Clinical parameters do not predict infection in patients with external ventricular drains: a retrospective observational study of daily cerebrospinal fluid analysis

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A retrospective review was conducted of patients with external ventricular drains (EVDs) *in situ* in order to ascertain the utility of daily cerebrospinal fluid (CSF) analysis in such patients. All laboratory requests for CSF analysis, which were sent to the Microbiology Department, Auckland City Hospital, New Zealand, were reviewed to identify patients with EVDs *in situ*. The patients' clinical records were reviewed and information was obtained regarding their age, ethnicity, indication for EVD, duration of EVD, CSF analysis results, daily temperatures, Glasgow Coma Scale (GCS) and the presence of other infections. For CSF samples that grew organisms, the patients' notes were reviewed to ascertain whether the organism was a contaminant or was representative of EVD-associated ventriculitis. A total of 454 CSF specimens from 60 patients were reviewed. Of the 56 CSF specimens that were culture-positive, 40 (71 %) were found to reflect clinical infection. Routine CSF analysis identified nine episodes of EVD-associated ventriculitis. Coagulase-negative staphylococci and *Staphylococcus epidermidis* were the most common isolates and were associated with ventriculitis approximately half of the time. Gram-negative isolates were less frequently isolated, but, when present, were always associated with ventriculitis. This study found that patient temperature and GCS did not allow early prediction of EVD-associated ventriculitis.

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INTRODUCTION

External ventricular drains (EVDs) are used to monitor and treat elevations in intracranial pressure. Rates of EVD-associated ventriculitis range from 3.4 to 21.9 % (Arabi *et al.*, 2005; Aucoin *et al.*, 1986; Hader & Steinbok, 2000; Ohlstrom *et al.*, 1989; Pfisterer *et al.*, 2003; Schade *et al.*, 2005; Stenager *et al.*, 1986). Our centre routinely performs daily analysis of cerebrospinal fluid (CSF) taken from the EVD of neurosurgical patients. The value of this practice, however, remains unproven (Meredith *et al.*, 1997). The aim of the current study was to determine whether clinical parameters are of value in predicting ventriculitis in patients with an EVD *in situ* and whether routine daily CSF samples are needed to detect EVD-associated ventriculitis.

METHODS

We performed a retrospective observational study of patients with EVDs *in situ* from July 2005 to March 2006. At our centre, EVDs are inserted by sterile technique in the operating theatre or in the high-dependency

unit of the neurosurgical ward, and are attached to a closed external-pressure monitor and drainage system. EVD samples are drawn daily by a senior neurosurgery staff nurse. The three-way stopcock is turned off from the external drainage system and the proximal outlet port is swabbed with 2 % chlorhexidine in alcohol. A sterile needle is inserted into the port and 3 ml CSF is withdrawn slowly from the patient.

CSF analysis and culture were performed using standard methods. The clinical records were reviewed and information regarding patient demographics, indication for EVD, duration of EVD, CSF analysis results, peak daily temperatures and daily Glasgow Coma Scale (GCS) when the EVD was *in situ*, and the presence of other infections were recorded. If an organism was isolated from a patient's CSF, the patient was reviewed by an infectious diseases specialist to determine the significance and to direct treatment if required. An organism was classified as a true pathogen if it was associated with the presence of ventriculitis. The criteria for diagnosis of ventriculitis included all of the following: (i) positive CSF culture from an EVD; (ii) CSF leukocytosis $>5 \times 10^6 \text{ l}^{-1}$; (iii) clinical diagnosis of ventriculitis by an infectious diseases physician. The Mann–Whitney test with a two-tailed *P* value was used to compare CSF protein, CSF glucose, temperature and GCS of patients with and without EVD-associated ventriculitis. CSF white cell count was corrected for red blood cells in the CSF by subtracting one white cell for every 1000 red blood cells.

A study proposal was submitted to the local ethics committee, who advised that formal ethical approval was not required for this laboratory-based quality-assurance audit.

Abbreviations: CSF, cerebrospinal fluid; EVD, external ventricular drain; GCS, Glasgow Coma Scale.

RESULTS AND DISCUSSION

During the study period, 60 patients had 454 CSF samples taken from their EVDs. The median age of the patients was 50 years (range: 2 months–87 years). Twenty-seven patients (45 %) were male. The indications for EVD placement are given in Table 1.

Of the 454 CSF samples, 56 (12.3 %) yielded organisms. Excluding duplicate isolates, there were 32 organisms identified. Only 13 (41 %) were considered true pathogens. These organisms accounted for 12 episodes of ventriculitis in 10 patients. One patient had two different organisms causing a single episode of ventriculitis and two patients had two episodes of ventriculitis with different organisms. Three episodes represented recurrence of previously known ventriculoperitoneal shunt infection and these were excluded. Thus we identified a total of nine new episodes of EVD-associated ventriculitis in 60 patients with EVDs *in situ*.

EVDs were maintained for a median duration of 6 days (range: 1–23 days). The median number of days from EVD insertion to EVD-associated ventriculitis was 10 days (range: 1–16 days).

The Gram stain was positive in almost half (45 %) of the CSF samples from patients with EVD-associated ventriculitis, but none of the specimens that grew contaminants had a positive Gram stain. All of the organisms that caused infection were isolated by direct culture as well as by enrichment culture, and all organisms that only grew on enrichment culture were contaminants.

More than one CSF culture result was positive in six out of nine episodes of EVD-associated ventriculitis, with a median of three (range: one to eight) positive CSF specimens. In contrast, all of the organisms deemed contaminants were only isolated in a single CSF sample.

Coagulase-negative staphylococci (including *Staphylococcus epidermidis*) were the most common organisms isolated and less than half (41 %) were considered significant. Gram-negative organisms were isolated infrequently, but, when present, were always clinically significant. Table 2

Table 1. Indications for EVD placement

Indications for EVD	No. of patients (%)
Subarachnoid haemorrhage	25 (41)
Intracranial haemorrhage	10 (17)
Tumour	11 (18)
Shunt malfunction	7 (12)
Hydrocephalus – other*	7 (12)

*Patients in this group included those who had hydrocephalus secondary to congenital malformations, post-operative hydrocephalus, normal pressure hydrocephalus and hydrocephalus secondary to a cerebrovascular accident.

Table 2. Organisms isolated from EVD CSF specimens

Organism	No. of isolates	No. of pathogens (%)
Coagulase-negative <i>Staphylococcus</i>	11	5 (45)
<i>Staphylococcus epidermidis</i>	6	2 (33)
<i>Staphylococcus aureus</i>	1	1 (100)
<i>Enterococcus faecalis</i>	1	1 (100)
<i>Micrococcus</i> species	4	0
<i>Corynebacterium</i> species	3	0
Aerobic sporing bacillus	1	0
Gram-variable bacillus	1	0
<i>Escherichia coli</i>	1	1 (100)
<i>Pantoea</i> species	1	1 (100)
<i>Acinetobacter</i> species	2	2 (100)
Total	32	13

shows the breakdown of organisms isolated in patients with EVDs *in situ*.

The median CSF glucose level was lower in patients with EVD-associated ventriculitis than in patients without infection, but the median CSF protein level was not different, as shown in Table 3. There was no difference in the median peak daily temperature and median GCS between patients with and without EVD-associated ventriculitis, as shown in Table 4.

In our study population of neurosurgical patients with EVD *in situ*, the incidence of EVD-associated ventriculitis was 15 %. This is similar to the incidence found in other centres (Arabi *et al.*, 2005; Aucoin *et al.*, 1986; Hader & Steinbok, 2000; Ohrstrom *et al.*, 1989; Pfisterer *et al.*, 2003; Schade *et al.*, 2005; Stenager *et al.*, 1986). The diagnosis of EVD-associated ventriculitis can be difficult as many of the patients in neurosurgical units are often unable to report clinical symptoms suggestive of ventriculitis such as

Table 3. CSF parameters in infected and non-infected CSF

CSF analysis	Infected CSF (n=40)	Non-infected CSF (n=335)*	P value
Median glucose (mmol l ⁻¹)	3.3 (0.31–6.8)	4.1 (0.08–8.2)	<0.001
Median protein (g l ⁻¹)	0.33 (0.17–10.4)	0.45 (0.03–16.6)	0.19
No. of culture-positive CSFs	40	16	NA
No. of CSFs with contaminants	2†	16	NA

NA, Not applicable.

*Culture-negative specimens from patients with known ventriculitis have been excluded.

†Two CSF specimens with pathogens also grew contaminant organisms.

Table 4. Clinical parameters in patients with and without ventriculitis

Clinical parameter	Ventriculitis (n=10)	No ventriculitis (n=50)	P value
Median temperature [°C, (range)]	37.4 (37.1–39.1)	37.4 (36.6–40.3)	0.52
Median GCS (range)	13 (3–15)	13 (3–15)	0.39

headache, neck stiffness and nausea (Lessing & Bowler, 1996). As a consequence, daily CSF sampling has become routine practice.

Published studies investigating the value of clinical signs and symptoms for predicting infection in this setting have conflicting results. In a paediatric population, routine CSF screening was not found to be necessary (Hader & Steinbok, 2000). Findings from this study indicated that if CSF cultures are performed for new fever ($>38.5^{\circ}\text{C}$), peripheral leukocytosis, neurological deterioration or a change in CSF appearance, infections will be identified in a timely fashion. In contrast, another study in adults found that no single clinical or laboratory parameter, including fever, leukocytosis, CSF protein and CSF glucose, could reliably predict or exclude a shunt infection (Meredith *et al.*, 1997). Our results support the conclusion of this study. We demonstrated that clinical parameters such as temperature and GCS were not reliable predictors of ventriculitis in patients with an EVD *in situ*. In our patient group, regular CSF sampling was necessary to identify patients with EVD-associated ventriculitis. However, a limitation of our study is that its observational nature precluded blinding of clinicians diagnosing EVD-associated ventriculitis in the neurosurgical patients.

Whilst acknowledging that this is a retrospective observational study, from the laboratory perspective there were a number of helpful clues for the clinician as to the likely significance of a positive CSF culture result. CSF samples from patients with confirmed EVD-associated ventriculitis were more likely to be positive in consecutive cultures and to have organisms seen in the Gram stain.

It needs to be noted that the technical time required for the processing of CSF samples is considerable and the use of enrichment broths did not provide any information additional to that of direct culture in the present study. In fact, all organisms isolated only from the enrichment broth were considered to be contaminants. Other authors

have also questioned the value of enrichment broths (Lessing & Bowler, 1996; Meredith *et al.*, 1997; Morris *et al.*, 1995). It has been suggested that the use of enrichment broth culture should be confined to CSF specimens with a high leukocyte count or positive Gram stain. Furthermore, any organism isolated from the enrichment broth alone should be isolated on repeat cultures to be considered significant (Lessing & Bowler, 1996).

In conclusion, we found that temperature and GCS are not reliable predictors of EVD-associated ventriculitis in patients with EVDs *in situ*. The use of enrichment broth cultures does not add to the diagnosis of EVD-associated ventriculitis, increases the number of contaminants isolated and should not be performed. A large randomized prospective study is required to determine whether the frequency of CSF sampling can be safely reduced from daily in patients with EVDs *in situ* without impacting on clinical outcome.

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