Bacterial meningitis caused by the use of ventricular or lumbar cerebrospinal fluid catheters

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Object. In the present study the authors compared the incidence and risk factors for external drainage–related bacterial meningitis (ED-BM) by using ventricular and lumbar catheters.

Methods. A cohort of 230 consecutive patients with ED was evaluated. Cerebrospinal fluid samples were obtained daily for microbiological culture, and ED-BM was defined based on culture results in combination with clinical symptoms. The incidence of ED-BM was 7% in lumbar and 15% in ventricular drains. Independent risk factors included site leakage, drain blockage, and most importantly duration of ED. Despite a higher infection rate, ventricular catheters did not have a significant higher risk of infection after correcting for duration of drainage.

Conclusions. Analysis of data in the present study showed that the incidence of ED-associated death is low (0.45%) in patients who do not receive continuous antibiotic prophylaxis during ED.

Key Words • cerebrospinal fluid drainage • risk factor • central nervous system infection • ventriculostomy catheter • lumbar subarachnoid catheter

Abbreviations used in this paper: BM = bacterial meningitis; CSF = cerebrospinal fluid; ED = external drainage; ICP = intracranial pressure; OR = odds ratio.

External drainage of CSF is frequently performed in the neurosurgical department. Common indications for its use include transient hydrocephalus in relation to intracranial hemorrhage or tumors, prevention of CSF fistulae after neurosurgical procedures, and monitoring of ICP. The preferred areas for insertion of a draining catheter are the lateral ventricle and the lumbar region. Both locations can be used to perform continuous CSF drainage and/or monitoring of ICP through a closed system.7,12

An important complication of external CSF drainage is bacterial colonization and subsequent infection in the catheter, which can lead to meningitis and encephalitis. Reported infection rates with the use of external CSF catheters differ considerably.1,3,5,8,10,11,13,14,19–23 The reported incidence of BM with ventricular drainage is between 6 and 22%.5,9,12,14,19,21,23 Bacterial meningitis caused by the use of lumbar catheters has been rarely studied, and reported incidences vary between 3 and 10%.3,5,12–14,20 These different infection rates may be explained by a number of reasons, such as variations in catheter types, definitions of drainage-related infection, and use of prophylactic antibiotic agents.12

Factors associated with an increased risk of ED-BM have been investigated.5,12–14,19,21,22 Duration of ED, indication for placement of the drain, and hemorrhagic CSF are commonly indicated as risk factors for drain infection.5,12–14,20,21 Factors that are directly drain related, such as manipulation of the drain and site leakage, are also important.3,5,12–14,22 Note, however, that there are considerable discrepancies among data from studies focused on risk factors for ED-BM. Such variations may be explained by different methods of analysis but are mostly due to different types of drains studied. So far, no authors have directly compared the use of ventricular and lumbar catheters in relation to risk factors for ED-BM.

Therefore, we performed a cohort study to investigate ED-BM in patients with ventricular catheters and lumbar catheters. During the drainage period, CSF samples were obtained daily to perform Gram staining and culturing as well as chemical analysis of CSF. No prophylactic antibiotics were given during the drainage period, except for a single dose of flucloxacillin or cefazolin in case of perioperative prophylaxis. We investigated the incidence of drain-related infections in this cohort of patients, and evaluated risk factors for ED-BM.

Clinical Material and Methods

Patient Population

A single-center cohort of 280 consecutive patients who had ED of CSF for more than 24 hours during the period from July 1999 to January 2003 was evaluated. Cultures and Gram stains of CSF samples were performed daily, and chemical analysis (cell counts and protein and glucose levels) every weekday. Clinical records were examined for patient characteristics, clinical data (fever, signs of meningitis, headache, and neurological status), drain characteristics (blockage, site leakage, and involuntary disconnection), diagnostic tests, and treatment information. All clinical data were recorded onto standard data-entry forms and subsequently entered into a database. The study was approved by the Ethics Review Committee of the Leiden University Medical Center.
Definitions and Exclusion Criteria

External drainage–related infections were defined using microbiological data of daily CSF monitoring in combination with clinical data. An ED-BM was defined as a CSF culture positive on 1 or more consecutive days in combination with one or more of the clinical signs of bacterial meningitis: fever, headache, stiff neck, and/or altered mental status. If a patient had two or more consecutive CSF cultures positive for the same pathogen but no clinical symptoms, the result was defined as bacterial colonization of the drainage catheter. If a patient had only one CSF culture positive for a common skin pathogen, results of consecutive samples were negative, and no treatment had been started, then the CSF result was considered a contamination (20 patients). Patients with negative cultures or cultures considered to be contaminated were categorized as having no ED-BM.

Thirty patients were excluded from the study with temporaraly externalized internal CSF drains, such as malfunctioning ventriculoperitoneal or ventriculostomy drains. Another 20 patients were also excluded because they demonstrated central nervous system infection (cerebral abscess or tuberculosis) prior to placement of the drain. Therefore, 230 patients were included in the final analysis.

Interrupted ED for more than 24 hours (12 patients) before placement of a new drain was considered a new ED period. We analyzed only the first ED period in each patient.

Insertion and Maintenance of Drainage Catheters

Placement of the drainage catheters occurred in the operating room or under sterile conditions at the patient’s bedside. For placement of ventricular catheters, the patient’s skull was shaved and prepared using standard sterile methods. A small incision was made over the coronal suture in line with the pupil of the ipsilateral eye. A 6-mm burr hole was made through the skull, and the dura mater was incised with the aid of a small knife. The catheter was inserted approximately 5 to 7 cm until CSF was obtained. The wound was closed with sutures, and the catheter sewn to the scalp to prevent dislodgement. To place lumbar catheters, a spinal needle was placed in the lower lumbar subarachnoid space. The remaining portion of the catheter was positioned transversely across the back and slightly up the side of the abdomen.

For drainage of CSF with ventricular and lumbar catheters, we used a closed ED and monitoring system (Exacta; Medtronic, Minneapolis, MN), which was connected to the catheter. Cerebrospinal fluid samples were obtained through a special valve incorporated into the drainage system. All patients who underwent craniotomy prior to placement of a drainage catheter or during ED received intravenously 1 g flucloxacillin before surgery. In case of transphenoidal/transsphenoidal surgery 1 g cefazolin was administered intravenously. No special antibiotic prophylaxis was dispensed if drain insertion took place outside the operating room. Patients did not receive prophylactic antibiotics during the period of ED.

Use of Corticosteroid Agents

Patients who underwent craniotomy received 10 mg of dexamethasone the day before surgery; on subsequent days, four 4-mg doses were administered, and this regimen was gradually decreased over the course of 5 days. Patients who underwent resection of the pituitary gland received four 1-mg daily doses dexamethasone during the period of ED.

Microbiological Testing

The CSF samples were sent daily to the microbiological laboratory for direct examination, Gram staining, and culture. The CSF was centrifuged, and the sediment was Gram stained and cultured on 5% sheep blood agar; chocolate agar; and cysteine, lactose, and electrolyte-deficient agar for 5 days at 35°C in a 5% CO2 enriched environment. The sediment was also cultured in brain–heart infusion broth as enrichment medium. Bacteria were identified using standard biochemical tests.15 Susceptibility testing was performed using VITEK 2 (bioMérieux, Marcy l’Etoile, France). Results of susceptibility tests were used to compare different isolates.

Risk Factor Analysis

The association of risk factors with infection rate was
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determined through logistic regression analysis. The following risk factors were assessed: indication for ED, duration of ED, catheter type, site leakage, severe drain blockage, blood in the CSF, surgery prior to ED, and involuntary disconnection of the drain. Two analyses were performed: 1) patients with ED who had been classified as having bacterial colonization were not included in the risk factor analysis; and 2) these patients were redefined as having bacterial infection. All clinical and laboratory information was entered into SPSS, version 11.0 (SPSS, Inc., Chicago, IL). A probability value less than 0.05 was considered to be significant.

Results

Indications for ED With Lumbar or Ventricular Catheter

Two hundred thirty patients (male/female ratio 1:1.3) included in the study had a median age of 52.5 years (range 0.1–87.6 years). Lumbar catheters were used in 125 patients (54%), ventricular catheters in 97 (42%) patients (Table 1). The most frequent indications for ED were prevention and/or treatment of CSF leakage (54%) and cerebral hemorrhage (36%).

Lumbar catheters were predominantly (89%) used for prevention/treatment of CSF leakage, whereas ventricular catheters were mainly (76%) used in patients with cerebral hemorrhage. The median duration of ED was 6 days (range 2–47 days) among all patients with ED. More specifically, the median duration of ED was 5 days (range 3–12 days) in patients with a ventricular catheter, and 9 days (range 2–47 days) in patients with a ventricular catheter.

Incidence of ED-BM

Of the 230 patients with ED, 22 (9.6%) had ED-BM. In patients with ventricular catheters, the incidence of ED-BM was 15% (14 patients); in patients with lumbar drains, the incidence was 7% (eight patients). Bacterial colonization of the drainage catheter occurred in eight of the patients (3.5%) with ED; in four patients (4.1%) with a ventricular catheter and in four patients (3.1%) with a lumbar catheter.

Microbiological Findings

In the 22 patients with BM, isolated bacteria were mainly (82%) Gram positive (Table 2). Coagulase-negative Staphylococci and Staphylococcus aureus were the most frequently encountered pathogens, that is, in 44 and 22% of all patients with ED-BM, respectively. Gram-negative pathogens were encountered in four patients (18%) with ED-BM. In one patient, two pathogens were repeatedly cultured from the CSF samples: coagulase-negative Staphylococci in combination with S. aureus. No difference was observed in the spectrum of encountered pathogens between the two catheter types. The Gram staining showed a positive result during the period of ED-BM in 13 (59%) of 22 patients with meningitis.

In the eight patients with bacterial colonization of the external drain, mainly (75%) Gram-positive bacteria were found: coagulase-negative Staphylococci (three patients), coagulase-negative Staphylococci in combination with S. aureus (one patient), coagulase-negative Staphylococci in combination with Corynebacterium (one patient), and Cor- ynebacterium (one patient). Two patients had Gram-negative ED-BM with Enterobacter cloacae.

Clinical and Laboratory Findings in Patients With ED-BM

The median time from the start of ED until the occurrence of infection was 6 days (range 2–17 days) in the 22 patients with ED-BM. In patients with ventricular catheters, the median time to infection was 11.5 days (range 2–17 days); in patients with lumbar catheters, 5 days (range 2–7 days).

All patients with BM (22 patients) had fever during the period of positive CSF cultures. In seven patients (32%), accompanying signs of meningitis were present: headache, stiff neck, and/or altered mental status. In one patient (5%), signs of infection at the drain site were also present. Fifteen of the patients (68%) with ED-BM had two or more (consecutive) positive CSF cultures. In seven patients (32%), only one positive culture was demonstrated, but treatment had already been started using antibiotics for which the cultured pathogen was susceptible. All patients with ED-BM received antibiotics. Of these 22 patients, one (4.5%) died because of the consequences of the cerebral infection with Klebsiella pneumoniae. Treatment was begun when the patient developed clinical symptoms and demonstrated a positive Gram stain of CSF. The patient died the following day due to complications of raised ICP. Results of a postmortem examination showed signs of acute encephalitis caused by BM.

Eight (3.0%) of the 230 patients with ED had two or more consecutive CSF cultures positive for the same pathogen but no clinical symptoms and were classified as having bacterial colonization of the drainage catheter. Five (63%) of these patients received antibiotic treatment, whereas in three patients (27%) the drain was removed. All patients with ED-BM had pleocytosis in the CSF. Chemical analysis of CSF in all 22 patients with ED-BM showed a median glucose level on Day 1 of the infection of 4.35 mmol/L (range 0.3–6.7 mmol/L), a median cell count of 311 (range 0–10,240), and a median total protein content of 0.52 g/L (range 0.12–2.09 g/L).

Risk Factors for ED-BM

First, we analyzed the relationship between duration of
ED and risk of infection (Fig. 1). Results showed that the daily rate of infections increased from 0.9% on Day 3 to 12.5% on Day 17. Univariate regression analysis data (Table 3) subsequently demonstrated a significant association between ED duration and infection rate, both at cut-off points of 5 days (OR 4.1) and 15 days (OR 7.3). Severe drain blockage (OR 5.1), blood in the CSF (OR 3.3), and cerebral hemorrhage as indications for ED (OR 3.3) were also significantly correlated with a higher infection rate. There was a borderline significant difference between the risk of infection in ventricular catheters compared with that in lumbar catheters (p = 0.049). Risk factors including pre-ED surgery, involuntary drain disconnection, and site leakage were not associated with a higher risk of infection.

Because of the clear association between duration of ED and the risk of infection, all risk factors were subsequently tested in a bivariate model by using ED duration as the covariate, to adjust for the effect of ED duration on infection risk (Table 3). Results of this adjusted analysis showed a marked decrease in the significance for catheter type; that is, the type of catheter used is not an independent risk factor for developing ED-BM. Similar results were demonstrated for the risk factor of blood in the CSF: adjusted analysis showed that hemorrhagic CSF is not an independent risk factor for ED-BM. In contrast, the time-adjusted analysis revealed a significant result for the risk factor of site leakage, indicating that site leakage is an important risk factor for ED-BM, as is severe drain blockage. Both risk factors were also significant in a multivariate logistic regression model (data not shown)—they are both independent risk factors for the development of ED-BM.

A separate risk-factor analysis was performed in patients who had been classified as having bacterial colonization of the external drain. The subanalysis in these patients redefined as having infected drains did not change the recognized risk factors in the bi- and multivariate logistic regression analyses (data not shown).

Discussion

The present study is the first to compare the incidence and risk factors for ED-BM associated with ventricular and lumbar catheters. A cohort of 230 consecutive patients with external CSF drainage in the period between 1999 and 2003 was evaluated. We found an infection rate of 15% in patients with a ventricular drain, and 7% in those with a lumbar drain. In our study, no prophylactic antibiotics were administered during the period of ED. Microbial growth in CSF was monitored daily, and the incidence of drain-related BM was defined based on the results of these samples. The incidence of ED-BM in this cohort may therefore be considered as the baseline incidence of infections that occur in an unprotected group of patients with ED who are fitted with ventricular or lumbar drains and who are monitored daily.

The bacteriological findings showed that most patients (82%) with ED-BM had a Gram-positive pathogen causing the meningitis. We observed predominantly Gram-positive cocci, that is, coagulase-negative Staphylococci and S. aureus, and a few cases with Gram-positive rods. These results are comparable to those of previous studies demonstrating that the major proportion of ED-BM is caused by common Gram-positive skin flora. Interestingly, in one of the patients (4.5%) with ED-BM, a mixed infection of two different Gram-positive pathogens was diagnosed. These bacteria were not considered as contaminants because they were present on two or more solid culture media of two CSF samples. Mixed infections have not been previously reported in the literature but may be important for appropriate antibiotic treatment. The proportion of Gram-negative bacteria in our study was small (18%) and consisted of three members of Enterobacter and one nonfermenting bacterium. These results are in accordance with the spectrum of Gram-negative bacteria found in previous studies in which prophylactic antibiotics were not used.16,22

The results of the risk-factor analysis in this cohort showed that the duration of catheterization is a major risk factor for the development of drain-related BM. There was a significant increase in the infection rate during the period of drainage. Regression analysis even showed that patients with ED for more than 15 days had a risk of developing an infected drain that was seven times that in patients with an ED duration of less than 15 days. Data from most previous studies have identified duration of ED as a major risk factor for drain infection.3,9,12–14,19 In a recent review, Lozier, et al.,12 summarized data from 10 studies including 1698 patients and confirmed the clear association of drainage duration and rate of drain-associated infections. Given this associa-
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Table 3
Risk factors for ED-BM*

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>% Incidence of Infections</th>
<th>Univariate (crude) OR (95% CI) p Value</th>
<th>Bivariate (adjusted)† OR (95% CI) p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>duration of ED &gt;5 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>4 (4/99)</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>yes</td>
<td>15 (8/123)</td>
<td>4.1 (1.3–12.5)</td>
<td>0.014</td>
</tr>
<tr>
<td>duration of ED &gt;15 days</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>7 (15/203)</td>
<td>1.0</td>
<td>—</td>
</tr>
<tr>
<td>yes</td>
<td>37 (7/19)</td>
<td>7.3 (2.5–21.3)</td>
<td>&lt;0.001</td>
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<tr>
<td>catheter type</td>
<td></td>
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<tr>
<td>lumbar</td>
<td>7 (8/121)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>ventricular</td>
<td>15 (14/93)</td>
<td>2.5 (1.0–6.3)</td>
<td>0.049</td>
</tr>
<tr>
<td>site leakage</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>no</td>
<td>9 (14/150)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>yes</td>
<td>20 (8/41)</td>
<td>2.4 (0.9–6.1)</td>
<td>0.077</td>
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<td>severe drain blockage</td>
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<td></td>
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<tr>
<td>no</td>
<td>8 (17/206)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>yes</td>
<td>31 (5/16)</td>
<td>5.1 (1.6–16.2)</td>
<td>0.007</td>
</tr>
<tr>
<td>blood in CSF</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>6 (10/157)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>yes</td>
<td>19 (12/65)</td>
<td>3.3 (1.4–8.2)</td>
<td>0.009</td>
</tr>
<tr>
<td>surgery prior to ED</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>8 (5/60)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>yes</td>
<td>11 (17/162)</td>
<td>1.3 (0.5–3.7)</td>
<td>0.633</td>
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<tr>
<td>involuntary disconnection</td>
<td></td>
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</tr>
<tr>
<td>no</td>
<td>12 (21/179)</td>
<td>1.0</td>
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<tr>
<td>yes</td>
<td>8 (1/12)</td>
<td>0.7 (0.8–5.6)</td>
<td>0.723</td>
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<td>use of corticosteroids</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>no</td>
<td>11 (5/45)</td>
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<td>1.0</td>
</tr>
<tr>
<td>yes</td>
<td>10 (17/177)</td>
<td>0.9 (0.3–2.4)</td>
<td>0.763</td>
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<td>ED indication</td>
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<td></td>
<td></td>
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<tr>
<td>CSF leak</td>
<td>6 (7/119)</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>hemorrhage§</td>
<td>17 (14/81)</td>
<td>3.3 (1.3–8.7)</td>
<td>0.013</td>
</tr>
<tr>
<td>tumor</td>
<td></td>
<td></td>
<td>9 (1/11)</td>
</tr>
</tbody>
</table>

* CI = confidence interval.
† External drainage duration used as covariate.
‡ Drainage for prevention or treatment of CSF leakage.
§ Drainage for cerebral hemorrhage.
|| Drainage for hydrocephalus caused by tumor or other noninfectious cause.

The results of the present study show that drain type and indication for ED are not independent predictors for drain infection. To our knowledge, this is the first report of a direct comparison of the incidence of ventricular and lumbar drain types. Authors of many previous reports have asserted that the indication for ED—for example, placement of a catheter for the drainage of cerebral hemorrhage—is a determining factor for the development of drain infection. Note, however, that in none of these studies did the researchers correct for the duration of catheterization. Results from the present study indicate that, when adjusted for ED duration, the factors of indication for drainage and blood in the CSF are not significantly associated with drain infection. The same holds true for the factor catheter type. In general, just as in our study, reported infection rates in ventricular drains are higher than those in lumbar drains. Note, however, that ventricular drains are mostly used for cerebral hemorrhage and other indications in which the average time of drainage is longer. The higher infection rates in ventricular drains can therefore only be attributed to the longer duration of catheterization. The results from our study support the recommendation that clinicians be aware of the increasing risk of drain infection for every day that the drain remains in place. Therefore, drainage catheters and external pressure-monitoring devices should be removed as soon as possible.

Although ED-BM may cause the death of a patient, the BM-related mortality rate was low in our cohort; only one (0.45%) of the patients with ED died as a result of ED-BM. Mortality rates reported in the literature are generally higher: 0.5 to 2.8%. One of the reasons for the discrepancy between our results and those of others might be the fact...
that we performed daily monitoring of the CSF. We assumed that because of this policy, the delay in diagnoses was minimal, which may have resulted in better outcomes in patients who suffered a drain infection. Some authors have advocated the use of prophylactic antibiotics to reduce the rate of drain infection and thus the frequency of infection-related death. One of the major disadvantages of the prolonged administration of prophylactic antibiotics, however, is the potential of increased resistance of bacteria. For this reason we do not recommend the use of prophylactic antibiotics.

Conclusions

In summary, the results of our study showed that the incidence of ED-BM in a cohort of patients with ED is between 7 and 15% by using our insertion conditions and no continuous antibiotics. There was no significant difference between the infection rate in ventriculostomy and lumbar catheters, nor between the various drainage indications. Drain-related factors like site leakage and drain blockage are significant risk factors for infection, but the most important is the duration of catheterization. The previous reported differences in the infection rate between ventricular and lumbar catheters can therefore only be attributed to the time that the drain remained in place. The frequency of ED-associated death is low (0.45%) in a population of patients who do not receive continuous prophylactic antibiotics during ED.

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References


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