RESEARCH PROTOCOL OUTLINE

Instructions: Protocols should be formatted according to the following outline and include all of the elements indicated.

Title of Project: Quality Control: A prospective analysis of external ventricular drain effectiveness.

Principal Investigator: Abdal Cheema, MD, Department of Neurosurgery

Abstract

In an effort to decrease the number of external ventricular drain (EVD) catheter related infections, this research will compare the efficacy of the standard EVD catheters utilized by Oklahoma University Medical Center (OUMC). These catheters will be compared in three principle areas: 1) incidence of infection, 2) cost analysis, and 3) average durations of placement, without deviation from existing standard of care (SOC). The three EVD catheters being compared in this study are 1) the Integra External Drainage Catheter (non-impregnated), 2) the Ventriclear EVD Antibiotic Catheters (antibiotic-impregnated), and 3) Codman Bactiseal EVD Catheter Set (antibiotic-impregnated). The goal of this prospective study is to determine whether the use of antibiotic impregnated EVDs vs non-impregnated EVDs will result in lower infection rates.

A. Specific Aims

The hypothesis for this research study is that antibiotic impregnated EVDs are more effective in reducing the number of EVD catheter related infections. The long-term objective is a reduction in the number of EVD catheter related infections.

B. Background and Significance

While use of sterile techniques and periprocedural antibiotics have traditionally been used to combat infection, infection rates remain above goal, leading to the question of whether the antibiotic impregnated catheter should be added to the standard of care. With the knowledge gained, we hope to decrease the amount of EVD catheter related infections and reduce use of prolonged antibiotics.

C. Preliminary Studies/Progress Report

Glenn C, Conner A, **Cheema AA**, Burks J, Case J, O'Neal C, Sughrue M. Use of Frameless Neuronavigation for Bedside Placement of External Ventricular Catheters. November 28, 2015. PMID 26642952.

Buster B, Bonney P, **Cheema AA**, Glenn C, Conner A, Safavi S, Andrews M, Gross N, Mapstone T. Proximal Ventricular Shunt Malfunctions in Children: Factors Associated with Failures. Journal of Clinical Neuroscience. October 22, 2015. PMID: 26601815.

D. Research Design and Methods

All patients, both male and female, ages 18-75, requiring EVD placement will be solicited for enrollment into this study, except those who are incarcerated and/or

may be pregnant. The indications for EVD placement are 1) increased intracranial pressure, 2) hydrocephalus, 3) interventricular hemorrhage, and 4) subarachnoid hemorrhage with poor clinical exam. Upon receipt of informed consent, participants will be randomly assigned to receive one of the three EVDs being studied. The EVDs being studied are 1) the Integra External Drainage Catheter, 2) the Ventriclear EVD Antibiotic Catheter, and 3) Codman Bactiseal EVD Catheter Set. A random number generator will be utilized to randomly assign participants to one of three EVDs. Study data will be collected from patient's electronic medical record (EMR) both at OU Medical Center and OU Physicians. Study data will include participant information, infection outcomes, equipment cost, and duration of placement will be added to a secure database for later analysis. The study will enroll a total of 252 participants, after which study enrollment will be closed. The database will be maintained by the Project Contact: Beverly Roy, M-HR. Patients who require placement of an EVD are, by nature of their condition (which includes altered mental status), unable to consent for the procedure. As such, a Legally Authorized Representative (LAR) must consent for the procedure on behalf of the patient. The LAR is either the patient's next of kin, or if available, the designee on the patient's living will, power of attorney, or advance directive. The same LAR will be asked to consent for this study, on behalf of the patient.

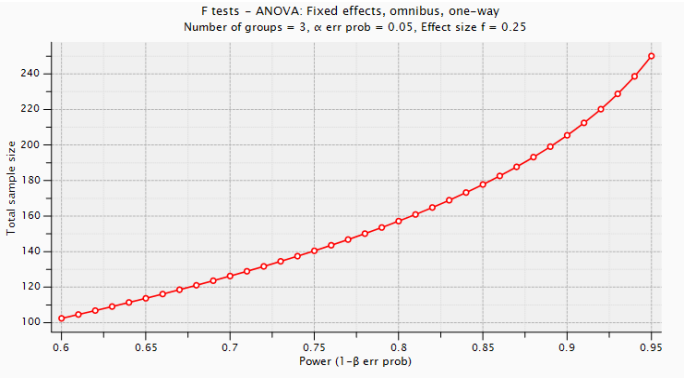
E. Statistical Methods

The statistical method for this study will be a one-way ANOVA. Utilizing G*Power 3.1.9.2 software, a priori power analysis provided the following results:

[1] *-- Friday, December 12, 2014 -- 10:25:39*

F tests – ANOVA: Fixed effects, omnibus, one-way

Analysis:	A priori: Compute required sample size		
Input:	Effect size f	=	0.25
	α err prob	=	0.05
	Power (1-β err prob)	=	0.95
	Number of groups	=	3
Output:	Noncentrality parameter λ	=	15.7500000
	Critical F	=	3.0320649
	Numerator df	=	2
	Denominator df	=	249
	Total sample size	=	252
	Actual power	=	0.9514888



F. Gender/Minority/Pediatric Inclusion for Research

This project will include both men and women age 18-75.

G. Human Participants

1. This project will recruit 252 participants, age 18-75, who require placement of an external ventricular drain. All adult patients who require an EVD will be included.
2. Research material will consist of records and data.
3. Recruitment will take place at the bedside or within a consultation room in the OUMC and will be administered by the assigned resident. The bedside is frequently within the emergency department, intensive care unit, or step down care unit. Recruitment of non-English speaking participants will be done via a translator. Given that there is no deviation from the existing standard of care, participant coercion is not a significant concern.
4. This research does not involve more than minimal risk to the patient.
5. Patient records, including PHI, will be stored in a secure database on a secure network that is password protected. Access to this database will only be granted to essential personnel.
6. While use of sterile techniques and periprocedural antibiotics have traditionally been used to combat infection, infection rates remain above goal, leading to the question of whether the antibiotic impregnated catheter should be added to the standard of care. With the knowledge gained, we hope to decrease the amount of EVD catheter related infections and reduce use of prolonged antibiotics.
7. The three EVD catheters being studies are part of the existing standard of care at OUMC and therefore do not produce any additional risk to the patient.

H. Data and Safety Monitoring Plan

1. All electronic data will be maintained in a password protected database on a secure server. All non-electronic data (i.e. consent form) will be stored in a locked file cabinet in the Project Contact's office.
    a. Should any type of breach occur, this will be immediately reported to the IRB and study PI.
2. The study Principal Investigator will be responsible for monitoring the study.
3. Additionally, Dr. Bappaditya Ray, Neurologist, will monitor study data.

I. Literature Cited

Bohnstedt BN, Ziemba-Davis M, Edwards G, Brom J, Payner TD, Leipzig TJ, Scott JA, DeNardo AJ, Palmer E, Cohen-Gadol AA. Treatment and outcomes among 102 posterior inferior cerebellar artery aneurysms: a comparison of endovascular and microsurgical clip ligation. World Neurosurg 2014 Dec 23. PMID 25541085

Lane B, **Bohnstedt BN**, Cohen-Gadol AA. A prospective comparative study of microscope-integrated intraoperative fluorescein and indocyanine videoangiography for clip ligation of complex cerebral aneurysms. J Neurosurgery; 122(3):618-26, 2015 Mar. PMID 25526265

Kulwin C, **Bohnstedt BN,** Payner TD, Leipzig TJ, Scott JA, DeNardo AJ, Cohen-Gadol AA. Aneurysmal acute subdural hemorrhage: Prognostic factors

associated with treatment. J Clin Neurosci 21(8): 1333-6. 2014 Aug PMID 24679648

Ziemba-Davis M, **Bohnstedt BN**, Payner TD, Leipzig TJ, Palmer E. Cohen-Gadol AA. Incidence, epidemiology, and treatment of aneurysmal subarachnoid hemorrhage in 12 midwest communities. J Stroke Cerebrovasc Dis; 23(5): 1073-82, 2014 May-Jun PMID24144595.

Cohen-Gadol AA. **Bohnstedt BN**. Recognition and evaluation of nontraumatic subarachnoid hemorrhage and ruptured cerebral aneurysm. Am Fam Physician; 88(7): 451-6, 2013 Oct 1 PMID 24134085

Bohnstedt BN, Nguyen HS, Kulwin CG, Shoja MM, Helbig GM, Leipzig TJ, Payner TD, Cohen-Gadol AA. Outcomes for clip ligation and hematoma evacuation associated with 102 patients with ruptured middle cerebral artery aneurysms. World Neurosurg 80(3-4):335-41, 2013, PMID 22465372