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Characteristics and Outcomes of a Population of Pediatric Patients with Traumatic Brain Injury Before and After Initiation of Guidelines for Management

a. Study Purpose and Rationale

Traumatic brain injuries (TBI) are the most common acquired cause of death and disability in children in developed countries¹. These injuries disrupt the normal function of the brain and can lead to death or cognitive, behavioral, emotional and physical disabilities. Each injury affects the lives of individuals, families, communities, and the economy. Head trauma in children <18 yo results in ~7400 deaths, and 60,000 ED visits.² The overall health care cost of traumatic brain injury is approximately 56.3 billion dollars per year³, and there are approximately 145,000 children and adolescents currently living with long-lasting functional limitations after sustaining TBI⁴.

The pathophysiology of TBI follows a two hit model, and there is emerging evidence to show that the traumatized pediatric brain has unique responses. This leads to age-dependent injury patterns. In infants and young children, diffuse cerebral swelling and subdural hematomas are more common than focal injury, such as contusions in older children. Subsequent ischemia and hypoxia also appear to be more common in infants and young children^{5,6}. In this two hit model, the primary insult is direct parenchymal damage caused by the trauma. This can be open head trauma with a penetrating injury, closed head trauma, or acceleration-deceleration injury leading to axonal shearing. The primary injury then leads to hypoperfusion of the brain while at the same time requiring increase metabolic demands⁸. This leads to a cascade of secondary insults from biochemical, cellular, and metabolic responses, and exogenous responses. There is also significant cerebral swelling and increasing intracranial hypertension 24-72 hours after the injury, all decreasing cerebral perfusion⁹.

The key to management of severe traumatic brain injury is to minimize the potentially avoidable secondary insults and to break the cycle of continued injury. The desire to minimize the second hit is the basis behind the study of and initiation of guidelines for the treatment of severe traumatic brain injury, initially published in 2003⁸. It is important to evaluate if these guidelines, which improved clinical knowledge, translated to improved outcomes for patients. To the best of our knowledge, no study exists addressing the question of the severe traumatic brain injury guidelines improving outcomes. As such, this study poses the question; did the institution of the guidelines for the management of severe traumatic brain injury published in 2003 improve the outcome of patients? The null hypothesis being, there will be no statistical difference in GOS scores before and after the institution of the guidelines for the acute medical management of severe traumatic brain injury in pediatric patients.

This study also characterizes a large population, 124 patients from 2001 to 2004, and 185 patients from 2005 to 2013, for 309 total patients, who presented to one center with accidental trauma only. The second hypothesis of this study is that some of their stated characteristics, such as age, GCS on arrival, number of days on a ventilator, etc. will have significant association with outcomes and GOS scores.

b. Study Design and Statistical Analysis

This study is a retrospective analysis of data compiled by a database at Children's Medical Center Dallas, called the Brain Nerve Injury and Repository Database. Data on patients was collected from 2001 to 2013, on children who were admitted to their institution for head injury cause by blunt force.

Patients were included in this study if enrolled in this database, between the age of 0-21, and suffered severe traumatic brain injury, defined by the GCS score at presentation to the ED of less than or equal to 8. Patients were excluded if there was no documented GOS score upon discharge, and those with mechanisms of injury secondary to non-accidental trauma.

GCS Score (Appendix 1) has been an externally validated measure of severity of traumatic brain injury. GCS Scores <9 were defined as severe traumatic brain injury, 9-12 were moderate traumatic brain injury, and 13-15 were mild traumatic brain injury.

Primary outcome measured was GOS score. GOS scores have also been externally validated means of measuring outcomes of those with traumatic brain injury. GOS score of 1 defined as death. GOS score of 2 indicated a vegetative state defined as being unaware of self and environment. GOS score of 3 indicated severe disability, defined as unable to live independently. GOS score of 4 indicated moderate disability, defined as able to live independently, and GOS score of 5 indicated mild disability, defined as able to return to work/school. Secondary Outcome measured is length of PICU stay, and length of hospital stay.

An unpaired T-Test will be used to compare pre 2003 GOS scores to post 2003 GOS scores. A statistical significance is defined as <0.05. A graphical representation of the data will be created to look at the slope of GOS scores over time, and Regression analysis will be applied to determine if there is a significant difference in the slope of the GOS scores over time prior to and after the initiation of management guidelines.

A power analysis was conducted using a $p < 0.05$, and a power of 80%, to determine the necessary N to see a statistical significance, with an effect of a change in the mean GOS score of 0.3. Based on this analysis we should have 52 subjects before the guidelines and 59 subjects afterward in order to detect a difference in proportion of patients who do well with 80% certainty. In the database, we have 139 subjects from 2001-2003, 121 with GOS scores, compared to 184 subjects from 2003 to current, 137 of which have GOS scores. These numbers assure this study is adequately powered.

A second hypothesis is that some of the characteristics of the patient population (age, sex, intubated on arrival, GCS on arrival, etc.), will have a significant impact on their outcome. Primary outcome is defined as GOS at 6 months and secondary outcomes as GOS at discharge, length of stay in the hospital and in the ICU. Unpaired t tests will be used for continuous variables and chi square proportions will be used to assess categorical variables to look for significance in their association with outcome.

Finally, a logistic regression analysis will be performed to both test all input variables for significance. This will help to guide future research efforts in deciding areas of focus.

c. Study Procedure

No procedures were performed for this study.

d. Study Drugs

No drugs were given for this study.

e. Medical Devices

No medical devices were used for this study.

f. Study Questionnaire

No questionnaires were used during this study.

g. Study Subjects

Subjects who were enrolled in the BNIRD database were included in this study if their presenting GCS score was less than or equal to 8. Patients were excluded from this study if GOS scores were not documented upon discharge, if mechanism of injury was secondary to non-accidental trauma, or if mechanism of injury was not recorded.

h. Recruitment of subjects

No requirement was done for this study.

i. Confidentiality of Study Data

Investigators involved in the BNIRD database only receive de-identified samples and data. Therefore, No information will be published that could be directly linked to a donor-participant.

j. Potential Conflict of Interest

No investigator or university has proprietary interest in or might stand to benefit in any other way from the results of the investigation.

k. Location of Study

Brain and Nerve Injury Center Repository and Database database is located at Children's Medical Center Dallas. Analysis of the data for this study was completed at Children's Hospital of New York, Pediatric ICU.

l. Potential Risks

No potential risks are present for this study.

m. Potential Benefits

Although individual subjects will not benefit from this study, there is a system wide benefit to determining if clinical knowledge and standards, translates to improved patient outcome.

n. Alternative Therapies

No alternative therapies exist.

o. Compensation to Subjects - N/A

No compensation to subjects made by this study.

p. Costs to Subjects

This study was of no cost to subjects.

q. Minors as Research Subjects

Database coordinators for BNRID obtained IRB approval and clearance by their pediatric committee.

r. Radiation and Radioactive Substances

No radiation or radioactive substances used during this study.

Appendix

Appendix 1. Glasgow Coma Scale Score

	Adult	Pediatric
Eye Opening	4 Spontaneous 3 To verbal Stimuli 2 To painful stimuli 1 No eye opening	4 Spontaneous 3 To verbal stimuli 2 To painful stimuli 1 No eye opening
Verbal Response	5 Oriented 4 Confused 3 Inappropriate words 2 Incomprehensible 1 No verbal response	5 Appropriate coo & cry 4 Irritable cry 3 Inconsolable cry 2 Grunts 1 No verbal response
Motor Response	6 Obeys commands 5 Localizes pain 4 Withdraws to pain 3 Flexion to pain 2 Extension to pain 1 No motor response	6 Normal spontaneous 5 Withdraws to touch 4 Withdraws to pain 3 Flexion to pain 2 Extension to pain 1 No motor response

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