Disposition of Critically Ill Patients In Acute Care Setting Following Botulinum Injections to Salivary Glands.

Author: **Aaron Charnay, MD**
Faculty Mentors: **Heakyung Kim MD, John Rausch MD**
Date: **August 3rd, 2018**

A. Study purpose and Rationale:

Excessive salivation (sialorrhea) is a common issue for patients with neuromuscular disorders like Cerebral Palsy (CP), Spinal Muscular Atrophy (SMA), and many other genetic conditions predisposing to abnormal muscle tone. Ultrasound guided salivary gland injections with botulinum toxin A have been shown to be a safe and effective way to reduce hospitalizations and decrease the risk of aspiration pneumonia in these patients[1-3]. Due to their underlying complexity, when acutely ill, these children are often admitted to an intensive care unit (ICU) setting and typically take longer to return to their pre-admission respiratory baseline than compared to children without underlying neuromuscular disorders and salivary regulation. There is a paucity of evidence looking at botulinum injections to enhance care in critically ill patients. This study aims at looking at the effects of treatment with ultrasound guided botulinum toxin A injection to the salivary glands in acutely hospitalized patients by comparing time to discharge from the PICU for patients who received the injections to those who were considered but ultimately did not receive the treatment. A secondary aim will be to identify primary factors that precluded the use of botulinum toxin treatment in acute hospitalization for the latter cohort of patients.

B. Study Design and Statistical Analysis

This will be a retrospective analysis of pediatric patients w/ neuromuscular disorders with concurring sialorrhea admitted to the Morgan Stanley Children's Hospital pediatric intensive care unit between 2011 and 2017. Patients will be included who:

    A.) Underwent a rehabilitation medicine consult for sialorrhea and

    B.) Did or did not receive ultrasound guided salivary gland botulinum toxin injections.

Data will be gathered through the New York Presbyterian TRAC database, a repository of hospital specific clinical data, and will include demographic information as well as specific characteristics such as:

       1.) Admission diagnoses (respiratory failure/distress, aspiration pneumonia)

       2.) Specific underlying neuromuscular condition (CP, SMA, congenital hydrocephalus, other genetic disorders)

       3.) Type and level of increased respiratory support from baseline (oxygen, continuous positive airway pressure, biphasic positive airway pressure, intubation)

       4.) Presence of comorbidities at time of consult (active bloodstream infection, vital sign instability, newly trach dependent, undergoing w/u for gastroesophageal reflux)

       4.) Suctioning requirement compared to baseline

       5.) Other medications utilized to decrease drooling (glycopyrrolate, scopolamine)

6.) History of prior botulinum injections
7.) Length of PICU stay
8.) Length of time intubated (if requiring intubation)
9.) Discharge status (general ward v home v acute rehab v subacute rehab)
*The data will be de-identified prior to statistical analysis.
The goal of the study will be to determine length of stay, length of intubation, and factors associated with patients who did not receiving botox injections (i.e. active bloodstream infection, vital sign instability, incomplete reflux workup, poor response to prior injections).

To identify predictive measures of patients who receive treatment, we will utilize a logistic regression with the binary dependent variable being "botox" or "no-botox" compared to the above mentioned co-factors/comorbidities taken into account while evaluating a patient for eligibility. This will help determine which and how many variables were necessary to change a patient's likelihood of receiving treatment. Then we will use unpaired, two group t-test (or nonparametric test such as Wilcoxon as needed) to measure differences in length of stay and length of intubation between those who either did of did not receive treatment with botulinum toxin injections.

C. Sample Size Determination and Power Analysis
Based on reviews by pediatric rehabilitation specialists, an estimated 10-15 patients per year received this treatment while hospitalized in this specific institution. So we are estimating between 70 and 100 patients (or treatment events one patient received multiple treatments) to be included in this study. If these numbers are correct, using a two group, unpaired t-test to measure mean length of stay, with an estimated standard deviation of 7 to 10 days, with an alpha of 5% and 80%, we are powered to detect a difference of 7 days difference in LOS.

D. Study Procedures
The study will be a retrospective chart review. Patients will be identified via internal departmental databases. Chart review will be performed on all patients. The data described above will be gathered from the electronic medical record and placed into a spreadsheet with identifying data removed. A separate password protected file will correlate the patient identifiers to the unique study ID numbers used in the spreadsheet. The collected data will then be analyzed using the statistical measures outlined in the previous section.

E. Study Drugs/Medical Devices
No new drugs or medical devices are being used as part of this study. All subjects received botulinum toxin injections as part of their care course while admitted to the Morgan Stanley Children's Hospital Intensive Care Unit.

F. Study Questionnaires
No Questionnaires will be employed in this study.

G: Study Subjects

Subjects chosen for this retrospective chart review will include pediatric patients admitted to the Morgan Stanley Children's Hospital Intensive Care Unit between June of 2011 and June of 2018.

H: Recruitment of Subjects
No recruitment will take place as this is a retrospective chart review.

I. Confidentiality of Study Data
Study data will be stored in a secure database located on NYP/CUMC hospital computers. Only study investigators who have completed the appropriate HIPPA and clinical research training will access data. Any unneeded identifying information (such as hospital MRN, birth date) will be removed from the database once data collection is complete.

J. Potential Conflict of Interest
None of the investigators have any conflicts of interest to report.

K. Location of the Study
All data was collected as part of routine clinical care. Patients were admitted to the Pediatric ICU at CHONY

L. Potential Risks
There are no potential risks for this retrospective chart review except the possibility of loss of confidentiality. However, this risk will be minimized by limiting access to the database to qualified study personnel, maintaining the data on secure network encrypted devices, limiting the identifying data abstracted from the medical record; and removing any unnecessary identifying information from the database as soon as possible.

M. Potential Benefits
As a retrospective chart review, there are no immediate benefits to the patients in this study. The information gained from this study may have an impact on the management of patients with sialorrhea secondary to neuromuscular disease/dysfunction.

N. Alternative Therapies
Patient's received therapy as a part of the standard ICU care and no alternative medications will be considered in this retrospective study.

O. Compensation/Cost to Subjects
No compensation or additional cost to subjects as this is a retrospective study.

P. Minors as Research Subjects
Data will be collected retrospectively from the electronic medical records of pediatric patients in with chronic illnesses admitted to the ICU who received treatment as a component of their medical necessity. A waiver of consent has been given through the CUMC IRB and numerous precautions will be taken to protect the data, as detailed above.

Q. Radiation or Radioactive Substances
This study will not employ radiation or radioactive substances

Citations:

1.   Faria J, Harb J, Hilton A, Yacobucci D, Pizzuto M. Salivary botulinum toxin injection may reduce aspiration pneumonia in neurologically impaired children. *International Journal Of Pediatric Otorhinolaryngology* [serial online]. December 2015;79(12):2124-2128.
2.   Lungren, Matthew P. et al. Ultrasound-Guided Botulinum Toxin Type A Salivary Gland Injection in Children for Refractory Sialorrhea: 10-Year Experience at a Large Tertiary Children's Hospital. *Pediatric Neurology* 2016;54:70 – 75.
3.   Pena AH, Cahill AM, Gonzalez L, Baskin KM, Towbin RB. Botulinum toxin A injection of salivary glands in children with drooling and chronic aspiration. *J Vasc Inter Radiol* 2009; 20: 368–373.