Cerebrospinal Fluid Infection with External Ventricular Drainage: Analysis of the Risk Factors in 110 Patients of a Single Institution*

Infecção liquórica em drenagem ventricular externa: Avaliação dos fatores de risco em 110 pacientes de uma única instituição

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Abstract

Objectives External ventricular drainage (EVD) is extensively used in the neurosurgical practice with the purpose of monitoring the intracranial pressure and draining the cerebrospinal fluid (CSF). Despite its remarkable benefits, the technique is not devoid of risks, notably infections, which have been reported in up to 45% of the cases.

Methods A retrospective analysis of the main risk factors for CSF infection in neurosurgical patients submitted to EVD at a single institution. We recorded and submitted to statistical comparison every risk factor for CSF infection present or absent in each of the 110 EVD patients enrolled, 53 males and 57 females, with an average age of 52.9 years, with different underlying neurosurgical conditions.

Results Infection of the CSF occurred in 32 patients (29%). The rate of mortality related to CSF infection was of 18.7% (6 of 32). The risk factors that showed statistical significance for CSF infection in this series were: emergency surgery; length of stay at the intensive care unit (UCI); duration of the EVD; parenchymal and/or intraventricular hemorrhage; simultaneous infections; time of bladder catheterization; and the use of non-disposable adhesive drapes as part of the preparation of the wound area.

Conclusions Infection of the CSF in patients submitted to EVD is multifactorial and a challenge in terms of prevention. Further studies proposing scores with blended risk factors may be useful to prevent and reduce the morbidity and mortality associated with CSF infection.

Keywords

- external ventricular drainage
- cerebrospinal fluid infection
- risk factors

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Resumo

Objetivos A derivação ventricular externa (DVE) é frequentemente utilizada na prática neurocirúrgica para monitorização da pressão intracraniana e drenagem de líquido cefalorraquidiano (LCR). Apesar dos evidentes benefícios, a utilização do método não é isenta de riscos, notadamente infecção, podendo atingir incidência de até 45%.

Métodos Realizamos análise retrospectiva dos principais fatores de risco para infecção do LCR em pacientes neurocirúrgicos com DVE em uma única instituição. Registramos e analisamos, através de comparações estatísticas, todos os fatores de risco para infecção do LCR presentes ou ausentes em uma série de 110 pacientes submetidos à DVE, onde 53 eram homens e 57 mulheres, com idade média de 52,9 anos.

Resultados Infecção do LCR ocorreu em 32 pacientes (29%). A taxa de mortalidade relacionada diretamente à infecção liquórica foi de 18,7% (6 de 32). Os fatores de risco que se mostraram significantes para infecção do LCR nesta série foram: cirurgia de emergência, tempo de permanência em UTI, tempo de permanência da DVE, hemorragia parenquimatosa e/ou intraventricular, foco infeccioso distante concomitante, uso prolongado de sonda vesical e o uso de campos cirúrgicos não adesivos durante a confecção da DVE.

Conclusões A infecção do LCR em pacientes com DVE é multifatorial e um desafio para sua prevenção. Estudos adicionais, com propostas de escores que combinem vários fatores de risco podem ser úteis na prevenção e redução dos índices de infecção liquórica com repercussão positiva sobre morbidade e mortalidade associadas.

Palavras-chave

- derivação ventricular externa
- infecção liquórica
- fatores de risco

Introduction

Ventricular catheters are essential for the treatment of patients with intracranial hypertension. Besides monitoring hypertension, these devices also play a role in its treatment through cerebrospinal fluid (CSF) drainage. External ventricular drainage (EVD) is frequently used for the treatment of patients with disturbances in CSF circulation. Most patients present subarachnoid or parenchymal hemorrhage. Some patients present acute expansive lesions that require CSF derivation before the definitive treatment. Monitoring the intracranial pressure (ICP) and concomitant CSF drainage have been used more frequently over the past years. However, continuous CSF drainage may increase the exposure of the patients to risks. The main disadvantages of the permanence of these catheters are the potential risk of fatal ventriculitis and/or meningitis, and the mortality rate of the patients varies, reaching up to 45% according to a literature review.[1–4] Continuous monitoring of the ICP,[1,5] and continuous manipulation[1,6–8] and frequent collection of CSF for laboratorial tests[9] are factors frequently related to the contamination of the derivation system of the CSF. Other risk factors are related to the long-term use of the ventricular catheter, such as presence of an infectious site at distance and the surgical technique. Due to the fact that the influence and incidence of such risk factors for CSF infection may vary between groups of patients and regarding different procedures, it is relevant to know the data to improve the results related to CSF infection in patients submitted to EVD as individually as on specialized assistance provided by a neurosurgery service.

The present study aimed to identify and quantify the potential individual risk factors for infection related to the device in a series of patients submitted to EVD, to monitor the ICP or to perform CSF drainage.

Patients and Methods

The present study was performed in the Neurosurgery Service of Hospital de Clínicas, Universidade Federal do Paraná (UFPR). The project was evaluated and approved by the Ethics Committee on Human Beings of the hospital under technical report CAAE N° 0184.0.208.000–08. Out of 142 patients submitted to EVD with registered data, 110 patients whose records had full information related to the study were included. These patients had a ventricular catheter implanted for CSF drainage. Their underlying diseases were cerebral aneurysms, intracranial tumors, hydrocephalies, and strokes. All patients were aged 16 years or older. All of them were submitted to frontal or parietal EVD, and the same surgical technique was used, with catheter exteriorization by counter incision with a subcutaneous tunnel, and always using the same model of EVD system. Patients with active central nervous system (CNS) infection were excluded from the study. The minimum period of follow-up for inclusion in the study was of 6 months.

The potential risk factors associated to CSF infection in patients submitted to EVD were chosen after a review of the world literature and based on the experience of the service, and they were divided into 4 groups for didactical purposes: 1) factors related to the patients submitted to EVD; 2) factors related to the disease/neurological condition of the patients

Table 1 Factors with potential influence on the onset of cerebrospinal fluid (CSF) infection in external ventricular drainage (EVD)*

Group 1–Factors related to the patients submitted to EVD			
Age (110)	Gender (110)	Comorbidities (108)	Distant-site infection prior to the EVD procedure (108)
ICU permanence (104)	Use of prophylactic antibiotics (108)	Use of hormonal anti-inflammatory drugs (108)	Bladder catheter permanence (102)
Group 2–Factors related to the disease/neurological condition			
Surgery indication (108)	Glasgow Coma Scale at admission (109)	Treatment of underlying disease (110)	Intraventricular hemorrhage (102)
Presence of hydrocephalus (100)		Postoperative Glasgow Coma Scale (108)	Postoperative ICP alteration (98)
Group 3–Factors related to the neurosurgical treatment			
Concomitant procedures (108)	Emergency surgery (110)	Surgery time (106)	Anesthesia time (106)
Surgeon experience (110)	Number of surgeons (110)	Operating room (98)	Number of professionals in the operating room (108)
Change of assistants in the operating room (108)	Presence of a technician (108)	Use of surgical adhesive film (110)	Trepanning site (104)
Number of suture plans (110)			
Group 4–Factors related to the EVD device			
Previous manipulation of the EVD system (108)		EVD time (106)	Change of the prophylactic catheter of the EVD (110)

Abbreviations: ICP, intracranial pressure; ICU, intensive care unit.
*The figures in parentheses refer to the numbers of patients used in the specific statistical analysis of each factor.

submitted to EVD; 3) factors related to the neurosurgical treatment to which they were, including the implantation of the device; and 4) factors directly related to the EVD device. ►**Table 1** shows all potential factors for CSF infection investigated in the study subdivided into 4 categories, as well as the number of patients who participated in each individual analysis of the factors.

Epidemiological data about the studied population were obtained, such as age and gender; clinical data such as comorbidity, symptoms and sign of sickness, fever, interval between the onset of the symptoms and the diagnosis, level of consciousness according to the Glasgow Coma Scale (GCS), and location of associated lesions through imaging tests, such as computed tomography or encephalic nuclear magnetic resonance. We also obtained data related to the treatment, such as surgical time, qualification of the professional who performed the procedure, use of disposable surgical adhesive film, number of professionals in the surgical room, and use of prophylactic antibiotics. Laboratorial data obtained from biochemical CSF tests, CSF cultures and hemograms were also recorded. According to literature review,[10] for the purpose of analysis, in the present study the presence of positive CSF culture was considered ventriculitis, this fluid was taken from the ventricular catheter or by lumbar puncture, associated to fever, clinical signs of meningitis, including stiff neck, photophobia, decrease in the level of consciousness, seizures, as well as low levels of glucose, high protein, and CSF pleocytosis. Manipulation and/or changes of catheter were performed only due to demand in specific individuals. In order to analyze each parameter, the patients were subdivided regarding the occurrence or non-occurrence of CSF infection. At the hospital release, the functional state of the patients was evaluated and classified in categories A, B or C according to the Karnofsky Scale, which was adapted by Crooks et al.[11]

The statistical analysis consisted of determining the positive and negative predictable values, the specificity, the sensibility, and the accuracy of several parameters of the study; comparative tests for each risk factor in the study were also applied. Regarding the qualitative parameters, the Chi-squared (χ^2) test and/or frequency distribution tables were used. As for the quantitative parameters, we first observed the prerequisite of normal distribution (Gauss) to later choose the statistical tests (Student *t* test or the Mann-Whitney test). In all of the analyses, p-values < 0.05 were considered statistically significant.

Results

In the present series, the age ranged from 16 to 82 years, with an average of 52.9 years, and the sample was composed of 53 men and 57 women. In total 32 (29%) patients filled the criteria for the diagnosis of CSF infection required by the study. The CSF cultures were positive for *Staphylococcus epidermis* in 59.37% of the patients, followed by *Staphylococcus aureus* in 18.75% of the cases. *Acinetobacter baumanni*, *Enterococcus faecalis*, *Enterobacter cloacae* and *Staphylococcus hemoliticus* were the etiological agents agents of the 7 remaining cases (21,88%).

The most common comorbidity was systemic arterial hypertension in 16 patients, followed by the effects of

smoking in 8 patients, the effects of alcoholism in 4 patients, and type-2 diabetes mellitus in 4 patients. Emergency surgeries were performed in 77% (85 out of 110 patients) of the cases. The average permanence of the EVD was of 10 to 14 days. The trepanning site was predominantly frontal (87 cases). Disposable surgical adhesive film was used in 49 of the 110 patients (44,54%) patients during the surgical procedure. In total, 92 (83%) cases of hydrocephalus were verified. Prophylactic antibiotics were used in 86 (78%) cases, and cefazolin was the most administered drug.

►**Table 2** shows the results obtained in the analysis of the factors related to the patients, with the respective statistical comparison between carriers and non-carriers of CSF infection.

Neither age nor gender or the comorbidities influenced on the onset of CSF infection in the patients submitted to EVD in the present study. Similarly, the use of prophylactic antibiotics or hormonal anti-inflammatory drugs did not show a significant effect. However, the existence of distant-site infection prior to the insertion of the system, the length of stay of the patient in intensive care, as well as the time of permanence of the bladder catheter were factors that potentially had an influence on the onset of CSF infection (►**Table 2**).

►**Table 3** presents the analysis of the factors related to the illnesses that may correlate with CSF infection in the patients submitted to EVD.

In general, the studied aspects of the underlying diseases of the patients submitted to EVD did not influence the onset of CSF infection. However, the CNS hemorrhage links both factors with positive data. Sick patients with hemorrhage in the CNS and/or inside the ventricles are more prone to present CSF infection in case they need EVD (►**Table 3**).

We analyzed many different aspects and characteristics related to the neurosurgical treatment administered to the patients submitted to EVD (►**Table 4**).

Some of the factors evaluated in this study and listed on ►**Table 4** are rarely found in the available literature. What draws attention is that the concomitant execution of other procedures, such as tracheostomy, central venous access, invasive mean arterial pressure monitoring, phlebotomy and cystostomy, did not influence the rate of CSF infection.

Table 2 Factors with potential influence on the onset of cerebrospinal fluid (CSF) infection related to the patients submitted to external ventricular drainage (EVD)

Evaluated factor	Factor distribution among patients with and without CSF infection			Statistical test (univariate analysis)
Age (years)	CSF infection	Average age		Student *t* test
	With	53.88		$p = 0.57$
	Without	52.12		
Gender	CSF infection	Male	Female	Chi-squared test
	With	15	17	$p = 0.97$
	Without	38	40	
Comorbidities	CSF infection	Absent	Present	Chi-squared test
	With	3	29	$p = 0.09$
	Without	20	56	
Previous infection distant from the EVD system	CSF infection	With previous infection	Without previous infection	Chi-squared test
	With	28	4	$p < 0.0001$
	Without	34	42	
Permanence in the intensive care unit (ICU)	CSF infection	Average of days in the ICU		Student *t* test
	With	20.97		$p < 0.0001$
	Without	11.81		
Use of prophylactic Antibiotics	CSF infection	Yes	No	Chi-squared test
	With	25	7	$p = 0.99$
	Without	61	15	
Use of hormonal anti-inflammatory drugs	CSF infection	Yes	No	Chi-squared test
	With	21	11	$p = 0.10$
	Without	35	41	
Permanence of the bladder catheter	CSF infection	Average (days)		Student *t* test
	With	21.25		$p < 0.0001$
	Without	10.71		

Table 3 Factors with potential influence on the onset of cerebrospinal fluid (CSF) infection related to the underlying disease of the patients submitted to external ventricular drainage (EVD)

Evaluated factor	Factor distribution among patients with and without CSF infection					Statistical test (univariate analysis)
Surgical indication	**CSF infection**	**Subarachnoid hemorrhage and brain aneurysm**	**Hemorrhagic stroke**	**Brain tumor**	**Other**	**Chi-squared test**
	With	16	13	0	3	$p = 0.001$
	Without	29	16	8	23	
Glasgow Coma Scale at admission	CSF infection	3 to 8	9 to 14	15		Chi-squared test
	With	18	10	4		$p = 0.50$
	Without	43	18	16		
Treatment of underlying disease	CSF infection	Only EVD	EVD + operation			Chi-squared test
	With	19	13			$p = 0.21$
	Without	37	41			
Intraventricular hemorrhage	CSF infection	Hemorrhage	Without hemorrhage			Chi-squared test
	With	32	-			$p < 0.001$
	Without	51	19			
Presence of hydrocephalus	CSF infection	Yes	No			Chi-squared test
	With	32	-			$p = 0.10$
	Without	60	8			
Postoperative Glasgow Coma Scale	**CSF infection**	**3 to 8**	**9 to 14**	**15**		**Chi-squared test**
	With	**19**	**11**	**2**		$\boldsymbol{p = 0.10}$
	Without	**46**	**15**	15		
Postoperative alteration in intracranial pressure	CSF infection	Yes	No			Chi-squared test
	With	28	–			$p = 0.14$
	Without	62	8			

Curiously, from this specific group of factors, the only ones that showed influence on the onset of CSF infection in patients submitted to EVD were the emergency catheter for the neurosurgical treatment and the lack of use of surgical adhesive films (►**Table 4**).

Since certain aspects and characteristics of the manipulation of EVD systems may also influence the onset of CSF infection, they were also analyzed in the present study (►**Table 5**).

The total amount of time that the EVD system remained installed in the patient had an influence on the onset of CSF infection. Nevertheless, previous manipulation of the system did not have a negative influence, and the prophylactic change of the catheter did not have a positive influence; the patients who remained longer with the EVD system presented a higher rate of CSF infection (►**Table 5**).

Discussion

The most serious and potentially fatal complications of the onset of CSF infection are constituted by meningitis, ventriculitis or both. The concern about the risk factors that can determine CSF infection has grown in the world literature related to this subject. Among the several risk factors that are more frequently mentioned in the literature as relevant to CSF infection in patients submitted to EVD are the continuous monitoring of the ICP,[1,5] frequent manipulation,[1,6–8] collection techniques for regular laboratory evaluations,[9] prolonged permanence of the device,[2–4,7,9,12–14] concomitant infection,[13] the surgical technique used, CSF leak,[2,4,8,13,15] catheter change,[8] underlying diagnosis, as well as the factors related to the neurosurgical procedure of the treatment of the patients.[2,12] Despite the presence of some risk factors on the world literature, there is no consensus about which factors would be relevant, nor about the individual performance of each one of them in the many studies in which the topic is approached.

From the eight factors related to the patients submitted to EVD (►**Table 2**) whose statistical analysis was possible in this study, three of them were considered relevant to CSF infection. We verified that patients with infections in other sites, previous to the installation of the device, as well as those who remained with a bladder catheter for more than three weeks, or in an intensive care unit (ICU) for more than three weeks, developed CSF infection with significant superiority in relation to the others. In this sense, we find recent reports in the literature that support concomitant infection[13] and prolonged hospitalization in an intensive care environment[6,14] as relevant risk factors for CSF infection in patients submitted to EVD.

Table 4 Factors with potential influence on the onset of cerebrospinal fluid (CSF) infection related to the neurosurgical treatment of the patients submitted to external ventricular drainage (EVD)

Evaluated factor	Factor distribution among the patients with and without CSF infection				Statistical test (univariate analysis)
Concomitant procedures	CSF infection	Yes		No	Chi-squared test
	With	25		7	$p = 0.87$
	Without	60		16	
Emergency surgery	CSF infection	Emergency		Non-Emergency	Chi-squared test
	With	30		2	$p < 0.01$
	Without	55		23	
Surgery time	CSF infection	Average (minutes)			Student *t* test
	With	64.69			$p = 0.61$
	Without	74.39			
Anesthesia time	CSF infection	Average (minutes)			Student *t* test
	With	105.16			$p = 0.36$
	Without	128.18			
Surgeon experience	CSF infection	R2	R3/R4	Preceptor	Chi-squared test
	With	20	8	4	$p = 0.83$
	Without	44	22	12	
Number of surgeons	**CSF infection**	**Average**			**Student *t* test**
	With	**1.47**			$\mathbf{p = 0.39}$
	Without	**1.60**			
Operating room	CSF infection	Own surgical service room		Other	Chi-squared test
	With	26		4	$p = 0.46$
	Without	53		15	
Number of professionals in the operating room	CSF infection	Average			Student *t* test
	With	4.56			$p = 0.38$
	Without	4.88			
Change of assistants in the operating room	CSF infection	With change		Without change	Chi-squared test
	With	4		28	$p = 0.97$
	Without	8		68	
Presence of surgical instrument technician	**CSF infection**	**With**		**Without**	**Chi-squared test x^2**
	With	**4**		**28**	$\mathbf{p = 0.19}$
	Without	**20**		**56**	
Use of disposable	CSF infection	With surgical adhesive		Without surgical adhesive	Chi-squared test
Surgical adhesive film	With	2		30	$p < 0.0001$
	Without	47		31	
Trepanning site	CSF infection	Frontal		Parietal	Chi-squared test x^2
	With	25		5	$p = 0.81$
	Without	62		12	
Number of suture plans	CSF infection	Single		Double	Chi-squared test x^2
	With	27		5	$p = 0.64$
	Without	61		17	

Abbreviations: R2, second-year resident; R3, third-year resident; R4, fourth-year resident.

Table 5 Factors with potential influence on the onset of cerebrospinal fluid (CSF) infection related to the external ventricular drainage (EVD) system

Evaluated factor	Factor distribution among patients with or without CSF infection			Statistical test (univariate analysis)
Previous manipulation of the EVD system	CSF infection	Yes	No	Chi-squared test
	With	4	28	$p = 0.97$
	Without	8	68	
EVD time	CSF infection	Average of days with the EVD device		Student *t* test
	With	15.39		$p < 0.0001$
	Without	7.86		
Prophylactic change of the catheter of the EVD system	**CSF infection**	**With change**	**Without change**	**Chi-squared test**
	With	**8**	**24**	$\boldsymbol{p = 0.09}$
	Without	**8**	**70**	

We did not expect that factors such as age, gender and the comorbidities of the patients submitted to EVD had influence on the onset of CSF infection as shown on literature,[12] neither the number of days of hospitalization before an elective procedure, nor the number of hours before emergency procedures.

The use of prophylactic antibiotics did not have statistical relevance, and the literature is conflicting regarding their use. Some authors did not observe a decrease in the rates of infection with the administration of prophylactic antibiotics to populations who were victims or not of traumas, and they do not recommend their use.[16] The precise medical recommendations for the administration of prophylactic antibiotics are not well-defined, because their indiscriminate use may theoretically result in infections with resistant germs, anaphylactic reaction, prolonged bleeding time, and systemic toxicity. However, recent evidence[16,17] has suggested the use of catheters impregnated with antibiotics in the installation of the EVD device, which is justified by the significant increase in the time of infection-free stay achieved with such devices in comparison to catheters that were not impregnated.

Curiously, after the statistical analysis of the data, two other factors related to the patients submitted to EVD with potential influence on the onset of CSF infection – prolonged time of permanence in the ICU and prolonged time of permanence of the bladder catheter – were statistically significant risk factors for CSF infection. Despite the fact that none of the literature data corroborate these results, we believe that such data, mainly due to the nature of these factors, are related to the long-term manipulation of "multi-invaded" critical patients in ICUs.

In the present study, when we analyzed the potential risk factors for CSF infection that are related to the illness of the patients submitted to EVD (►**Table 3**), two factors that showed possible influence on the onset of CSF infection are linked by their origin – CNS hemorrhage. The patients submitted to EVD whose underlying disease presents hemorrhagic stroke or cause bleeding into the ventricle present higher risk of developing CSF infection. In spite of the fact that some literature reports do not agree with such information,[12,18] there are scientific records favoring the role of those factors in the onset of CSF infection in patients submitted to EVD.[1,2,5,10,14,19]

The presence of hydrocephalus, the fact that the device is installed simultaneously to the neurosurgical treatment of the underlying disease, the alterations in the ICP measurement in the postoperative period regarding the score on the Glasgow coma scale of the patients, when at the admission or after the treatment, did not have an influence on the onset of CSF infection in the present study.

The aspects specifically related to the neurosurgical treatment (►**Table 4**) that may be attributed to the onset of CSF infection frequently arouse the curiosity of specialists. Some of these factors are not very frequently found in the studies, probably due to the difficulty in obtaining records of the data, or due to the presence or absence of these factors in the study samples. Regarding this, we believe that the present study contributed specifically to the knowledge on the topic, since it was possible to raise the data of a series and perform statistical analyses to determine these factors.

There is a tendency to admit that there may be a higher risk of CSF infection in patients who had their EVD device installed at the same time as other surgical procedures were being performed. In the present study, this was not confirmed when the underlying neurosurgical disease was approached at the same time. The same result was obtained regarding other small concomitant procedures that were very prevalent (78%) in our series, such as tracheostomy, cystostomy, central venous access, arterial access, phlebotomies etc.

Another very common trend is to attribute to the emergency neurosurgical procedures with EVD an incidence of CSF infection significantly superior to the one found in the elective procedures in which the device was implanted. In the present study, the cases of emergency surgery associated or not with EVD, at the same time or isolated, presented a higher incidence of CSF infection than the elective surgical procedures with the same characteristics. However, there is always the possibility of interaction of factors that may influence the analysis and the results. A typical example would be the occasional and plausible higher incidence of illnesses involving hemorrhage in the CNS in patients who

underwent emergency surgeries, since the rates of CSF infection are higher in patients submitted to EVD who have illnesses that entail parenchymatous and/or ventricular hemorrhage. However, it is important to consider the simple argument that, in general, during emergency procedures, neurosurgical or non-neurosurgical technical errors, either isolated or in chain, are more likely to occur.

In the present study, we performed a sensible investigation of the occasional occurrence of CSF infection resulting from factors related to the surgical procedures in patients submitted to EVD. We did not find a significant statistical relationship between CSF infection and the following situations: prolonged duration of the surgery and anesthesia; the level of experience of the surgeon and the number of surgeons in the operating room; procedures performed in the operating rooms of specialties other than neurosurgery; procedures performed with a higher number of professionals or with changes of assistants; absence of surgical instrument technicians; frontal or parietal trepanning; and single or double suture plan of the surgical wound.

Curiously, the technical factor related to surgery with relevant results was the use of surgical adhesive films. The rate of CSF infection was higher in patients who underwent neurosurgical procedures without the use of surgical adhesive films. Evidence from recent researches[6,20] shows that CSF infection associated with EVD is acquired more frequently by the introduction of the bacteria during the insertion of the catheter than by the subsequent retrograde colonization. The world literature[3,15,16,21] and the present study ratify the fact that the etiology of this infection is widely dominated by *S. epidermidis*, which compose the cutaneous bacterial flora. Therefore, the use of more efficient physical barriers in the isolation of the surgical site may benefit the patients who need the insertion of the EVD device.

Similarly to other factors that were already discussed, it is valid to argue that the longer an invasive via remains open in the CNS, the higher the probability of CFS contamination and its consequences, mainly if the catheter is frequently manipulated, and if there are not prophylactic protocols regarding catheter change. This means that the technical manipulation of the EVD device should also be adequately analyzed in terms of its role in the development of CSF infection (►**Table 5**).

The present study shows that the rate of CSF infection was significantly higher in patients in whom the permanence of the EVD device was superior to 2 weeks.. Despite the fact that this is the most studied risk factor for CSF infection, it is still an issue that generates debate, and it is not accepted by all of the authors who study the topic. Park et al[18] observed a daily increase in the rate of infection after the insertion of the catheter. In the beginning, the infection is mild, but it worsens daily in a non-linear fashion, reaching its peak on the 4th day, though it may still worsen at rates of 1% and 2% a day until the 14th day. After that, many researchers believe that the infection rates remain stable. Holloway et al[5] also found a daily initial increase in the rate of infection after the insertion of the catheter, but the rate continued to increase by as much as 4.1% and 4.9% on days 12 and 14. But there are other authors who report that there is no relationship between the rate of infection and the time of permanence of the catheter.[19]

Some authors did not report the association between the number of manipulations of the EVD system and subsequent infection using a strictly aseptic technique.[1,13] Other authors reported greater rates of infection with the systematic irrigation of the system with antibiotics or saline solution, frequent handling or collection of samples, and scheduled exchanges.[6–9] In the present study, manipulation of the EVD device was rare (►**Table 5**). In the cases in which manipulation was necessary, we did not observe an increase in the rate of CSF infection.

Due to the reported increase in the rate of CSF infection after the insertion of the EVD catheter, some authors recommend changing the catheter prophylactly. The results of a controlled and randomized study[13] did not show a decrease in the rate infection rates with or without regular catheter changes. Several authors do not recommend changing the prophylactic EVD catheter.[2,10,12] In addition, in a recent study,[6] the authors demonstrated that maintaining an elective change protocol for the drainage system was an independent risk factor, increasing the chances of infection by ~ 4.6 times. We did not observe a protective effect against CSF infection regarding the prophylactic measures followed in this series.

Finally, we believe the present study contributes to a better comprehension of several factors that may influence the onset of CSF infection in patients submitted to EVD, it emphasizes the multi-factorial nature of the issue, and it suggests that recording the behavior of several factors involved in CSF infection in patients submitted to EVD is also relevant to neurosurgery services. We hope that in the future this data may be used to establish the profile of the patients who are more prone to develop infection, so physicians can provide them with attentive care, aiming to reduce the risk morbidity and mortality.

Conclusion

The individualized and detailed analysis of various relevant factors in the onset of CSF infection in patients submitted to EVD enabled us to establish a more probable profile of the patients who are more likely to develop it during the treatment: individuals with CNS disease with parenchymatous and/or ventricular hemorrhage who present previous distant-site infection, operated in an emergency situation without the use of surgical adhesive film, in whom the permanence in the ICU and/or of the bladder catheter is prolonged for more than 3 weeks, and in whom the EVD device is used for more than 2 weeks.

We suggest the performance of more in-depth studies with statistical multivariate analysis of relevant factors to enable a better prediction of the individual risk of developing CSF infection, with the proposal of a risk score; such studies would benefit a large number of patients.

Conflict of Interests
The authors have no conflict of interests to declare.

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