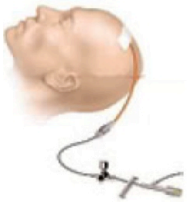

External Ventricular Drainage

BNTRC National Audit

National Audit Protocol

Prospective Multi-centre Audit of External Ventricular Drainage Management and Infection Rates in the United Kingdom and Ireland

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Protocol version 2.0

Website: www.bntrc.org.uk

BNTRC British Neurosurgical Trainee Research Collaborative

Advancing Research through Collaboration

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I. STEERING GROUP

Trainee Steering Group:

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II. PROPOSED TIMELINE

Date	Objective
March 2014	Presentation at BNTA meeting
April - May 2014	Development of audit proposal
May 2014	Submission of proposal abstract for presentation in autumn SBNS meeting
July 2014	Completion of formal audit proposal and submission to BJNS
Aug - Nov 2014	- Development of audit database - Local audit registration by lead trainees
September 2014	Present proposal at SBNS meeting
Nov 2014	Testing of Orion database
Nov 14 – Feb 15	National data collection
May 15	Complete data follow-up

III. ABBREVIATIONS

EVD	External Ventricular Drainage
ERI	EVD-related infection
CSF	Cerebrospinal Fluid
VP shunt	Ventriculoperitoneal shunt
BNTRC	British Neurosurgical Trainee Research Collaborative
RoSERI	Reduction of Shunt- and EVD-related infections collaborative group
CI	Confidence Interval
RCT	Randomized Controlled Trial

IV. ABSTRACT

Objectives:

We aim to establish the demographics, current practice patterns, and infection rates of External Ventricular Drain (EVD) insertion across the UK and Ireland.

Design:

We propose a prospective, multi-centre audit of EVD management in the United Kingdom (UK) and Ireland. The audit will be run under the auspices of the British Neurosurgical Trainee Research Collaborative (BNTRC), Society of British Neurological Surgeons (SBNS), the British Neurotrauma Group (BNG), the UK Shunt Registry, the Reduction of Shunt- and EVD-related infections collaborative group (RoSERI collaborative group) and the UK Neurosurgical Research Network.

Methods:

All neurosurgical units in the UK and Ireland will be invited to enroll and data will be collected over a 3-month period. The audit aims to include patients of all ages who have an EVD inserted in participating units. Our proposed outcome measures include: (1) EVD-related infection (ERI) rates; (2) duration of EVD placement; (3) need for a ventriculoperitoneal (VP) shunt; (4) length of stay in neurosurgical unit; (5) GCS on discharge; (6) number of EVD replacements and (7) patient mortality. Follow-up for ERI and patient mortality will be 30 days from EVD insertion while follow-up for need for VP shunt will be 90 days from insertion. The ERI audit standard has been set from the literature at below 15%.

Conclusions:

This audit will determine contemporary EVD practice and will establish national benchmarks. Alongside this, it aims to identify standards that may be associated with improved outcomes. This will guide future research under the British Neurosurgical Trainee Research Collaborative and the UK Neurosurgical Research Network.

V. INTRODUCTION

In neurosurgery, cerebrospinal fluid (CSF) diversion through a ventriculostomy using an external ventricular drain (EVD) is an important procedure for patients with acute hydrocephalus or elevations of intracranial pressure. However, the placement of EVDs comes with the significant risk of introducing EVD-related infections (ERIs). The incidence of ERIs within the literature varies from 0.8% approaching up to 22%[123]. In addition to the increased risk of mortality, ERIs increase hospital stays and costs, commit patients to extended courses of antibiotics and increase the likelihood of requirement of permanent CSF diversion[45]. A number of parameters have been identified to increase the risk of ERIs including systemic infection, craniotomy, duration of catheter dwelling, frequency of sampling and location of insertion[1]. The drive to reduce ERIs has included technical modifications such as extending tunneling lengths and strict sampling protocols[3]. The use of prophylactic antimicrobial agents is an important strategy in reducing ERIs with two approaches: systemic or local antimicrobial use. To evaluate systemic use of antibiotics, a meta-analysis of six studies (including two RCTs and four observational studies) demonstrated that prolonged prophylactic systemic antibiotics reduced ERIs compared to patients having only peri-procedural antibiotics by a relative risk of 0.45 (95% CI: 0.27-0.74)[6]. However, the major RCT within the meta-analysis showed that though patients who were exposed to prolonged systemic antibiotic prophylaxis had reduced ERIs; they were more likely to grow resistant organisms and had a higher overall mortality compared to the control group[7].

Local use of antibiotics can be achieved either by intrathecal injection of the antibiotic directly into the ventricle or by using catheters impregnated with antimicrobial agents. The recent focus of local antibiotic delivery has been on impregnated EVD catheters. A randomized controlled trial (RCT) by Zabramski et al demonstrated that antibiotic impregnated (AI) catheters resulted in a statistically significant reduction in ERIs compared to non-impregnated control catheter [1.3% vs 9.4%; p=0.02][8]. Similarly, Keong and colleagues demonstrated that catheters impregnated with silver nanoparticles reduced ERI rates compared to control from 21.4% to 12.3% (p=0.04)[5]. A single centre pilot study by Winkler et al comparing AI and silver catheters demonstrated a 10% confirmed infection rate in both cohorts (p=0.71)[9]. These early results demonstrated no difference in efficacy between the two types of catheter however further multi-centre RCTs are required. Similarly, the BASICS trial (British

antibiotic and silver-impregnated catheters for ventriculoperitoneal shunts multi-centre randomised controlled trial) - a three-way comparative trial of standard, silver and AI catheters in ventriculoperitoneal (VP) shunting is underway[10]. This work will help improve our understanding of the comparative efficacy and safety of the differing antimicrobial impregnated catheters in CSF diversion.

The majority of studies investigating ERIs have concentrated on either a single unit's experience or the pooled results of a handful of neurosurgical units. This limits the generalizability of the results and does not provide information on national variation. Recently, there has been a drive to establish trainee-led surgical research networks to buttress nation-wide audit and research[11]. The British Neurosurgical Trainee Research Collaborative (BNTRC) recently completed its first national audit of chronic subdural haematoma management[12]. Data were collected on over 1200 patients - the largest prospective multi-centre cohort of such patients in the literature - demonstrating its grass-root effectiveness [unpublished data]. We aim to build upon this experience and infrastructure to prospectively determine EVD management and infection rates in the United Kingdom and Ireland, and here, we outline a proposal to undertake a prospective nationwide multi-centre audit.

VI. OBJECTIVES

The audit has three primary objectives:

1. Establish the demography, contemporary practice patterns, and complications (including rate of infections) of EVDs across the UK and Ireland.
2. Identify practices that may be associated with improved outcomes.
3. Use collected data to guide future research questions and studies.

VII. MATERIALS AND METHODS

We propose to undertake a prospective, multi-centre audit of EVD management in the United Kingdom (UK) and Ireland. The audit will be run under the auspices of the British Neurosurgical Trainee Research Collaborative (BNTRC), the UK Shunt Registry, the Reduction of Shunt- and EVD-related infections collaborative group (RoSERI collaborative group) and the UK Neurosurgical Research Network. The audit will be part of the National Neurosurgical Audit Programme of the Society of British Neurological Surgeons (SBNS). A Steering Committee, which will include representatives from the above groups and other relevant non-corporate stakeholders, will have the overall responsibility for overseeing the strategic direction and running of the audit. All neurosurgical units within the UK and Ireland are eligible to participate. Each unit will have a trainee and consultant lead and will register the audit in accordance with their local clinical governance policies.

Patient eligibility

The audit aims to include **ALL** patients of any age who have had an EVD inserted within the participating neurosurgical units in the UK and Ireland during the study period. The EVD can be inserted as a standalone procedure or as part of another procedure.

Outcome measures and audit standards

The audit will focus on the following primary and secondary outcome measures (**Table 1**):

1. *Primary outcome*: EVD-related infection rate (confirmed and suspected cases)
2. *Secondary outcomes*:
    a. Glasgow Coma Score (at 30 days or discharge if sooner)
    b. Time to discharge (duration of neurosurgical stay)
    c. Patient mortality (up to 30 days)
    d. Mofied Rankin Score (at 30 days or discharge if sooner)
    e. Need for permanent CSF diversion (up to 90 days from audit data and shunt registry)

EVD-related Infections Rate

EVD-related infection (ERIs) will be defined under two categories: 'confirmed' ERI will be defined as a gram stain positive or culture positive CSF sample that is not deemed a contaminant by the managing team and prompts antibiotic therapy and/or catheter

removal. 'Suspected' infection will be allocated when the managing team has a clinical suspicion of meningitis (clinical signs, serum inflammatory markers, CSF pleocytosis) that prompts the use of antibiotics and/or catheter removal but is culture and gram stain negative. The final infection rate will be a combination of both the confirmed and suspected cases. Importantly, patients who have evidence of a CSF infection at the time of EVD insertion will be assessed for time to infection resolution and will be analyzed as a sub-cohort in the final analysis. The audit aims to follow-up patients for infection up to 30 days from EVD insertion. The infection rate within the literature varies widely. This is likely due, in part, to differing definition of ERIs. Stringent definitions of ERIs that necessitate two separate cultures or both gram stain and culture positive aren't reflective of daily practice and ignore the importance of clinical suspicion. The SILVER study used a pragmatic definition of ERI similar to our definition and found an infection rate of 12.3% in the treatment group[5]. We have therefore opted to set our audit standard at a VRI rate below 15%.

Ventriculoperitoneal Shunt conversion

Conversion to long-term CSF diversion with a ventriculoperitoneal (VP) shunt is an important clinical end-point. ERI has been demonstrated to increase the risk of VP shunt requirement[5]. Within the literature, the incidence of permanent CSF diversion following EVD insertion varies between 4-32%[5 8 9 13]. The follow-up time for VP shunt insertion will be 90 days from EVD insertion. This can be obtained from the UK Shunt registry rather than duplicated within the audit.

Patient mortality

Studies investigating EVD management have not routinely included mortality within their outcome measures. Of the few reports that have, a study by Flint and colleagues found a patient population mortality rate of 33.6%[3]. This is very high, however Flint's study looked only at an intensive care population that likely skewed the results due to the more critical nature of their pathology. Two recent RCTs by Keong and Winkler found mortality rates of 18.3% and 16% respectively[5 9]. Patient mortality will be assessed for up to 30 days from EVD insertion.

Data collection

Preliminary data collection will be piloted in two neurosurgical units. Once the pilot period is complete, the data collection will be rolled out across all participating units and will run for a three-month period. Patients will be identified prospectively through

on-call and theatre lists. We anticipate that 6-10 patients will be recruited per unit per month. Every EVD insertion will be treated as a single data-set entry to overcome issues with EVD reinsertion in the same patient. The audit will aim to collect a range of data including patient age, gender, comorbidities and indication for EVD insertion. Alongside this baseline data, we also plan on collecting procedure specific information that includes: the type of EVD catheter, level of surgeon, location of surgery, length of tunneling and use of peri-operative antibiotics. Patients will then be prospectively followed up to 30 days from the time of EVD insertion for ERI/mortality and up to 90 days for VP shunt requirement. Those identified as having developed a ERI will have further infection specific data collected including cultured organism (if present), CSF white cell count, time of infection and antibiotics used. Finally all patients will have outcome data collected as outlined above. Operating theatre registers and other clinical management systems will be used for the identification of eligible patients. Data will be submitted directly by members of the local clinical team to the secure online platform hosted by the Outcome Registry Intervention and Operation Network (ORION), which already hosts the UK CSF shunt registry. The ORION platform complies with the Department of Health Information Governance policies and standards for secure processing of patient healthcare data as set out in the Information Governance Toolkit of the Health and Social Care Information Centre. The audit will be implemented within the established ORION governance and administration structure.

Data analysis

Data analysis will be undertaken on anonymized patient data. Qualitative analysis will be done in the first instance to give whole cohort information including patient demographics and the main outcome parameters. Simple comparative analysis (unpaired *t*-test and Chi Squared) can be used to look at difference between different cohorts for the outcome parameters. The analysis can be extended to include survival analysis such as Cox proportional Hazard Modelling and Kaplan Meier Curves. SPSS will be used and the p value set at <0.05.

VIII. CONCLUSIONS

EVD-related infections are a major cause of morbidity and mortality. There have recently been a number of important clinical trials providing a growing evidence base for EVD management. However, there still remain a number of questions about the comparative effectiveness of different impregnated catheters and the efficacy of a number of operative techniques. Our audit aims to assess contemporary practice patterns and infection rate. It will allow the identification of parameters related to infection and help establish national benchmark to guide future trial design.

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X. TABLES

Primary outcome measures	Secondary outcome measures
1. Confirmed EVD-related Infection: gram stain positive and/or culture positive CSF sample that is not deemed a contaminant by the managing team and prompts antibiotic therapy and/or catheter removal. 2. Suspected EVD-related infection: clinical suspicion of meningitis (clinical signs, serum inflammatory markers, CSF pleocytosis) that prompts antibiotic therapy and/or catheter removal but is CSF culture and gram stain negative	1. Glasgow Coma Score (at 30 days or discharge if sooner) 2. Time to discharge (duration of neurosurgical stay) 3. Patient mortality (up to 30 days) 4. Mofied Rankin Score (at 30 days or discharge if sooner) 5. Need for permanent CSF diversion (up to 90 days)

Table 1: Audit primary and secondary outcome measures

XI. APPENDIX

Appendix I: Data collection proforma

Patient parameters					
Demographics	Surname Forename Gender DOB NHS number (identifiers only for local use as per Orion policy) Hospital number (identifiers only for local use as per Orion policy)				
Comorbidities	Baseline mRS (or pre-intubation) Physical Status (ASA grade) I II III IV Presenting GCS (E V M)				
Primary Reason for EVD insertion	Hydrocephalus/Congenital Infection/Inflammation Trauma Tumour Cerebrovascular Misc Unknown				
Ventricle Size prior to EVD insertion	Normal	Large	Small		
Did the patient have evidence of meningitis before insertion?	Yes	No	(If yes – was there a previous infected EVD)		
Operation Details					
Start + end time	Knife to skin	Final Suture			
Was the procedure performed as	Elective	Scheduled	Urgent	Emergency	
Location of insertion	Theatre	Intensive Care	Emergency Department		
Primary surgeon level	Name Grade				
Did the patient get systemic prophylactic antibiotics	At Induction	<24 hours	>24 Hours	Pre-existing therapy	No

Type of catheter	Conventional	Antibiotic Impregnated	Silver-bearing	Other
Type of drain	Tunnelled	Bolt drain	Ommaya reservoir	Other
Length of tunneling (cm)	0-5	5-10	>10 (including long tunneled EVDs)	
Insertion site	Left Frontal	Left Parietal	Left Occipital	Left Parieto-Occipital
	Right Frontal	Right Parietal	Right Occipital	Right Parieto-Occipital
	Cyst	Bilateral	Other	
Assisted EVD insertion?	Navigation	Ultrasound	No	
Number of passes	1	2	3	>/= 4
Peri-operative CSF sample?	Yes		No	
Old Implants Removed?	Yes		No	
Op Note included	Yes		No	
Surgical Update (Day 30)				
Post-insertion CT?	Yes		No	
If yes, what was the location of the catheter tip?	Free floating in CSF	Touching choroid/ventricle wall	In brain parenchyma	
Average CSF sampling frequency?	Never	1-2/week	Alternate days	Daily	Other
Date drain removed				
CSF leak encountered from EVD site?	Yes	No	Don't Know	
Reason for removal?	• Stopped working • No longer required clinically • Dislodged accidentally • EVD became infected • Elective replacement			
Further CSF diversion within 30 days of EVD insertion?	• Shunt • Serial LPs • Reinsertion of EVD			

Infection parameters				
Did the patient develop an ERI?	No	Yes Confirmed	Yes Suspected	
Date of diagnosis?				
If yes, did they meet the criteria for confirmed ERI?	Confirmed (Yes/No)		Suspected (Yes/No)	
	Gram Stain Positive	Culture Positive		
If yes, what did the gram stain show?	Gram positive cocci, Gram positive bacilli (rods) Gram negative cocci, Gram negative bacilli (rods) Yeast			
What was seen in the culture growth?	No Organisms	Mixed	Positive Tick Box of *Staphylococcus aureus* *Staphylcoccus epidermidis* *Staphylococcus* spp (please specify in other if species given) Coagulase negative staphylococcus *Streptococcus* spps (please specify in other if species given) *Enterococcus* spps (please specify in other if species given) *Propionibacterium acnes* *Pseudomonas aeruginosa* *E. coli* *Klebsiella pneumonia* Other ……	
Same organism from 2 or more CSF samples	Yes	No		
CSF results	Polymorphs	RBC	Lyphocytes	Glucose
Inflammatory markers on diagnosis	WCC		CRP	
Clinical Signs	Fever >38^{o}C	Change in consciousness	New onset of seizures	Signs of meningeal irritation

What antibiotics were commenced?	IV (Y/N) Cefotaxime/Ceftriaxone, Cefuroxime, Ceftazidime Flucloxacillin, Meropenem Gentamicin, Amikacin, Linezolid, Vancomycin Other IT (Y/N) Gentamicin, Amikacin, Linezolid, Vancomycin Other PO (Y/N) Cefuroxime Flucloxacillin Other (Please State) Duration (total)	
Evidence of concurrent infection	Yes	No
Outcome parameters		
30 day mRS (or D/C if earlier)		
30 day GCS (or D/C if earlier)		
Did patient die within 30 days from EVD insertion?	• No	• Yes – if yes, to complete DoD on ORION