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COMMUNICATIONS C4
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Reducing external drainage-related cerebrospinal fluid infections through implementation of a multidisciplinary protocol: experience in a paediatric hospital

Ridurre le infezioni correlate alle derivazioni liquorali esterne con l'applicazione di un protocollo condiviso: l'esperienza di in un ospedale pediatrico

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Abstract

Objective. To assess the frequency of external cerebrospinal fluid (CSF) drain-related CNS infections before and after implementation of a protocol for their prevention.

Design. Quasi-experimental study, with comparison of incidence before and after the implementation of the intervention.

Setting and participants. Bambino Gesù Children's Hospital in Rome, Italy. Children receiving an external cerebrospinal fluid drain from 1 January 2013 to 31 March 2015.

Main outcome measures. Drain-related infections.

Results. Fifty-two patients were included in the study. Before protocol implementation, cumulative incidence was 14 per 100 drains. Incidence rate was 8/1,000 catheter-days. After protocol implementation, cumulative incidence and incidence rate were 6.7 per 100 drains and 4.6 per 1,000 catheter-days (p=0.61 and p=0.2 *versus* the pre-intervention period, respectively). Infected patients were significantly younger (median age: 16.5 days *vs* 13.4 months; p=0.026), had a significantly higher number of procedures (5 *vs* 1 procedure per patient; p <0.0001) and were most frequently affected by post-haemorrhagic hydrocephalus of premature newborns (50% *vs* 16.7%; p=0.039), compared to non-infected patients.

Conclusions. After protocol implementation, we observed a reduction of incidence of CSF drain-related infections, though the short post-intervention period limited the power of the study to detect a significant difference. Patients <1 year of age, with multiple interventions and post-haemorrhagic hydrocephalus had higher risk of CSF drain-related infections.

(*Epidemiol Prev* 2015; 39(4) Suppl 1: 113-118)

Key words: external cerebrospinal fluid (CSF) drains, protocol, prevention

Riassunto

Obiettivo. Valutare la frequenza delle infezioni del sistema nervoso centrale correlate ai drenaggi liquorali esterni (DLE) prima e dopo l'applicazione di un protocollo per la loro prevenzione.

Disegno. Studio quasi-sperimentale, con comparazione dell'incidenza pre-post attuazione dell'intervento.

Setting e partecipanti. Bambini che hanno ricevuto un drenaggio liquorale esterno dal 1-1-2013 al 31-3- 2015, nell'Ospedale Pediatrico Bambino Gesù, Roma.

Principali misure di outcome. Infezioni correlate a drenaggi liquorali.

Risultati. Sono stati valutati 52 pazienti, con 136 drenaggi totali. Nel periodo pre-intervento, l'incidenza cumulativa è stata 14 infezioni/100 drenaggi e il tasso di incidenza 8/1.000 giornate di derivazione. Nel periodo post-intervento, l'incidenza cumulativa e il tasso di incidenza sono state rispettivamente 6,7/100 e 4,6/1.000 (p=0,61 e p=0,2 rispetto al periodo pre-intervento). I pazienti con infezione erano più piccoli (età mediana: 16,5 giorni contro 13,4 mesi; p=0,026), con un maggior numero di procedure (5 contro 1; p<0,0001) e più frequentemente affetti da idrocefalo postemorragico del prematuro (50% rispetto al 16,7%; p=0,0039), rispetto ai pazienti non infetti.

Conclusioni. Dopo l'intervento abbiamo osservato una riduzione di incidenza di infezioni DLE correlate, sebbene il breve pe-

riodo post-intervento limiti la potenza dello studio. I pazienti di età <1 anno, con interventi multipli e idrocefalo post-emorragico hanno avuto un più alto rischio di infezioni correlate a drenaggi liquorali.

(*Epidemiol Prev* 2015; 39(4) Suppl 1: 113-118)
Parole chiave: drenaggi liquorali esterni, protocollo, prevenzione

INTRODUCTION

External cerebrospinal fluid (CSF) drains, including ventricular (EVD) and lumbar drains (ELD), are temporary devices used to perform CSF diversion in acute conditions, such as primary and secondary acute hydrocephalus, or for intracranial pressure monitoring.[1] Sometimes, clinical conditions cause patient dependence on CSF diversion and approximately one quarter requires conversion into permanent and implanted shunts.[2,3] Conversely, temporary drains may be inserted because of shunt complications, especially to prevent recurrent shunt infections.[4]
Use of external CFS drains is associated with risk of central nervous system (CNS) infections, such as ventriculitis and meningitis, which cause increased patient morbidity and mortality, length of hospital stay and costs.[5-7] These complications can also be associated with external subdural drains (ESD) employed to empty the subdural space of CSF pools, such as subdural hygroma or CSF layer.[8]
Predisposing factors for CSF drain-related ventriculitis or meningitis include intraventricular and subarachnoid haemorrhage, craniotomy, systemic infection, and underlying disease.[9] Other risk factors are catheter duration, multiple catheter insertions and exchanges, surgical technique of insertion, and multiple infections in other anatomical sites.[10,11] Coagulase-negative *Staphylococcus* and *Staphylococcus aureus* are the most common associated pathogens.[9,12] In adults, reported incidence of CSF drain-related infections ranges from 2% up to 25% of cases per drain placed, with mortality rates as high as 22% for ventriculitis caused by Gram-negative bacteria. Incidence rates range from 7.2 to 32 per 1,000 catheter-days.[12-14] In children, available data show that CNS infections occur in 9.4% of EVD insertions; reported incidence rate is 8.6 infections/1,000 catheter-days and mortality rate is 22.8%.[15-17]
Results reported from various studies are difficult to compare, because of differences in patient age, underlying diseases, case definition, and case ascertainment.[18,19] In order to prevent external CSF drain-related infections, several healthcare organizations have adopted standardized protocols and bundle approaches.[5,6,10,20] Despite possible severe consequences, there is little ongoing surveillance of external CSF drain-related CNS infections. In children, there is scarce evidence about the impact of preventive strategies.[16,21]
In this article, we present the results of surveillance targeting external CSF drain-related CNS infections in a tertiary care children's hospital in Italy, and we describe the impact of a multidisciplinary protocol for their prevention.

METHODS

Setting

The Bambino Gesù Children's Hospital (Ospedale Pediatrico Bambino Gesù, OPBG) is a 607-bed tertiary care research hospital in Rome, Italy. The hospital's acute inpatient admissions were 26,164 in 2013 and 26,716 in 2014. Hospital patient population includes children at high risk of acquiring healthcare-associated infections (HAIs), such as pre-term newborns and immunocompromised patients. In-hospital actions for prevention and control of HAIs have been implemented over time.[22] A multidisciplinary committee for infection control annually prioritizes interventions and monitors results of actions taken. In 2014, prevention of surgical site infections was identified as a priority for improvement.

Study design, case definitions, and data collection

This was a quasi-experimental study, with a pre- and post-intervention analysis. Patients with EVD, ELD, externalized catheter shunt, or ESD were identified through retrospective analysis of electronic records of surgical procedures, by extracting all procedures coded as ICD9-CM 01.26, 01.28, 01.31, 02.2, 02.31, 02.32, 02.39, 02.41, 02.42, 03.71-03.79, from January 2013 to March 2015.
Patients' clinical records were then reviewed to verify consistency of coding with description of the procedure and to collect the following information: age, gestational age for pre-term newborns, sex, first external drainage indication, catheter duration in days and removal causes, clinical symptoms compatible with diagnosis of ventriculitis or meningitis, CSF characteristics, and results of microbiological investigations.
Ventriculitis and meningitis were defined by the detection of a microorganism in the CSF, associated with compatible clinical signs (including fever >38°C, headache, stiff neck, meningeal signs, cranial nerve signs, and irritability, hypothermia <36.0°C, apnoea, bradycardia in patients ≤1 year) and at least one pathologic CSF finding (i.e., elevated cell count and/or decreased glucose level).
Infections were considered drain-related if at the time of microbiological confirmation the drain had been in place for at least 48 hours or had been removed within 48 hours prior to the diagnosis. CSF infections already present at drainage insertion were excluded from count of drain-related infections.

Preventive strategies

In 2014, a multidisciplinary group (neurosurgeons, neonatologists, clinical epidemiologist, microbiologists, pharmacist, infection control professionals, infectious disease physician) revised the recommendations for prevention of external CSF drain-related CNS infections and defined a specific protocol.[6,9,23] The protocol provides recommendations on patient preoperative preparation, surgical antibiotic prophylaxis, surgical technique, catheter type to be used, and postoperative

Steps	Actions
preoperative patient preparation	■ body showering or sponging with antiseptic soap (chlorhexidine or povidone iodine) the evening before and the morning of surgery ■ hair washing with cleaning soap or with a waterless shampoo cap ■ trichotomy with clipper the day of surgery, within 2 hours before surgery ■ head washing after trichotomy
antibiotic prophylaxis	■ single dose of antibiotic (cefazolin or vancomycin in MRSA carrier) within 60 minutes before incision ■ intraoperative antibiotic dose repeated if the operation duration exceeds antibiotic hemi-life ■ antibiotic prophylaxis continued for 24 hours after surgery
EVD insertion	■ physicians scrub up and wear cap, mask, sterile gown, and sterile gloves ■ all members of the staff wash their hands and wear cap, mask, and sterile gowns ■ head washing with antiseptic soap (chlorhexidine or povidone iodine) ■ full sterile draping of patient's head and body ■ skin preparation with gauzes soaked in 2% chlorhexidine and followed by gauzes soaked with povidone iodine ■ unsterile staff keeps at least 50 cm away from the surgical field. ■ rifampin/clindamycin-coated ventricular catheter in post-hemorrhagic hydrocephalus and in the absence of infection ■ non impregnated catheter in case of infection ■ catheter is tunnelled approximately 3 cm (patients weighing less than 1,500 g) to 5 cm from insertion site ■ collection of two CSF samples of 1 ml for chemical and microbiological analysis
dressing	■ catheter is secured using surgical staples ■ two patches are applied at 1 and 3 cm over catheter exit site and a three-way valve at the distal end of the catheter ■ a transparent patch is applied on the surgical scar ■ dressing should be kept intact for 72 hours, unless it is wet, dirty, or saturated with either blood or secretions
EVD manipulation	■ nurse checks dressing daily ■ all healthcare professionals involved in manipulation practice hand hygiene and wear cap, mask, sterile gown, and sterile gloves ■ every 72 hours, neurosurgeon checks dressing, replaces necessary parts, and collects a CSF sample of 1 ml for chemical analysis ■ before and after collection, access port and surrounding tubing are cleaned with 0.5% chlorhexidine in alcohol solution ■ height of the collection system is regulated by the neurosurgeon with the pressure level of "0" cm H_2O corresponding to the external acoustic meatus of the patient
EVD failure	■ in case of diastasis of the surgical incision, CSF leak, or accidental removal, neurosurgeon puts reinforcement stitches
EVD infection	■ in the presence of at least one sign or symptom of ventriculitis/meningitis and in the absence of other known causes, chemical and microbiological analysis, CSF Real-Time PCR, and blood cultures are performed ■ in the absence of signs and symptoms but with chemical or physical alterations of CSF found during routine testing, it is recommended to repeat CSF analysis with calculation of cell index, CSF culture, and Real-Time PCR

Table 1. Protocol for the prevention of EVD-related infections. / **Tabella 1.** Protocollo per la prevenzione delle infezioni DVE-correlate.

management, including infection and failure management (table 1). It was published on the Hospital intranet in September 2014.

Data analysis

We describe characteristics of CSF drain-related CNS infections by type and time period, before (January 2013-September 2014) and after (October 2014-March 2015) the implementation of preventive strategies.

Continue variables were described as median and range interval, and compared using the Mann-Whitney *U* Test. Categorical variables were described as proportions and compared using the Chi-square test or the Fisher exact test, as appropriate. Cumulative incidence of CSF drain-related infections was estimated as number of cases per 100 CSF drains (cumulative incidence) and as number of cases per 1,000 catheter-days (incidence rate). Estimates of cumulative incidence and incidence rate were compared using the Chi-square test or the Fisher exact test, as appropriate. Statistical analysis was performed with SPSS version 22.0 (SPSS Software, IBM, NY).

RESULTS

Over the study period, 52 patients (31 males and 21 females) had at least one procedure related to CSF drain placement. Patients' characteristics and type of inserted drain are reported in table 2. Five patients underwent placement of different types of drains. The vast majority of patients (46/52; 89%) had an EVD, mostly due to post-haemorrhagic hydrocephalus, or meningitis. Patients with EVD were younger than patients who had other types of drains (median age at first drain placement: 5.6 months versus 4.6 years for ELD and 10 months for ESD; p=0.004). The total number of drains was 136, with 2 drains per patient as median value. Median length of stay of catheter per patient was 28 days.

Patients' characteristics were similar in the two study periods, i.e., prior and after the implementation of the protocol with recommended interventions. No statistically significant differences were noted regarding sex, median age at first drain placement, or median duration of catheter either in the entire patient sample or in the EVD group.

Table 3 shows cumulative incidence and incidence rate of CSF drain-related infections by type of drain and study period. Before protocol implementation, there were 9 patients who had at least one CNS infection related to external CSF drains (19.1%) and 17 total infections, all in the EVD group. Cumulative incidence was 14 per 100 drains overall, and 15 per 100 EVDs.

	EVD	ELD	ESD	Total
number of patients	46	3	8	52[a]
number of males (%)	26 (56.5%)	3 (100%)	2 (25%)	31 (59.6%)
median age at first drain placement (range)	5.6 months (24 gestational week-13.3 years)	4.6 years (4.4-11.4 years)	10 months (4.9 months-7 years)	6.6 months (24 gestational week-13.3 years)
indication for first drain placement (%)				
post-haemorrhagic hydrocephalus of premature newborns	12 (26.1%)	0	0	12 (23.1%)
meningitis	9 (19.6%)	0	1 (12.5%)	10 (19.2%)
shunt infection	6 (13%)	0	0	6 (11.5%)
mechanical shunt complications	4 (8.7%)	0	0	4 (7.7%)
tumour	6 (13%)	3	1(12.5%)	10 (19.2%)
primary hydrocephalus	3 (6.5%)	0	0	3 (5.8%)
secondary hydrocephalus (other causes)	2 (4.3%)	0	0	2 (3.9%)
intraventricular haemorrhage	3 (6.5%)	0	0	3 (5.8%)
subdural hygroma or CSF layer	0	0	1 (12.5%)	1 (1.9%)
injury	1(2.2%)	0	0	1 (1.9%)
total number of drains	121	3	12	136
median number of drains per patient (range)	2 (1-13)	1 (1-2)	1 (1-1)	2 (1-13)
median duration of catheters in days per intervention (range)	17 (1-61)	7 (3-76)	8 (3-29)	16 (1-76)
median duration of catheters in days per patient (range)	28 (1-251)	5 (3-76)	8 (3-67)	28 (1-251)

[a] five patients inserted more than one type of drain / [a] cinque pazienti hanno inserito più di un drenaggio

Table 2. Characteristics of patients with external CSF drain, by type of drain.
Tabella 2. Caratteristiche dei pazienti con drenaggi liquorali esterni per tipo di drenaggio.

	EVD		ELD		ESD		Total	
	pre	post	pre	post	pre	post	pre	post
patients	42	6	2	1	6	2	47[a]	7[a]
drains	113	8	2	1	6	6	121	15
catheter-days	2012	115	79	5	45	96	2136	216
patients with at least one infection (%)	9 (21.4%)	0	0	0	0	1 (50%)	9 (19.1%)	1 (14.3%)
infections	17	0	0	0	0	1	17	1
infections/100 patients	40.5	0	0	0	0	50	36.2	14.3
infections/100 drains	15	0	0	0	0	16.7	14	6.7
infections/1,000 catheter-days	8.4	0	0	0	0	10.4	8	4.6

[a] five patients inserted more than one type of drain; two patients were involved in both study periods / [a] cinque pazienti hanno inserito più di un tipo di drenaggio; due pazienti sono stati coinvolti in entrambi i periodi di studio

Table 3. Cumulative incidence and incidence rate of CSF drain-related infections by type of drain and study period.
Tabella 3. Incidenza cumulative e tasso d'incidenza per le infezioni correlate alle derivazioni liquorali, per tipo e periodo di studio.

Incidence rates in all drains and in EVDs were 8 and 8.4 per 1,000 catheter-days, respectively. After protocol implementation, one patient had an infection (14.3%); the patient was in the ESD group. Cumulative incidence and incidence rate were 6.7 per 100 drains and 4.6 per 1,000 catheter-days (p=0.61 and p=0.2 *vs* the pre-intervention period, respectively).

As shown in table 4, patients who developed at least one infection were significantly younger compared to non-infected patients (16.5 days *vs* 13.4 months; p= 0.026). Median number of procedures and median duration of catheters per patient were significantly higher in infected patients than in non-infected patients (5 *vs* 1 procedure/patient p <0.0001 and 85.5 *vs* 23.5 catheter-days/patient, p <0.0001 respectively). Indeed, the 10 infected patients underwent 44.1% of all interventions. Indication for first drain placement also significantly differed between infected and non-infected patients, as post-haemorrhagic hydrocephalus of premature newborns was the indication in 50% of patients with infections *vs* 16.7% of patients with no infections (p=0.039).

CSF infections occurred after a median duration of 11 catheter-days. The majority of infections were sustained by Gram-positive bacteria (12/18; 72.2%), with Coagulase-negative staphylococci detected in 9 cases (50%), and *Enterococcus* species in 3 (16.7%). One positive CSF culture was observed for each of the following organisms: methicillin-resistant *Staphylococcus aureus*, *Klebsiella pneumoniae*, *Acinetobacter baumannii*, *Candida albicans*, *Escherichia coli*, and *Serratia marcescens*.

CONCLUSIONS

In our experience, the implementation of a multidisciplinary protocol for prevention of CNS infections in children with CSF drains was followed by a reduction of approximately 25% of infected patients and of 42% of the incidence rate per 1,000 catheter-days. Compared to the pre-intervention period,

	Patients with infections	Patients with no infections	Total
number of patients	10	42	52
number of males (%)	8 (80%)	23 (54.8%)	31 (59.6%)
median age at first drain placement (range)	16.5 days (24 gestational week-6.5 years)	13.4 months (31 gestational week-13.3 years)	7.5 months (24 gestational week-13.3 years)
Type of drain			
EVD	57 (95%)	64 (84.2%)	121 (89%)
ELD	0	3 (4%)	3 (2.2%)
ESD	3 (5%)	9 (11.8%)	12 (8.8%)
Indication for first drain placement (%)			
post-haemorrhagic hydrocephalus of premature newborns	5 (50%)	7 (16.7%)	12 (23.1%)
meningitis	1 (10%)	9 (21.4%)	10 (19.2%)
shunt infection	2 (20%)	4 (9.5%)	6 (11.5%)
mechanical shunt complications	1 (10%)	3 (7.1%)	4 (7.7%)
tumour	1 (10%)	9 (21.4%)	10 (19.2%)
primary hydrocephalus	0	3 (7.1%)	3 (5.8%)
secondary hydrocephalus (other causes)	0	2 (4.8%)	2 (3.8%)
intraventricular haemorrhage	0	3 (7.1%)	3 (5.8%)
subdural hygroma or CSF layer	0	1 (2.4%)	1 (1.9%)
injury	0	1 (2.4%)	1 (1.9%)
Indication for drain removal (%)			
death	0	3 (3.9%)	3 (2.2%)
persistent CSF infection	18 (30%)	8 (10.5%)	26 (19.1%)
drain failure	6 (10%)	6 (7.9%)	12 (8.8%)
no further clinical indication	7 (11.7%)	23 (30.3%)	30 (22.1%)
internalization operation	19 (31.7%)	33 (43.4%)	52 (38.2%)
replaced during other procedure	6 (10%)	2 (2.6%)	8 (5.9%)
accidental removal	4 (6.6%)	1 (1.3%)	5 (3.7%)
total number of drains	60	76	136
median number of drains per patient (range)	5 (2-13)	1 (1-6)	2 (1-13)
median duration of catheter in days per patient (range)	85.5 (17-251)	23.5 (1-127)	28.5 (1-251)
median duration of catheter in days per insertion (range)	17 (2-61)	14.8 (1-76)	16 (1-76)

Table 4. Characteristics of patients with external CSF drain, by CNS infection presence.
Tabella 4. Caratteristiche dei pazienti con drenaggi liquorali esterni, per presenza di infezione del SNC.

when we observed 17 CNS infections, only one infection occurred in the post-intervention period.

Our study focused on a paediatric population with a younger age and with different clinical indications than reported by other studies:[15,16] we observed mostly infants in the first year of life who had EVD for hydrocephalus, while other case series involve older children with tumours and trauma as prevalent clinical indications. In addition, the median catheter length of stay in our study (16 days) was more than twice that found in others (7 days).[3,15,16] These differences in patient population make comparison among studies difficult. In the pre-intervention period, our proportion of infected patients was higher than reported by other authors (19.1% *vs* 6%) however, due to longer duration of catheter use, EVD-related infection incidence rate per 1,000 catheter-days was similar (8.4/1,000 *vs* 8.6/1,000).

First EVD infections occurred at 11 catheter-days of median duration, confirming increased risk of EVD infection related to placement length beyond 10 days, reported by Kim et al., although a paediatric study and review recorded an increased risk during the first 10 catheter-days.[16,19] This apparent discrepancy may be due to the paucity of studies describing patients with drain duration longer than 10 days.[19] In our experience, the number of procedures per patient were significantly higher in patients infected. These results are compatible with those reported in other studies, where drainage contamination during placement is a recognized risk factor for infection.[17,24]

Our study also confirms that Coagulase-negative staphylococci are most frequently responsible for EVD-related infections.[15,21] Moreover, it seems to confirm the increased infection risk in cases of intraventricular haemorrhage, especially in post-haemorrhagic hydrocephalus of premature newborns, which represents the most frequent condition in our infected patients and may be due to their major clinical susceptibility.[25]

Our study is limited by the shortness of the post-intervention period, with a low number of patients who underwent external CSF drains, and by lack of other information that could influence infection risk, such as use of antibiotic-impregnated or standard catheters, surgical antibiotic prophylaxis, and antibiotic use in the postoperative period. An extended period of observation, along with collection of these data, could allow to better evaluate the impact of protocol implementation on prevention of external CSF drain-related infections.

Conflicts of interest: none declared

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