Surveillance of infection associated with external ventricular drains: proposed methodology and results from a pilot study

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SUMMARY

Background: The insertion of external ventricular drains (EVD) is necessary in some neurosurgical patients but increases the risk of meningitis/ventriculitis. While there are well recognised risk factors, the proportion of patients developing meningitis/ventriculitis varies partly due to differences in definitions. A multi-disciplinary working group was established to agree definitions for EVD-associated meningitis/ventriculitis and a surveillance system was piloted in four centres in the UK and Ireland.

Methods: Definitions were agreed based on those previously published and on clinical and microbiological criteria. An agreed dataset was developed to monitor patients after the insertion of an EVD and until the EVD was removed. Risk factors and the microbial aetiology were recorded.

Findings: Four neurosurgical centres participated with between 61 and 564 patients being surveyed in each unit. The vast majority of drains were cranial. Intra-cranial haemorrhage was the most common indication for the EVD insertion. Between 6 and 35% were inserted by consultants compared to junior doctors. The proportion developing meningitis/ventriculitis varied from 3-18% and from 4.8-12.7/1000 EVD days. Coagulase negative staphylococci were the most common microbial causes.

Conclusions: The routine and on-going monitoring of patients with an EVD *in situ* to detect meningitis/ventriculitis presents logistical difficulties and few units undertake this. We believe that a national system of surveillance with agreed definitions and a methodology to enable unit-to-unit comparisons of EVD meningitis/ventriculitis, based on this pilot study, is both needed and feasible. This will in turn inform quality improvement processes leading to the minimisation of infection.

Introduction

Patients undergoing neurosurgery are at increased risk of healthcare-associated infections (HCAI). In the 2006 four - country prevalence survey of HCAI, the prevalence rate in neurosurgery was 10.5%.[1] Incidence studies of neurosurgical units in Italy and Germany found that meningitis occurred in 4-8% of patients.[2,3] Post-operative meningitis/ventriculitis is particularly a risk when an external ventricular drain (EVD) is inserted to monitor or control intracranial pressure.

Beer and colleagues conducted a Medline literature search of ventriculitis/meningitis and the rate of infection varied from 5 to 20%.[4] This wide variation may relate to the diagnostic criteria used. Amongst the risk factors they identified were: the duration of EVD, the frequency of EVD manipulations, the presence of intra-ventricular haemorrhage and the surgical technique used in inserting the device; the rate is lower when the device is tunnelled under the skin after exit from the cranium with skin puncture distally from this.[4] A retrospective cohort study using data from national surveillance in the Netherlands was used to develop prediction models that would assist in the detection of EVD-related meningitis.[5] Observed and predicted rates of infection were compared and the correlation was approximately 95% between both. Predictive factors for meningitis were abnormalities of the CSF such as raised white cell count, the type of drain (ventricular or lumbar), and whether admission to an intensive care unit was required.[5]

A wide variety of criteria to diagnose meningitis/ventriculitis are used, some of which are exclusively microbiologically based, i.e. a positive CSF culture, while others include microbiology findings, clinical presenting features and CSF abnormalities such as increased CSF leukocyte count.[6] For surveillance purposes, it is preferable not to include a decision to treat with antibiotics because meningitis/ventriculitis may be mimicked by other conditions,

e.g. intra-cranial haemorrhage, and antibiotics may be given to treat infection at other sites in a seriously ill patient. A further challenge for surveillance is selecting an appropriate denominator. Rates of infection are often calculated as numbers of patients with infection as a percentage of the total with an EVD. However, the use of denominators that account for the duration of the device are preferable, e.g. per 1,000 EVD days as the risk of infection increases the longer the EVD is *in situ*.

Most causes of meningitis/ventriculitis are skin organisms and therefore staphylococci, i.e. *Staphylococcus epidermidis* and *S. aureus*, account for nearly 80% followed by a variety of other organisms that include aerobic Gram negative bacilli (AGNB) and occasionally fungi.[4] The isolation of *S. epidermidis* or other coagulase negative staphylococci (CoNS) in the CSF needs to be interpreted with caution as this may represent contamination and can result in over-treatment.

In the absence of a national surveillance system of neurosurgical meningitis/ventricultis, a multi-disciplinary working party was established and funded under the auspices of the Healthcare Infection Society to: agree definitions, identify the challenges in establishing a national surveillance system and highlight preventative strategies. The purpose was to test the feasibility and practicality of a surveillance system to measure the incidence of ventriculitis associated with EVD in neurosurgical patients. Here we report on the agreed definitions and their use, a suggested dataset, and the results from a multi-centre UK and Ireland pilot surveillance system.

Methods

While the insertion of an EVD is a surgical procedure, the device provides an external route by which pathogens may gain access to the ventricles. The risk of infection is therefore likely to be influenced by the length of time that the device remains *in situ* and the extent to

which it is manipulated during this period, rather than specifically to the insertion procedure. The methodology developed for this surveillance was therefore based on the methods used for central vascular catheters, rather than surgical site infection, and used device days as a primary denominator to calculate the risk of EVD-associated ventriculitis.[7,8] The data captured were used to calculate the following metrics:

- Rate of ventriculitis/1000 EVD days
- Percentage of patients with EVD who developed ventriculitis

The number of EVD days was determined as the days between device insertion and device removal for all patients included in surveillance.

A patient-level surveillance method was employed and each patient with a newly inserted drain was followed prospectively to identify if ventriculitis occurred.[9] Table I indicates the variables captured for each patient included in the surveillance. Surveillance was continued until the device was removed or the patient was transferred/discharged or died.

The case definitions for EVD-associated ventriculitis were developed after much discussion and consideration of existing published ones, and were adapted from Horan *et al* 2008, to distinguish probable from definite meningitis/ventriculitis (Table II).[10] Cases of ventriculitis clearly associated with a recently removed EVD were included, and if an EVD was replaced this was considered as a new device and a new surveillance record commenced. A new episode of infection was recorded if a different microorganism was isolated from the CSF or the same microorganism was isolated from the CSF but at least 4 weeks had elapsed from a previous infection and there was evidence that the first infection had resolved.[11] When definite or probable venticulitis met the definition, the causative pathogen was recorded.

Local policies and demographic data

Local policies for the insertion and management of EVD vary. Data were therefore captured from units participating in the surveillance related to local policies on the type of EVD used, whether devices were tunnelled, type of dressing, and protocols for sampling, manipulation and replacement of EVDs. For each EVD included in the surveillance, a set of patient data (age, gender, BMI) and device data were captured (see Table I). If the EVD was manipulated the date and reason for manipulation were recorded.

Data collection

Data were collected locally by medical microbiologists, neurosurgeons or other clinical staff by prospective surveillance of all patients who had an EVD inserted during the study period, using a standard protocol.

Ethics

Since this study comprised the capture of routinely available data for the purpose of surveillance of infection, ethical approval was not required.

Results

Four centres participated in the pilot surveillance project ranging in size from a unit performing 1063 procedures a year (unit 1) to the largest unit which performed 2643 procedures annually (unit 2). In all of the units (Table III), EVDs were tunnelled. There was variation in the frequency of CSF sampling between the unit even if it is was mainly carried out as clinically indicated. However, in one unit, it also varied according to the individual consultant neurosurgeon. Likewise, data captured in the unit questionnaire demonstrated variations in unit protocols for the frequency of EVD manipulation from less than once a week in unit 2 to weekly and one or more times per week in unit 1 (Table III). We were not able to reliably record the reasons for EVD manipulation during prospective data capture.

The number of patients that were surveyed varied from 61 in unit 3 to 564 in unit 4 where there was an ongoing programme of surveillance of infection following the insertion of EVDs. Also, some patients had more than one EVD inserted due to the need to remove and replace an EVD because of blockage. The duration of EVDs *in-situ* varied (Table IV) from 5 days or less to greater than 10 days. The vast majority of drains were inserted cranially. In unit 3 only cranial EVDs were surveyed. Antibiotic-impregnated devices accounted for 73.7% (660/895) EVDs whilst silver coated EVDs were used in only two units and accounted for 0.44% (4/895). However, two units (1 and 4) frequently used both standard and antibiotic-impregnated devices.

The main indications for the insertion of the EVD were haemorrhage (47.3% 473/895) followed by tumour (21.6% 193/895). A minority of EVDs were inserted by consultants (21%, range 6%-35%). A total of 45 patients with an EVD developed an infection, a rate of 5.02%, ranging from 3% in unit 4 to 18% in unit 1. The latter unit also appeared to perform the most manipulations of EVDs. The rates per 1,000 EVD days were: 12.7 in unit1, 5.17 in unit 2, 4.8 in unit 3 and 5.9 in unit 4. The median duration of EVD use for patients with an infection compared to those without was: 19 versus 10 days in unit 2, 9.6 versus 13.67 days in unit 3 and 10.5 versus 2 days in unit 4. The corresponding data for unit 1 were not available. All nine infections in unit 1 were definite, seven of eight were definite in unit 2 with one probable, all three infections in unit 3 were definite and finally, the 17 EVD infections in unit 4 were not categorised as either definite or probable. A total of 47 isolates from EVD infections were recorded. Of these, 24 (52.2%) were *S. epidermidis* and 16 (37.8%) were AGNB.

Discussion

This pilot study was designed to look at the feasibility of the ongoing collection of data following the insertion of EVDs in neurosurgical units. Currently, this occurs in only a minority of units. The working group spent a considerable amount of time reviewing previously published definitions and then drafted ones for use in this pilot study that were felt to be robust for routine use. In particular, we did not allow for the inclusion of a decision to start antibiotics empirically for the treatment of meningitis/ventriculitis as a criterion for definite or probable infection.

The data were collected by whoever was available in each particular unit. However, the number of units involved, the number of patients surveyed and the details collected were less than had originally been intended indicating the resources necessary for on-going surveillance of these patients. Any future national surveillance system would need to provide guidance on logistics such as when and who is best positioned to collect data, how it will be analysed and shared, and what actions will ensue. For many units, this would need some additional resources to ensure the regular and comprehensive collection of data.

Not unexpectedly, there were variations in practice between the units such as how often EVDs were manipulated and the type of EVD used, i.e. standard, silver- or antibiotic-impregnated catheters. Despite using defined criteria to identify infections, the proportion of patients with meningitis/ventriculitis associated with an EVD varied between units from 3% to 18% and from 4.8-12.7/1,000 EVD days, although the type of microbes responsible was largely similar throughout.

Ventriculitis/meningitis following EVD insertion is a relatively common healthcare-acquired infection in neurosurgical patients if less prevalent than respiratory tract, urinary tract and

bloodstream infections.[12-14] A variety of recent studies reveal a variation in the proportion of patients with meningitis/ventriculitis after EVD insertion and also the actual incidence per 1,000 catheter-days. In a study from New York of 343 patients, the proportion of patients developing ventriculitis was 3.5% and 10/12 patients with positive CSF cultures also had infections elsewhere. The most common pathogens associated with EVD infection were mainly skin flora and in terms of risk factors patients developing ventriculitis were more likely to have a prolonged duration of EVD *in-situ*.[15] In a Brazilian study of 119 patients, the proportion of patients developing infection was 18.3% or 22.4 per 1000 catheter days but the majority of infections were due to AGNB.[16]

Many of the studies reported in the literature are limited by being single centre studies or involving relatively small numbers of patients. There are logistical difficulties in conducting multi-site studies and in collecting data over a prolonged period of time unless adequate resources are in place, as our study also highlights. However, in an Italian study of 13 ICUs where each unit recruited 10 or more patients over a period of 6 months or more, data were collated on 271 patients involving a total of 311 catheters.[17] Fifteen patients (5.5%) had confirmed ventriculitis/meningitis and 15 patients (5.5%) had suspected infection. Gram-negative bacteria were equally as likely to be the cause of infection as Gram positive bacteria and risk factors for infection included placement of the EVD outside the operating room, a co-existing extra-cranial infection and a combination of both an EVD and a lumbar drain *in-situ*.[17] This study included more sites than ours but collected data on fewer patients. Nonetheless, the overall proportion of patients with meningitis/ventriculitis was similar even if there were fewer infections due to AGNB in our study. The British Neurosurgical Trainee Research Collaborative (BNTRC) is in the process of completing a multicentre audit of EVDs throughout the UK and Ireland, including rates of infection but using different definitions, and the results from this may further inform ongoing surveillance systems and how they can best be delivered.

The collection of local data and its comparison with other centres facilitates the identification of those factors which may be contributing to infection and what measures are necessary to manage infection. This requires agreed definitions for infection. We reviewed those already available and decided on the ones above because we believe they are feasible and allow for the variables involved. Unlike those from the Centre for Disease Prevention and Control and the National Healthcare Safety Network in the USA, we had two categories, i.e. definite and probable, and our definitions require two culture positive CSFs for microbes that can colonise the skin to be deemed probable meningitis. Also, we do not specifically include meningitis/ventriculitis in the newborn in our pilot study.[18]

As with measures to reduce bloodstream infection and ventilator-associated pneumonia, there is increasing use of a healthcare bundle to minimise EVD-associated infection. A bundle consisting of education, meticulous EVD handling, CSF sampling only when clinically necessary and the routine replacement of the EVD on the 7th day was instituted in an ICU in Greece.[19] This resulted in a fall in the proportion of patients infected from 28% to 10.5% with *Acinetobacter baumannii* being the most common cause. In another study of 2928 EVDs inserted over a six year period, a comprehensive protocol or bundle for EVD placement was developed and its efficacy evaluated.[20] The protocol included the use of pre-operative prophylactic antibiotics, use of antimicrobial catheters, and CSF sampling only when infection was suspected. Following the implementation of the bundle, the proportion of patients infected fell from 1.5% to 0.46% with the highest incidence being between days 4-14 after EVD insertion. Gram positive bacteria such as CoNS were more common than Gram negative bacilli as the cause of infection.[20] In a Dutch study where a very high baseline proportion of patients were infected, i.e. 37%, a comprehensive bundle was aggressively implemented between 2004 and 2006. This included measures to reduce infection following the insertion of both EVDs and lumbar drains.[21] This led to a statistically significant fall in

the infection rate to 11.3% but even after the intervention, the proportion of patients receiving antibiotic prophylaxis at the time of EVD insertion had increased only from 31% to 56%.[20] One of the possible reasons for the relatively high background rate of EVD-associated infections in this centre was that catheters were often inserted at the bedside but this was changed to having them inserted in a separate room dedicated for this procedure.

There is clearly significant variation in the proportion of patients developing infection and the rate per thousand catheter days, as well as the causative organisms between some studies and for reasons that are not always obvious. Nonetheless, the collection of data, its analysis and comparison with similar units is useful in identifying where improvements can be made. As these are difficult to treat infections, sometimes causing death but often causing prolonged length of hospital stay and impaired intellectual capacity in some patients, there is a significant clinical need to improve practice and to improve the safety of patient care.

Practice varies in terms of using standard, antibiotic or silver-impregnated EVDs; two of the four units did not use standard EVDs. A recent meta-analysis of the impact of silver-impregnated EVDs found only one randomised controlled trial (RCT) and six prospective or retrospective non-RCTs.[22] There was a significantly lower infection rate associated with the silver-impregnated EVD in the RCT but not in the pooled non-RCTs. However, infections caused by Gram positive bacteria were lower in patients with silver-impregnated EVDs. In a recent post-hoc analysis from the Netherlands involving two units, with plain EVDs and those coated with rifampicin and clindamycin, there was no significant difference in the rate of EVD-associated infection using both CDC and culture-based definitions.[23] However, many studies in this clinical area are hampered by insufficient numbers of patients or by flawed design. Data from comprehensive surveillance performed at national level might indicate whether silver- or antibiotic-impregnated EVDs should be routinely used or only after other infection prevention measures have failed to reduce infection rates.

The purpose of our pilot study was to investigate the feasibility of on-going surveillance in neurosurgical units of infective complications following the insertion of EVDs with a view that such a system or a variation of it could be implemented nationally with an acceptable protocol. Furthermore, not all aspects of infection prevention were surveyed such as the use of antibiotic prophylaxis and whether antibiotics were administered before insertion and or throughout the duration of EVD placement. However, the study was not large enough to make recommendations on preventative measures, one of the original objectives of the working group. As a pilot study, the study has limitations including being able to collect data from only four neurosurgical units and deficiencies in the data collected, e.g. one centre did not distinguish between definite and probable cases. Also, the number of patients varied between the units as did practice such as the type of EVD used. We were not able to investigate risk factors for infection given the lower number of units involved than had been expected. However, the study emphasises the need for regular and comprehensive surveillance of patients at the time of EVD insertion until removal using agreed and robust definitions to help explain differences in infection rates and microbial aetiology. The data collected and the difference in the proportion of patients infected, highlights the need for on-going surveillance, the sharing of data with comparisons allowing for differences in case-mix and ultimately the identification of factors which can be modified to reduce infection.

In conclusions, we believe that the results of this pilot study and the BNTRC study confirm the need for and the feasibility of a national surveillance programme which would require some support locally. The use of an agreed set of definitions, a practical dataset and the sharing of data would identify risk factors, increase awareness and subsequently lead to the development of a set of guidelines, all contributing to reducing these important infections.

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Table I. Denominator data variables collected during pilot study of external drain-related meningitis/ventriculitis

Data item	Options	Data collection
Patient demographics	Age; gender; BMI; underlying disease	On insertion
Site of insertion	Cranial; lumbar	On insertion
Date of insertion		On insertion
Reason for EVD	Intracranial haemorrhage; tumour; blocked ventriculo-peritoneal shunt; trauma; other	On insertion
Type of EVD	Standard; silver coated; antimicrobial/other	On insertion
Tunnelled	Yes; no	On insertion
Emergency	Yes; no	On insertion
Surgeon	Consultant; junior doctor	On insertion
ASA score	1 to 5/unknown	On insertion
EVD access	Date and reason (CSF; drugs; other)	Duration of EVD
Reason surveillance discontinued	EVD removed; EVD removed & replaced; patient transferred; patient discharged; patient died	On completion of surveillance
Date surveillance discontinued		On completion of surveillance

BMI, body mass index; EVD, external ventricular drain; ASA- America Society of Anaesthesiology; CSF, cerebrospinal fluid

Table II. Definition of meningitis/ventriculitis used

1. Definite post-operative bacterial meningitis/ventriculitis

The patient needs to meet **either** of the following criteria based on positive culture results:

A The isolation of a recognised pathogen, e.g. *Staphylococcus aureus,* Gram negative bacilli or yeasts from at least one CSF sample

B The isolation of the same coagulase negative staphylococcus, diphtheroid or other skin organism from two or more CSF specimens.

2. Probable post-operative bacterial meningitis/ventriculitis

The patient needs to meet **at least two** of the following criteria: -

A Positive culture/ microscopic results:

- The isolation of a potential skin isolate, e.g. coagulase negative staphylococci from only one CSF, **OR**
- the isolation of bacteria/yeast from the tip of an indwelling neurosurgical device, e.g. EVD, or a positive CSF Gram stain in the absence of positive culture.

B Clinical features: One or more of the following, fever, change in consciousness, new onset of seizures, signs of meningeal irritation

C CSF inflammation: Raised or increasing white cell count or low CSF glucose, i.e. CSF: blood ratio of <60%

CSF, cerebrospinal fluid; EVD, external ventricular drain.
Note: A new episode of infection was recorded if a) a different microorganism is isolated from the CSF or b) the same microorganism was isolated from the CSF but at least 4 weeks had elapsed from the previous infection and there was clear evidence that the symptoms of the first infection had resolved e.g. higher Glasgow Coma Scale, reduced white cell count by >50%, and the eradication of the organisms on Gram stain and culture in one or more follow-up CSF specimens, if the EVD remained in place.

Table III. General details of neurosurgical units involved in pilot surveillance project

	Unit 1	Unit 2	Unit3	Unit 4
No. of neurosurgical procedures/year	1063	2643	2493	2274
No. of EVDs inserted/year	82	131	90	74
Whether EVDs are tunnelled or not	Yes	Yes	Yes	Yes
Sampling protocol	*Daily and as clinically required	As clinically indicated	As clinically indicated	As clinically indicated
Frequency of EVD manipulation	≥ 1/week	< 1/week	Weekly	Weekly

*varied according to consultant
EVD, external ventricular drain

Table IV. Data collect on external ventricular drain-associated ventriculitis in four neurosurgical units[o]

	Unit 1	Unit 2	Unit 3	Unit 4
No. of patients surveyed	82[+]	131	61	564
Duration of EVD *in-situ*				
≤ 5 days	39 (26%)	36 (26%)	16 (20%)	348 (62%)
6-9 days	71 (47%)	23 (16%)	41 (51%)	99 (17%)
≥ 10 days	40 (27%)	82 (58%)	23 (29%)	117 (21%)
Site of insertion				
Cranial	80	129	61	515
Lumbar	7	2	- *	49
Type of EVD				
Standard	10	0	0	209
Silver-coated	0	0	2	2
Antimicrobial-impregnated	127	131	49	353
Other	2	0	10	0
Indication for EVD				
Haemorrhage	43 (41%)	66 (55%)	26 (43%)	370 (66%)
Tumour	40 (38%)	17 (14%)	11 (18%)	125 (22%)
Blocked shunt	12 (12%)	8 (7%)	0	13 (2%)
Trauma	8 (8%)	2 (2%)	1 (2%)	53 (9%)
Other	1 (1%)	27 (22%)	23 (37%)	3 (1)%)
Status of operator				
Consultant	8 (6%)	25 (19%)	14 (24%)	202 (35%)
Junior doctor	123 (94%)	106 (81%)	43 (76%)	362 (65%)
Frequency of EVD access				
≤ 5 times	36 (60%)	124 (95%)	57 (92%)	N/A
6-9 times	19 (32%)	6 (4%)	4 (6%)	N/A
≥ 10 times	5 (8%)	1 (1%)	1 (2%)	N/A
No. (%) of infections	17 (18%)	8 (6%)	3 (5%)	17 (3%)

Rate/1,000 EVD days	12.7	5.17	4.8	5.9
Microbiology aetiology **				
CoNS	10	3	3	8
S. aureus	1	0	0	1
AGNB	4	4	0	4
yeasts	1	0	0	1
others	1	1	0	1

[ϕ]For some of the data, the denominator is number of patients and for others it is the number of EVDs; some patients had more than one EVD.

EVD, external ventricular drain; CoNS, coagulase negative staphylococci; AGNB, aerobic Gram negative bacilli, N/A - not available

* only cranial drains surveyed

** for some infections ≥ 1 isolate was recovered