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Ventriculostomy related infection in intensive care unit: Diagnostic criteria and related conditions

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ABSTRACT

Objective: To evaluate the usefulness of clinical signs, blood tests, microbiological cultures and cerebrospinal fluid (CSF) analysis to detect ventriculostomy related infections (VRI), and to describe related conditions.

Methods: A retrospective study was carried out including all patients with external ventricular drain admitted to intensive care unit from January 2000 to December 2006. Diagnosis of VRI, mortality, demographic and clinical data, time and number of drains, microbiological and biochemical CSF results and blood test were recorded. Difference between infected and uninfected patients was statistically significant at $P < 0.05$.

Results: The results revealed 136 drainages in 120 patients with 22 (18.33%) infected (15.39 infections per 1 000 days of drainage). This group was on overage older, had more severe systemic response syndrome and a significantly higher number of drains and longer duration of drain insertion. We found statistical differences in proteinorrachia, glycorrhachia, and glycorrachia/glycemia ratio during 8.5-day drain insertion (interquartile range 7–10.25). A total of 31 cultures were positive in patients without VRI and 47 were negative in patients with VRI. Furthermore, 35 patients died (2 belonging to the infected group). Significantly higher risk of VRI in intraventricular fibrinolysis and subarachnoid haemorrhage was observed. We made a multivariate regression model resulting in a prediction rule with 55.7% area under curve (95% *CI* 0.43–0.70).

Conclusions: CSF routine cultures and biochemical studies are not recommended to diagnose VRI. Clinical signs, external ventricular drain manipulation and a drainage insertion over a week justify the routine measurement of proteinorraquia, glycorrhachia and the ratio of glycorrachia/glycemia.

1. Introduction

The external ventricular drain (EVD) constitutes a clinical standard for the continuous monitoring of intracranial pressure (ICP) and facilitates the drainage of cerebrospinal fluid (CSF). Indications for an EVD include primary hydrocephalus, obstructive hydrocephalus secondary to expansive processes or intracranial haemorrhage, ICP control in patients with cranioencephalic trauma and prevention of postoperative CSF fistulas[1,2]. It facilitates the treatment using intraventricular fibrinolysis (IVF) and the administration of local antibiotics [1,3]. Its indications are limited by the risk of bleeding during the insertion procedure and the risk of ventriculostomy-related infection (VRI)[1–6]. The published indication on the VRI seems to be conflicting since incidence rates vary between 0% and above 50% depending on the authors[1,2,4–10]. There are no universal criteria to establish its diagnosis; strategies focus on clinical monitoring and blood and CSF microbiological and citobiochemical results[1,2,4,6–14]. The clinical assessment of the patient and certain test results that suggest infection (leucocytosis, CSF pleocytosis, hypoglycorrhachia, *etc*.) lose their predictive value due to the particular characteristics of the neurocritical patient[15–17], and they can cause delay in its detection and early treatment; the lack of rentability of the cultures and the fact that waiting is needed for their results to be available are also obstacles to an early diagnosis[18,19].

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The need to establish uniform criteria which are both highly sensitive and specific for the diagnosis of VRI seems necessary, and, also, to determine CSF parameters to predict its development[12]. The etiological agent most commonly involved is the coagulase-negative staphylococci[1,2,11–13,18,20], however, the detected amount of Gram-negatives is increasing. Many factors that could contribute to the development of VRI have been identified (associated craniotomy, systemic infection, depressed cranial fracture, intraventricular haemorrhage, catheter manipulation, and instillation of local treatments)[1,2,4,11,13,14,21,22], whereas some others are subjects of continuous debate (use of prophylactic antibiotics, the number of devices, corticosteroids administration, lengthy stays in critical care units, placement site of the catheter, prophylactic replacement of the catheter, duration of the derivation, *etc*.)[1,4,14,20–28].

The main objective of this study is to evaluate the usefulness of CSF and blood clinical, cytobiochemical and microbiological parameters to detect VRI, and the secondary objective is to describe possible related conditions to such infection.

2. Materials and methods

2.1. Patients

The setting is a 13 bed intensive care unit (ICU) located in a tertiary referral hospital, which is reference for an area of 400 000 citizens. A retrospective review was conducted on the patient prospective database of our unit and their clinical history, and those patients who were admitted between 2000 and 2006 and carried one or more EVD were included. Two of the authors, working independently from one another, registered the following variables: demography, main diagnosis, score on severity scales 24 h after admission [Acute Physiology and Chronic Health Evaluation II (APACHE)[29], and Simplified Acute Physiology II Score (SAPS II)[30]], VRI diagnosis, EVD duration (number of days from insertion until removal), number of catheters per patient, intraventricular haemorrhage (IVH) stratified using the Graeb scale[31], treatment with IVF and administration of systemic antibiotherapy prior of after treatment. The presence of systemic inflammatory response syndrome (SIRS)[32], at the same time of VRI and mortality while in ICU were also registered.

2.2. Insertion technique and care of EVD

While this study was conducted, the clinical guidelines for the management of EVDs did not suffer any significant alterations.

For insertion, a Lundberg technique modified by the neurosurgery staff was used in theatre or in the ICU, under asepsis and sterile conditions. Always according to availability and the preferences of the neurosurgeon in charge of the procedure, either silicon tunnelled ventricular catheters (Becker® PS Medical® by Medtronic Neurosurgery; Minneapolis, MN, USA) or clindamycin or rifampicin covered catheters (Codman Bactiseal®; Raynham, USA) were used. Ventricular drainage systems (LCR EDS 3 external drainage system; Codman®, Switzerland) and transducers for the monitoring of intracranial pressure were also used (CAMINO® laboratories; NeuroCare San Diego, USA).

For IVF, those patients with a Graeb score above 5 for IVH were given 10 000 intraventricular units of urokinase, for a length of time determined by clinical and tomographic criteria (a decrease in the amount of intraventricular blood along with a Graeb score below 6)[31].

For nursing care, watertight drainage system was strictly preserved and only broken to drain and obtain samples of CSF or for the instillation of local treatments, and strict asepsis measures were kept at all times.

For catheter removal, the time of EVD treatment was determined by the clinical evolution of the patient and the need of CSF drainage or ICP monitoring. If malfunction or accident occurs when removing catheter, but the catheter was still needed, the insertion of a new EVD on an alternative location was carried out. VRI did not justify the removal of the EVD when there was no indication for such removal.

Those patients with mechanical ventilation for a period longer than 48 h were subjected to selective digestive decontamination with a pool of amphotericin B, polymyxin, gentamicin and excipients, and a 3-day course of 2 g of intravenous ceftriaxone every 24 h.

2.3. Microbiological tests and test results

All EVD patients were subjected to a cytobiochemical test and CSF culture every 24–72 h from the insertion of the catheter until its final removal, accompanied by a simultaneous blood test. The CSF samples were cultured in a specific 35 °C and 5% CO_2 environment; germs were identified and the corresponding antibiogram with standard microbiological tests was carried out.

For collection and statistical analysis purposes, the moment of catheter insertion was defined as Day 0. The microbiological and cytobiochemical results were registered (glycorrhachia, proteinorrhachia, leucocyte count in CSF, blood sugar levels, leucocytes in blood and erythrocyte in blood and CSF) noting the drainage day corresponding to each simple. Several patients needed EVD during many days, then led to collect many samples; for data analysis purposes, for each one, five samples were selected following uniformity criteria. Discrepant data were corrected using an overall review of the computerised clinical history.

2.4. VRI definition and exclusion criteria

The VRI diagnosis was documented in the medical history of the patient, and the criteria for its diagnosis was established as follows: a known pathogen on CSF cultures with the association of at least two SIRS criteria[32], or, cytobiochemical suspicion[1] (less than 45 mg/dL hypoglycorrhachia and neutrophilic pleocytosis higher than 100 per mL) and SIRS symptoms with a negative culture[32]. The specificity of the positive cultures and the SIRS symptoms were subjected to the judgement of the doctor in charge of the patient who could interpret the symptoms as EVD colonization or contamination of the culture (in absence of symptomatology) or as symptoms related to another condition (pneumonia, urinary tract infection, *etc*.).

2.5. Data analysis

SPSS 11.0 (SPSS Ic. Chicago, Illinois) was used. Qualitative variables were expressed as frequencies and continuous variables were expressed as mean ± SD and median and interquartile

range (P_{25}–P_{75}) according to their distribution. The Fisher's test, *Chi*-square, student's *t*-test and Mann-Whitney *U* test were used to compare variables of VRI patients and non-VRI patients according to statistical criteria. A value of $P < 0.05$ was considered statistically significant. A multivariate logistic regression analysis was carried out using the backward Wald iterative method where the dichotomous dependent and categorical variable was the VRI diagnosis and the independent variables were age, drainage length in days, number of EVD, catheter indication, third CSF sample indication, proteinorrhachia, glycorrhachia and the glycorrhachia/blood sugar level quotient. Out of them, the continuous variables were dichotomised using the median as cut-off point: 60 years old, stay at ICU for 13 days, proteinorrhachia of 120 mg/dL, glycorrhachia of 80 mg/dL, and glycorrhachia/blood sugar level quotient of 0.5. The data analysis program detected automatically those variables which must be eliminated from consecutive interactions and finally selected the indication for EVD (subarachnoid haemorrhage, obstructive hydrocephalus, IVH and ICP monitoring) and low glycorrhachia/blood sugar levels. The area under the curve for the measuring ruler and the confidence interval (*CI*) were determined as 95%.

3. Results

3.1. Sample

Table 1 summarizes the sample characteristics. A total of 120 patients with an average age of 56.84 years (SD 15.77) were treated with 136 EVD between 2000 and 2006. About 62.5% of those patients were male. The APACHE II[29] average score was 16.70 (SD 7.36) and the SAPS II[30] average score was 39.23 (SD 15.77).

A total of 1364 derivation days in 119 patients were counted (one of those patients was already carrying a drain when admitted from another hospital), scoring a median of 11 EVD days (range 1–33 days); 9 of those patients had the EVD for less that 48 h. A total of 22 patients who suffered VRI were identified (18.33%), the infection rate being 15.39 cases per 1 000 drainage days. The percentage of infected inserted catheters was 16.17%.

3.2. Indications for insertion of EVD

Most of the EVD were inserted due to IVH and obstructive hydrocephalus. Statistical significance was proven for the indication cause and the development of VRI ($P = 0.001$).

3.3. Risk factors for VRI

Age, derivation length of time and number of drains were significantly higher in VRI patients ($P = 0.008$, 0.003 and 0.03 respectively). VRI incidence was significantly higher in the group of patients that carried two or more EVD (RR = 2.67, *CI* 95% 1.09–6.58) (Table 2), had subarachnoid haemorrhage (SAH) or IVH (RR = 5.20, *CI* 95% 1.94–13.95 and RR = 1.44, *CI* 95% 0.91–2.28 respectively); IVF resulted in 2.33 times risk increase (*CI* 95% 1.33–4.20). The administration of antibiotics (related to the treatment of other issues) prior to the diagnosis decreased the VRI risk with no statistical significance (RR = 0.79, *CI* 95% 0.25–2.45).

3.4. IRV diagnosis

3.4.1. Cytobiochemical findings in CSF and blood

Out of all the CSF checked samples, 359 were selected for the final analysis: 99 belonged to Day 3 of drainage (P_{25}–P_{75}: 2–5) and were classified as "first sample". A total of 86 belonged to drainage Day 6 (P_{25}–P_{75}: 2–30) and were labelled "second sample"; 74 belonged to Day 8.5 (P_{25}–P_{75}: 7–10.25) and were classified as "third sample", 58 belong to day 11 (P_{25}–P_{75}: 9.5–14.25) as "fourth sample". And finally 42 were obtained on Day 14 (P_{25}–P_{75}: 12–20.25) and were considered "fifth sample". Both VRI and non-VRI groups were very similar on simple days. In 21 patients no samples were obtained due to shortened time of drainage or death within the first hours of evolution; none of them had the VRI diagnosis.

A higher proteinorrhachia with significantly lower glycorrhachia and glycorrhachia/blood sugar level quotient was found in those CSF samples that were obtained in EVD Day 9 patients who had IRV ($P = 0.008$, 0.03 and 0.0001 respectively). Within this group, the glycorrhachia was also significantly lower on sample Day 13.

3.4.2. Microbiological findings

Out of all the CSF samples examined, 296 were selected for a final analysis. Out of them, 69 (23.31%) were positive; out of those 69, 38 belonged to VRI patients and the rest were labelled as simple contaminations or catheter colonizations. Out of the negative samples, 180 belonged to non-VRI patients. On 25 patients no CSF culture was carried out due to a catastrophic outcome within the first hours or to early removal of the catheter; all of them belonged to the group that did not developed the infection.

Table 1
Characteristics of the study population.

Characteristics	120 Patients	22 VRI	98 Non-VRI	*P*
Age [m (SD)]	56.84 (18.75)	63.59 (10.49)	55.33 (19.87)	0.008[a]
Gender (men/women)	75/45	15/7	60/38	0.540
APACHE [m (SD)]	16.7 (7.36)	17.41 (5.57)	16.54 (7.72)	0.910
SAPS [m (SD)]	39.23 (15.77)	38.86 (13.21)	39.31 (16.35)	0.620
Length of EVD (days) [md (P_{25}–P_{75})]	11 (1–33)	14 (7–33)	10 (1–31)	0.003[a]
Number of EVD [m (SD)]	1.13 (0.34)	1.27 (0.45)	1.1 (0.3)	0.030[a]
Intraventricular haemorrhage [*n* (%)]	49 (40.8%)	12 (54.5%)	37 (37.5%)	
Obstructive hydrocephalus [*n* (%)]	46 (38.3%)	3 (13.6%)	43 (43.9%)	
Subarachnoid haemorrhage [*n* (%)]	13 (10.8%)	7 (31.8%)	6 (6.1%)	
Brain tumour [*n* (%)]	7 (5.8%)	0	7 (7.1%)	
Intracranial pressure monitorization [*n* (%)]	5 (4.2%)	0	5 (5.1%)	

[a]: Statistical significance; m (SD): Medial value (standard deviation); md (P_{25}–P_{75}): Median (interquartile range); *n* (%): Number of patients (%).

Table 2
Risk factors for VRI.

Risk factors	120 Patients	22 VRI	98 Non-VRI	RR	*CI* (95%)
Intraventricular haemorrhage	49	12	37	1.44	0.91–2.28
Subarachnoid haemorrhage	13	7	6	5.20	1.94–13.95
Intraventricular fibrinolysis	32	11	21	2.33	1.33–4.20
Previous antibiotherapy	20	3	17	0.79	0.25–2.45
2 or more EVD	16	6	10	2.67	1.09–6.58

RR: Relative risk.

Within the VRI, thirteen were monomicrobial, six polymicrobial infections and three resulted in sterile CSF samples (Table 3). We found 26 patients with one or more positive CSF cultures due to EVD contamination or colonization (92.3% were monomicrobial, and the rest of them were polymicrobial) with Gram-positive cocci being the predominant organisms.

Table 3
Microbiological findings in VRI.

Microorganism	*n* (%)
CSF culture negative	3 (13.63)
Monomicrobial infections	13 (59.09)
S. epidermidis	5 (22.72)
Pseudomonas sp.	3 (13.63)
S. aureus	2 (9.09)
E. faecalis	2 (9.09)
Stenotrophomonas maltophilia	1 (4.54)
Polymicrobial infections	6 (27.27)
S. epidermidis–S. faecalis	3 (13.63)
S. aureus–E. faecalis	1 (4.54)
S. aureus–S. enteritidis	1 (4.54)
E. agglomerans–E. faecalis	1 (4.54)

S. epidermidis: *Staphylococcus epidermidis*; *S. aureus*: *Staphylococcus aureus*; *E. faecalis*: *Enterococcus faecalis*; *S. enteritidis*: *Salmonella enteritidis*; *E. agglomerans*: *Enterobacter agglomerans*.

3.4.3. Clinical findings

SIRS was found in 86.4% of the patients with VRI. No significantly statistical differences were found between the use of antibiotics for treating an indication prior to the VRI diagnosis and non-infected patients (13.6% *vs.* 17.3%, $P = 0.673$). A total of 33 patients died, and 31 had no VRI and 2 had ($P = 0.032$).

3.4.4. Multivariate analysis

A Wald logistic regression model was carried out, using a measuring ruler that applied to all of them, but calculated on 72 of them, since only they have the information of all the variables included in the model. The obtained area under the curve was 55.7% (*CI* 95%, 0.403–0.709) (Table 4).

4. Discussion

VRI constitutes the most important EVD related complications, and results in an increase in morbidity and mortality. Multiple studies have been published describing VRI incidence and guidelines on how to prevent it. Furthermore, the development of standardized protocols and checklists has been thought to reduce infections through medicine and is used in this same manner for ventriculostomy placement and its maintenance; however, most of these studies do not provide a clear definition of the diagnostic criteria for this complication[9,13,19,22]. Our retrospective study on 120 patients who were subjected to an EVD, analysed the criteria that had to be followed in order to diagnose VRI (clinical, microbiological and CSF and blood cytobiochemical). We found that the cytobiochemical changes for VRI and non-VRI patients are similar during the first 8.5 days of admission, and those indications that require a higher degree of EVD handling (administration of local treatments, urokinase instillation and repeated sample extraction)[3,7,13], as well as IVH and SAH seem to increase the risk of developing VRI. A multivariate analysis was carried out with the purpose of establishing a VRI risk prediction rule with an under-curve area of 55.7% (*CI* 95% 0.439–0.709). Dependent variables were included in the model which, according to our review and published data[1,2,4,7,10,20,22], seem to be associated with a higher VRI incidence: advanced age, presence of two or more EVD, the use of IVF, the indication for ventriculostomy and some cytobiochemical results obtained from the CSF sample taken on EVD Day 8. Although the prediction rule has been applied to the whole sample, the automatic variable selection done by the Wald test conditions the fact that it was only calculated on 72 patients, which resulted in an important loss on the power of the model and ultimately this could justify the lack of statistical significance.

4.1. Diagnosis, definition and VRI incidence

Specific characteristics of the critical patient, some related complications and neurosurgical and intensive treatments (EVD insertion amongst them), make the interpretation of the clinical parameters traditionally used to diagnose meningitis difficult and alter the CSF composition[11,18,25,33]. Blood presence at intraventricular level favours the existence of sterile inflammatory events[3,19] known as aseptic or non-infectious postsurgical meningitis[15–17], which are associated with an increase of white cell count in CSF samples. These facts have brought a wide diagnostic controversy, which, with the use of antibiotics, the different study inclusion criteria and differences

Table 4
Backward Wald iterative method. Prediction rule.

Variables	Beta	OR	Real weith for prediction	Weith	*CI* 95%
Subarachnoid haemorrhage		1	0.00	0.0	
Obstructive hydrocephalus	3.03	20.88	2.46	2.5	2.52–172.42
Intraventricular haemorrhage	1.23	3.42	1.00	1.0	0.55–21.24
Intracranial pressure monitorization	22.88	8.69	18.57	18.6	0.00
Low sugCSF/sugBlood quotient	2.06	7.85	1.67	1.7	2.08–29.68

Beta: Statistical power; OR: Odds ratio; Low sugCSF/sugBlood quotient: Glycorrhachia/blood sugar level quotient < 0.5.

in the management of EVD, make the comparison of infection rates which can be found in the literature extremely difficult. Lozier *et al.*[1], conducted a review on more than thirty VRI-related articles and suggested that the most referenced VRI definition is the one by Mayhall[34], which is based on clinical, cytobiochemical and microbiological criteria[1,7,11,18,20,22,25,27]. It is very likely that such specific definitions involve a loss of sensibility and assume a smaller VRI incidence, like the one published by Bota *et al.* which was 9%[2]. Using strictly microbiological criteria (one or more positive cultures) groups can be found which resulted in incidences of 4%[11], 7%[35], and 16%[18] which have been heavily criticised because of the variable profitability that cultures have and the possibility that the sample had been contaminated or the device had been colonized. Although definitions are still being discussed [1,2,9,12,13,22], it is considered that colonization is the presence of one or more positive CSF cultures with no compatible symptoms and no cytobiochemical variations. Contamination, on the other hand, is the isolation of a cutaneous saprophyte germ that turns negative with no treatment.

Our research contained the criteria that the doctor in charge of the patient used to diagnose VRI; the incidence resulted in 18.33%, which is similar to the most commonly mentioned references[1,5,7,14,20,22], in spite of our diagnosis criteria being more sensitive. Although the majority of our diagnosis is made on SIRS and CSF positive culture patients, it is worth to highlight that more than 13% of our EVD patients had VRI with negative CSF cultures; the VRI diagnosis was based on cytobiochemical variations and clinical criteria. On those studies with incidences fewer than 10%[7,11,36–38], the average age, EVD length of time and the percentage of HIV and/or IVF were also fewer than the ones in our study.

4.2. Diagnostic utility of CSF analysis: Cytobiochemistry and cultures and sample extraction guidelines

In order to diagnose VRI on its early stages, the routine CSF sampling for analytical purposes has become a regular practice [1,2,4–6,11,12,15,24–26,37], although its utility has been questioned in children[11] and adult patients[12]; changes on symptoms or CSF appearance, or leucocytosis with no evident source make the CSF sampling advisable[38]. The EVD guidelines that were being used for the length of time that our data collection lasted, considered the extraction of samples every 48–72 h from the moment the EVD was inserted until the time of removal; we have only found statistically significant differences in some of the parameters checked on EVD Day 8.5; the glycorrachia and glycorrachia/blood sugar level ratio are significantly lower in infected patients, and their proteinorrhachia is higher. If we consider that VRI is more frequent in the first five days after EVD insertion, then it is likely that CSF sampling during the first day is only adding manipulation, thus, increasing the risk of drain infection.

Although some authors have published cutting points for CSF parameters used to differentiate VRI, the threshold is very variable: white CSF cell count higher than 11[34], 15[10], 50[18], 100[2] and 7500[17] per microliter, CSF lactate concentration higher than 4 mg/dL[33], hypoglycorrhachia lower than 10 mg/dL[17] and 40 mg/dL[2], hyperproteinrrhachia above 50 mg/dL[2] and glycorrachia/blood sugar level quotient lower than 0.5[2,10]. In view of this wide variability, other cytobiochemical markers such as alfa 1 antitrypsin, haptoglobin, fibronectin and CRP have been evaluated with no significant differences found[3].

Our review did not include these parameters, which are still being debated. Pfausler *et al.*[19], suggested cell-index (ratio of leucocytes to erythrocytes in CSF and leucocytes to erythrocytes in peripheral blood) as a predictive VRI parameter in HIV patients, although their methodology[10] has been questioned since it lacked a truly effective cutting point. In our study, the cell-index values have been similar when comparing VRI and non-VRI patient groups; however, we have not tested the cell-index in HIV patients.

4.3. Microbiological findings

In our review, microbiological results relate to the published literature[1,2,7,11,15,18,20,25,26,28,38,39], *S. epidermidis* and *E. faecalis* monomicrobial VRI are predominant and so are the colonisations and contaminations produced by the same germs. The fact that we obtained a high percentage of *E. faecalis*-related colonisations is favoured by the microbial selection associated to the digestive decontamination protocol applied in the unit to those patients on prolonged mechanical ventilation. Twenty-six patients with no VRI and one or more positive CSF cultures were identified. Half of these patients had an EVD in the context of a IVH (eight of them received intraventricular fibrinolysis treatment). The data suggest, as published in other series[1,7–9,14,22], that the repetitive manipulation of the EVD that is required when IVF is carried out could be a risk factor for the colonization of the drainage itself or the samples obtained from it.

4.4. Clinical signs of VRI

Phlogosis at the insertion point[23], headache and nuchal rigidity[6] are not easy to assess in neurocritical patients. High temperature has been pointed out as the fundamental clinical sign that indicates VRI, with values above 38 °C or 38.5 °C [11,34], although some authors reject it when diagnosing VRI [18]. Martinez *et al.* used the decreased level of consciousness and a temperature threshold of 37.5 °C as part of their diagnostic criteria[10]. In our clinical study the presence of SIRS[32] was considered as a clinical sign of VRI; in spite of being non-specific, it allows a high sensitivity infectious screening and it was present in 86% of the infected patients.

The mortality described in the studied simples in this study (9.1% of the VRI patients) is not fully comparable to the published data due to the sample heterogeneity and the lack of severity indicators described in the literature. The mortality in the non-VRI sample group was three times higher than that in the VRI group; this phenomenon could be explained by the conditions that the drainage time of these patients was shorter and, hence, a lower VRI risk developed.

4.5. Risk factors

The favourable factors for VRI have been highly questioned. Our team detected a statistically increased risk of developing VRI linked to indications such as IVF and SAH which required a higher manipulation (instillation treatment, prolonged sampling) or longer drainage time[7,22]; those indications seem to be

in accordance to published data[4,34]. In those patients presenting IVH, the risk increase did not reach statistical significance, a fact that was probably related to our restricted sample. We found that those patients older and with longer EVD time developed VRI more frequently; this is also a fact that has been observed in other samples[4,5,14,22,24].

Some EVD guidelines recommend the use of prophylactic antibiotics around the drain insertion timeframe, which is a practice that is considered controversial by other researchers[28]. In our study, the antibiotherapy prior to the diagnosis of VRI meant a certain degree of protective effect with no statistical significance. Although some authors suggest that antibiotic-impregnated drains reduce the incidence of VRI[40,41], more well-designed clinical trials are needed in order to evaluate their effect[26].

The retrospective nature of this study can restrict the validity of our results. Given the characteristics of its design, the exact diagnosis moment could not be documented, and the collection of some relevant factors that allow the development of infection such as inmunosupresor or steroid treatment or the existence of intercurrent infections that could interfere with the sample prognosis was not possible.

Our study did not evaluate whether craniotomies, closed cranio-encephalic traumas, depressed cranial fractures, coin-fections, routine drain changes or EVD insertion sites increase the risk of VRI or not.

VRI diagnosis is based on clinical and microbiological data. Routine CSF culture and cytobiochemical sampling for the diagnosis of VRI are not advised; compatible clinical signs, repetitive device manipulation and/or drainage time longer than a week can be interpreted as indications for CSF culture and study of proteinorraquia, glucorraquia and glucorraquia/blood sugar level quotient.

Those indications that mean a longer insertion and manipulation time (such as IVF, SAH and IVH) are especially prone to favour drain contamination, colonization and infection. More studies that help establish CSF parameters, which, along with clinical data, allow the prediction of the risk of developing or existence of meningitis in EVD patients are needed.

Conflict of interest statement

The authors report no conflict of interest.

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