant organisms, polymicrobial infection and antibiotic associated diarrhoea. These complications are associated with an increased length of intensive care stay, hospital stay and cost.

The antibiotic protocol for this study was modified from the Therapeutic Guidelines Ltd, publication "Antibiotic Guidelines".[6] In addition to a sterile insertion, short term (i.e. 24 hours) use of a first generation cephalosporin was prescribed, with the first dose administered before the surgical incision. This was designed to inhibit colonisation or infection of a skin-associated Gram-positive species (e.g. *Staphylococcus aureus*) during the insertion. Thereafter, a meticulous sterile technique for drain manipulation and daily CSF surveillance formed the cornerstone of management.

An increased incidence of EVD infection is associated with two independent factors. There is a correlation between infection and the duration of drainage, though it does not seem to be simple or linear.[7] There is an increased risk of infection over the first ten days suggesting that changing the catheter after 5 - 8 days may be associated with a decreased risk of infection, although this has not been validated and may be associated with morbidity due to re-insertion of the drain. Other studies, however, have failed to identify a relationship between duration of drainage and infection.[8]

Secondly, breakage of the drain circuit, either to monitor intracranial pressure or to drain CSF for therapeutic or surveillance reasons is associated with an increased incidence of infection. This relates primarily to loss of sterility by frequent handling of the catheter, but poses a dilemma where circuit disconnection is required for clinical reasons.

Our study identified that the promulgation of a protocol was associated with significantly improved antibiotic prescription compliance. Prophylactic antibiotics were discontinued after 24 hours in the majority of patients in the post-protocol group. Whilst there was an improvement in antibiotic prescription practice, the number of CSF samples taken for surveillance did not increase, as recommended by the protocol. There were valid reasons for not breaking the EVD circuit in the majority of the omitted samples in the post-protocol group, suggesting that routine CSF sampling needs to be determined on important clinical grounds.

Secondly, there was a statistically significant reduction in the incidence of positive CSF cultures following implementation of the protocol. No patients developed polymicrobial ventriculitis in the post-protocol group. Although the number of patients in this study was too small to make firm conclusions about this association, it may be concluded that a restrictive antibiotic prescription protocol was not associated with an increase in infection rates. Whether this practice translates to a clinically significant reduction in patient mortality, morbidity and reduction in associated costs due to prolonged antibiotic administration should be addressed in an appropriately powered randomised trial.

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