Abstract

Objective

We aim to evaluate whether intraoperative cerebrospinal fluid (CSF) sampling during ventriculo-peritoneal (VP) shunt insertion can predict future VP shunt infection or guide its management.

Methods

83 paediatric patients undergoing VP shunt insertion between February 2013 and July 2019 were retrospectively identified. Patient demographics, presence of pre-operative extra ventricular drain (EVD), pre-operative CSF results, and intra-operative CSF results were identified from patient case notes and electronic clinical databases. All included patients were followed up for a minimum of 6 months for identification of shunt infection.

Results

90 VP shunt insertions were performed in 83 patients. Age at time of shunt insertion ranged from 5 days to 15.8 years (mean 44.2 months). Tumours were the most common aetiology for hydrocephalus (n=24). 67 cases (74.4%) had intra-operative CSF samples, of which 2 revealed the presence of bacteria. Only 1 patient with intra-operative CSF sampling positive for growth developed shunt infection during follow up. Two cases developed a shunt infection despite normal intra-operative CSF results. Three cases did not have intra-operative CSF sampling but developed a shunt infection during follow up. Intra-operative CSF culture achieved 33.3% sensitivity and 98.4% specificity for predicting future shunt infection (p=0.154). The Receiver Operator Characteristic (ROC) curve of intra-operative white cell count (WCC) and shunt infection at 6 months follow up yielded an Area Under the Curve (AUC) of 50.3%.

Conclusion

Our results show that intraoperative CSF sampling as a method to predict future risk of shunt infection and to help inform future antibiotic prescribing is unreliable. Given an AUC of 50.3%, it is no better than chance as a diagnostic tool. Further larger studies are needed to substantiate this.

Introduction

Ventriculo-peritoneal (VP) shunting remains the mainstay of surgical treatment for paediatric hydrocephalus (Canadian Pediatric Neurosurgery Study 2010, Di Rocco et al. 2006). Despite the advancements in surgical technologies (Aschoff et al. 1999, Drake et al. 2000), VP shunting is still associated with complications such as obstruction, infection, mechanical failure, over drainage, and distal catheter site failures (Hanak et al. 2017). Shunt infection in paediatric patients is associated with increased mortality and morbidity, reduced intellectual performance, and seizures (Chadduck and Adametz 1988, Sagun et al. 2000). The incidence of shunt infection varies across institutions and ranges from 5%-15% (McGirt et al. 2003, Prusseit et al. 2009). Generally, most shunt infections occur as a result of colonization at the time of shunt insertion.

Although widely practiced as a routine step of VP shunt insertion, there is no published evidence for intra-operative cerebrospinal (CSF) sampling in the paediatric population to predict the future risk of shunt infections or to guide antibiotic management. Of the shunt insertion protocols for reducing shunt infections published in scientific literature, most did not report performing intra-operative CSF sampling (Faillace et al. 1995; Pirotte et al. 2007; Kestle et al. 2016; Lee et al. 2017). Sweeney et al (2019) chose to include intra-operative CSF sampling to exclude intra-operative inoculation and to confirm sterile technique, despite acknowledging that the use of intra-operative sampling to future risk of shunt infection may be unreliable. A single study of an adult population found no correlation between intra-operative CSF sampling and post-operative CSF for infected cases (Khalil et al. 2016). This brings into question the significance of intra-operative CSF sampling and whether it contributes to the future management of shunt infection in the paediatric population. The

objective of this study was to determine if routine intra-operative CSF sampling guided the management of future shunt infection at our institution.

Methods

We retrospectively identified 83 consecutive paediatric patients under 16 years of age undergoing VP shunt placement between February 2013 and July 2019 at the University Hospital of Wales, Cardiff. All data was obtained via a review of patient case notes and electronic clinical databases. Data collected included patient demographics, presence of pre-operative extra ventricular drain (EVD), pre-operative CSF results and intra-operative CSF results (including CSF culture and WCC). All patients were followed up for at least 6 months to identify shunt infection. Shunt infection was based on clinical grounds and/or identification of CSF leucocytosis or microorganisms on CSF microscopy/culture.

R (R Core Team, 2020) was used with the pROC package (Robin et al. 2011) to perform ROC curve analysis of intra-operative CSF white cell count to determine its reliability of predicting shunt infection at 6 months follow up. Pearson's Chi-squared test with Yates' continuity correction was used for statistical analysis, with a p-value <0.05 considered significant. Patients without intra-operative CSF samples were excluded from data analysis.

Results

A total of 90 procedures were performed in 83 patients (7 patients had removal and re-insertion of their shunt: 6 for infection and 1 for a non-infective cause). The demographics of this cohort are shown in Table 1. The age at the time of shunt insertion ranged from 5 days to 15.8 years, with a mean of 44.2 months. Tumours were the most common cause of hydrocephalus (28.9%) (Table 1).

Table 1: Patient demographics

DEMOGRAPHICS	NO. OF PATIENTS
TOTAL PATIENTS	83
GENDER	
MALE	43
FEMALE	40
AETIOLOGY	
TUMOUR	24
INTRAVENTRICULAR HAEMORRHAGE (IVH)	15
MYELOMENINGOCELE (MMC)	12
IDIOPATHIC INTRACRANIAL HYPERTENSION	8
CONGENITAL	7
AQUEDUCTAL STENOSIS	4
MENINGITIS	4
TRAUMA	2
HURLER'S SYNDROME	1
NEUROFIBROMATOSIS TYPE 2	1
POSTERIOR FOSSA CYST	1
POST MENINGIOMA	1
UNKNOWN	3

A total of 19 patients had EVDs placed pre-operatively. The aetiologies of patients with pre-operative EVDs are depicted in Figure 1.

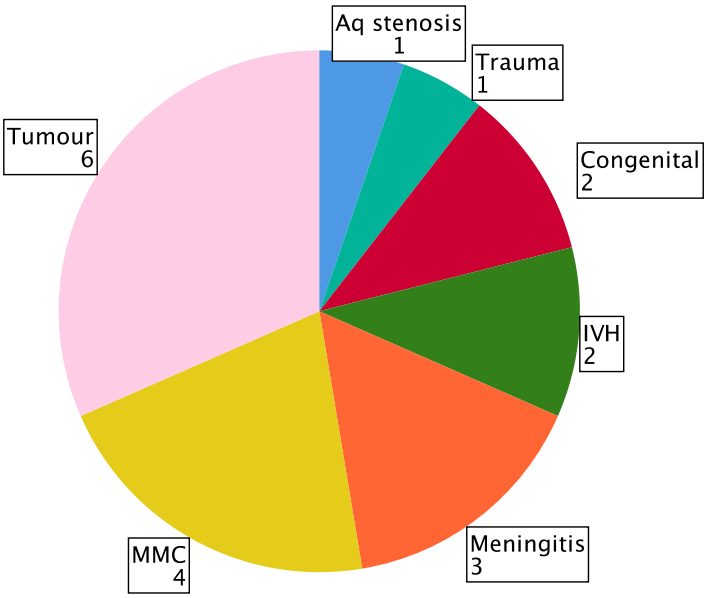

Fig. 1 Number of patients with pre-operative EVDs categorised based on aetiology of hydrocephalus

32 cases (35.6%) had pre-operative CSF samples taken (via EVD or lumbar puncture) before shunt insertion. Only 2 pre-operative CSF samples were positive for growth: 1) coagulase-negative *Staphylococcus* and 2) group A *Streptococcus*. However, neither case resulted clinically in shunt infection and thus were deemed contaminants.

67 cases (74.4%) had intra-operative CSF samples, of which 2 (2.2%) showed bacteria on microscopy and were subsequently positive for growth on culture media. One grew coagulase-negative *Staphylococcus.* This was deemed a contaminant as the sample was negative for leukocytes and the patient did not develop a clinical shunt infection. The second patient had *Enterobacter spp.* on microscopy and underwent shunt removal. In hindsight, this patient had undiagnosed meningitis that generated no septic symptoms or signs prior to shunt insertion.

Two patients developed clinical shunt infection despite normal intra-operative CSF samples and had their shunts removed, both of whom interestingly had no organisms on microscopy or any subsequent growth on culture medium but a marked CSF leucocytosis at the time of shunt removal.

Growth on CSF culture media for predicting shunt infection at 6-month follow up had a sensitivity of 33.3%, specificity of 98.4%, and a positive predictive value of 50% ($p = 0.154$). The contingency table is depicted in Table 2.

Table 2: Contingency table of Intra-operative CSF culture results and shunt infection at 6 months follow up

	Shunt infection at 6 months follow up	No shunt infection at 6 months follow up	Total
Positive intra-operative CSF culture	1	1	2
Negative intra-operative CSF culture	2	63	65
Total	3	64	67

Of the 23 cases (25.6%) who did not have intra-operative CSF sampling, 3 (3.3%) went on to develop shunt infection within 6 months. One (1.1%) patient developed a shunt infection with *Pseudomonas aeruginosa* and underwent shunt removal. The other two infections were in the

same patient 1 month apart. However, on both occasions, microscopy and growth were both negative. Each time the shunt was removed and then re-inserted after treatment.

Receiver Operator Characteristic (ROC) curve analysis of the effect of CSF white cell count on the outcome of shunt infection at 6 months yielded an Area Under the Curve (AUC) of 50.3% (Figure 2).

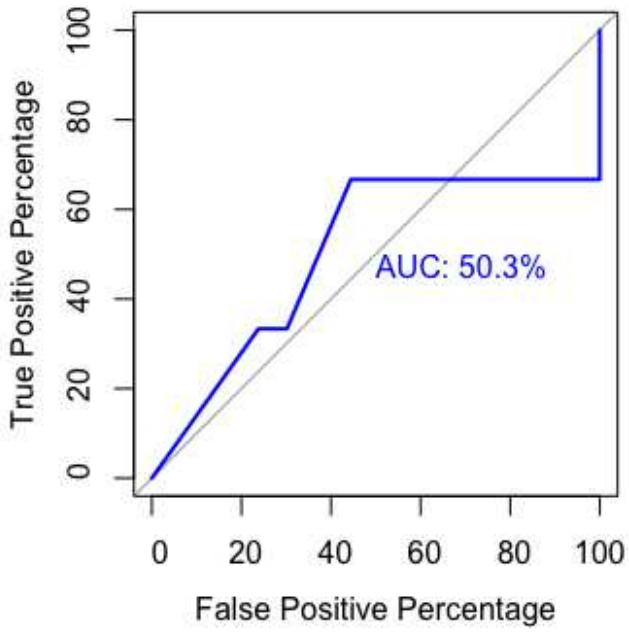

Fig. 2 ROC curve of intra-operative CSF WCC and shunt infection at 6 months follow up, with an AUC of 50.3%.

Discussion

Early recognition of shunt infection should reduce the neurological impact on children. Conversely, a delay in diagnosis of shunt infection might result in poorer outcomes and higher mortality. However, there is no evidence that intra-operative CSF sampling leads to earlier diagnosis of VP shunt infection. A study in the adult population showed no correlation

between intra-operative CSF sampling during VP shunt insertion and the subsequent development of shunt infection (Khalil et al. 2016). In our cohort of paediatric patients, only 1 patient benefitted from intra-operative CSF sampling. However, this was an unusual case as the patient had undiagnosed meningitis at the time of shunt insertion, as they presented with hydrocephalus with no objective signs of infection. Therefore, the intra-operative CSF sample revealed meningitis which resulted in shunt removal within 24 hours. Two patients developed shunt infection despite normal intra-operative CSF results. Despite the 98.4% sensitivity of intra-operative CSF culture for prediction of shunt infection, statistical analysis revealed that this was statistically insignificant. Moreover, the positive predictive value was 50%.

To determine if intra-operative CSF WCC could be a reliable marker for future shunt infections at 6 months follow up, we performed a ROC curve analysis to plot the sensitivity (true positive) against 1-specificity (false positive) of the values of each WCC cut-off value on a logistic regression that classified our patient cohort into those who had a shunt infection at 6 months follow and those who did not. A curve that lies on the diagonal baseline indicates a diagnostic performance that is no better than chance, as it has an equal true positive and false positive rate at all cut-off values. The area under the ROC curve (AUC) provides an overall assessment of the performance of the diagnostic test as a classifier. The maximum AUC of 1.0 indicates an ideal classifier whereby all positive outcomes are correctly identified with no false positive outcomes. However, an AUC of 0.5 indicates a classifier that is operating at chance level, with a 50% chance of sorting the variable into the correct outcome group. Based on our analysis, the AUC of the ROC curve of intra-operative CSF WCC was 50.3% which indicates it was performing at chance level.

This exemplifies the unreliability of intra-operative CSF sampling and casts doubt on its necessity especially as it contributes to the overall cost of patient care associated with the delivery, plating, analysis, and equipment costs of CSF sampling.

The decision for intra-operative CSF sampling was surgeon-dependent at our centre. As a result, a quarter of patients did not have intra-operative CSF sampling (25.6%). However, it is unclear whether intra-operative CSF sampling would have led to a more rapid diagnosis of shunt infection in the 3 cases that did not have intra-operative CSF sampling. In one of these cases, the post-operative CSF sample identified *Pseudomonas aeruginosa* 12 days after the date of surgery, so it could be argued that it would have. Intra-operative CSF sampling is unlikely to have been helpful in the other 2 cases as they did not show any bacteria even at the time of diagnosis of shunt infection.

Sweeny et al (2019) proposed the inclusion of intra-operative CSF sampling in their protocol for VP shunt infection reduction as a method of confirming sterile technique and to identify instances of intra-operative contamination during insertion. However, it is unclear if the costs associated with intra-operative CSF sampling (estimated £15/sample at our institution) is worth the confirmation of sterile technique or identification of intra-operative contamination when it does not affect future management strategies. Although our findings go against a widely practice neurosurgical routine, our results reveal that intra-operative CSF sampling solely for the prediction of future shunt infection is unreliable. However, other proposed uses of intra-operative CSF sampling include acting as documented proof of a functioning shunt at the time of placement, and prediction of shunt blockage secondary to raised CSF protein levels (Kamat et al 2018).

Limitations

This is a retrospective review of a single institution's results. Our definition of infection comprises a positive CSF culture and/or clinical signs and symptoms of shunt infection. Therefore, we may have over-estimated the infection rate, although we do not believe this would change the conclusion that CSF sampling was only useful in 1 patient.

Conclusion

Our results show that intraoperative CSF sampling as a method to predict future risk of shunt infection and to help inform future antibiotic prescribing is unreliable. Given an AUC of 50.3%, it is no better than chance as a diagnostic tool. This casts doubt on the need for intra-operative CSF sampling, which might add to the costs of healthcare in terms of materials used and costs of CSF analysis. However, until a prospective study is performed to fully answer this question, we suggest that intra-operative CSF samples should continue to be obtained at the time of shunt insertion.

Declarations of interest: none

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