Report

Pediatric Neurotrauma Center (PNTC)

University of Pittsburgh

June, 2011
Summary

Over the past 3 years, the Pediatric Neurotrauma Center (PNTC) of the University of Pittsburgh has continued to provide excellent care for children with traumatic brain injury (TBI) and advance its other goals in research, education and advocacy.

- The multidisciplinary clinical team cared for over 300 children demonstrating superior outcomes as a result of the hard work from Neurosurgical residents, Critical Care Fellows, Nurse Coordinators, Pediatric ICU nurses and the combined efforts of faculty members from Critical Care Medicine, Neurosurgery, Trauma Surgery, Pediatrics and other departments.

- Research is expanding at a vigorous pace, with the completion of the “Cool Kids” trial, the implementation of a new phase I/II clinical trial, the start of a comparative effectiveness study to discern barriers to implementation of evidenced-based guidelines, the continuing support of a T32-training grant in pediatric neurocritical care.

- Educational opportunities are myriad within the Center with weekly journal clubs, case conferences and lectures to staff within the hospital and across the country.

- Important advocacy initiatives were also completed including the development of a local community advisory board, leading the writing of new guidelines for medical management of traumatic brain injury for children and establishing common data elements necessary for future studies.

- Continuing challenges include developing long-term neuropsychological follow-up for children who are not on study protocols and continuing to search for therapies to mitigate injuries in this vulnerable patient population.

Cover photographs of star patients

Left – 18 month old who had a TV fall on her head (pictured with her mom). She suffered nearly fatal injuries to her skull base on Christmas Eve (including complete fracture of her clivus), enrolled in “Cool Kids” study, required multiple surgical procedures, pentobarbital coma and maximal medical therapies for months. In this picture, she is back for removal of her tracheostomy at approximately 6 months after injury and tests at only 1 month behind her age-group on neuropsychological evaluation.

Right – 15 year old who suffered severe TBI by falling from his motorcycle. He suffered an intracerebral hemorrhage and subdural hematoma, enrolled in “Cool Kids” study, required a medically-induced coma for 3 weeks and left the hospital with hemiparesis. Now 2 years after injury, he is getting excellent grades in high school and has fully regained strength in his extremities so that he can participate in sports.
Leadership
Michael Bell, Associate Professor, Critical Care Medicine and Neurological Surgery – Director, PNTC

Senior Advisors
Robert Friedlander, Chairman, Neurological Surgery
Derek Angus, Chairman, Critical Care Medicine
Ian Pollack, Chief, Pediatric Neurological Surgery
Robert Clark, Chief, Pediatric Critical Care Medicine

Senior Contributors
Jeff Balzer, Assistant Professor, Neurological Surgery
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Sue Beers, Associate Professor, Psychiatry
Rachel Berger, Associate Professor, Pediatrics
Ericka Fink, Assistant Professor, Critical Care Medicine
Barbara Gaines, Associate Professor, Surgery; Director, Trauma Surgery
Stephanie Greene, Assistant Professor of Neurological Surgery
Miguel E. Habeych, Assistant Professor of Neurological Surgery
Elizabeth Tyler-Kabara, Assistant Professor, Neurological Surgery
Patrick Kochanek, Professor, Critical Care Medicine
Mioara Manole, Assistant Professor, Emergency Department
Samuel Poloyac, Assistant Professor, Pharmacy
Mandeep Tamber, Assistant Professor, Neurological Surgery
Stephen Wisniewski, Professor, School of Public Health

Contributors
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Research Coordinators
Rachelle Bell, RN
Maria Sidoni, RN
The Pediatric Neurotrauma Center (PNTC) was formed to comprehensively provide care for children with traumatic brain injury in the catchment area that includes western Pennsylvania, West Virginia and eastern Ohio and to merge this effort in advanced care with research, education and advocacy efforts both within the Pittsburgh region and throughout the world. As one of the most established and comprehensive programs in the country, the PNTC has led the country in establishing clinical guidelines for caring for children and performing trials to improve outcomes.

Clinical Care/Education Summary

Clinical care of children with traumatic brain injury continues to be at the cutting edge within the Center at Children’s Hospital of Pittsburgh of UPMC. The physician care team is organized based on Pediatric Intensivists (including our Neurocritical Care team), Neurosurgeons, Trauma Surgeons, Pediatricians, Neuropsychologists and a host of other consultants required for the care of these patients with complex illnesses. All of these physicians (Drs. Pollack, Tyler-Kabara, Greene, Tamber, Bayir, Clark, Fink, Bell along with Dr. Gaines and the entire Surgery Faculty) have worked tirelessly to provide care for these children within the Center. In the past 3 years, we treated 351 children with moderate-severe TBI within the PNTC. Unfortunately, we had 13 fatalities within this group - 4 children who could not be resuscitated from multiple injuries (including presumed TBI) and died upon arrival to the ED/PICU and 1 had support withdrawn after surviving his moderate TBI with an unrecoverable high spinal cord injury. As a result, we have observed a mortality rate of 2.3% for children with TBI.
There were many educational sessions within the PNTC in the last several years. Rachelle Bell, RN and Maria Sidoni, RN provided in-services for the PICU nursing and respiratory staff regarding administration of hypothermia and providing consistent care to the head-injured child. Several lectures were given to the Benedum Trauma Center and as a part of Critical Care Orientation for Nursing Staff. Dr. Bell performed several visiting professorships to promote the work of the Center (Cornell University, New York, NY; Massachusetts General Hospital, Boston MA; New York Pediatric Critical Care Society, New York, NY; Children’s National Medical Center, Washington, DC, Department of Pediatrics of the University of Pittsburgh School of Medicine) among many other talks given by Senior Contributors to the PNTC. Several lectures were given to provide an orientation to Surgery, Neurosurgery and Critical Care Medicine trainees on the care for children with severe TBI. A unique T32 training grant from the NIH focused on pediatric neurocritical care supports our program was successfully renewed this year. Multi-departmental (critical care, neurological surgery, child neurology, pediatrics, neuroradiology, emergency medicine, and physical medicine and rehabilitation) and multidisciplinary investigation in traumatic brain injury in children is a central facet of this grant. And a vibrant journal club schedule and case conference series (Safar Journal Club, 9am Fridays at the Safar Center; Safar Rounds, 7am Wednesdays at CHP) has been implemented to discuss the latest advances of care. As a result, the clinical care and educational opportunities within the PNTC are broad and very active. We hope to recruit a dedicated fellow in Neurocritical Care from the specialties of Pediatric Neurosurgery, Pediatric Neurology and/or Pediatric Critical Care Medicine in the future to offer a broadened educational and clinical experience to talented young practitioners. Another remaining challenge for the PNTC is to
obtain neuropsychological outcomes from children who are not enrolled in clinical studies, as insurance providers have not been universally willing to support these vital tests for all children with moderate-to-severe TBI.

**Research Summary**

The ongoing research within the PNTC continues to be amongst the most active and productive of any center across the country. Dozens of important projects are ongoing, including observational and interventional trials. In the past several months, the Center completed work on the Pediatric Traumatic Brain Injury Consortium: Hypothermia Trial (the “Cool Kids Trial”). That trial, of which our center enrolled nearly one-third of all the subjects (24 patients enrolled within the PNTC out of the 78 total patients across 36 clinical sites in 3 countries), was stopped due to the inability of the trial to detect a difference in the primary outcome (overall mortality). Nevertheless, a clearer understanding on the role of hypothermia after TBI was discerned and several other advances were made in organizing interventional clinical trials and several ancillary studies performed within the PNTC.

Two additional funded studies have begun in the past year. A phase I/II trial of combinational drug therapy for TBI (using Probenecid and N-acetyl cysteine) began enrollment in January 2011. In this study, 20 children will be randomized to receive the combination of drugs or placebos, with the hypothesis that the combination therapy will not cause increased adverse events but will lead to increased anti-oxidant reserve within the serum and CSF. Another study (Implementation Science to Increase Implementation of Evidenced-Based Guidelines in Pediatric TBI: PI, Monica Vavilala, University of Washington) has
begun in the past year as well. In this study, adherence to the TBI Guidelines will be measured and barriers to implementation of these guidelines at several sites (including the PNTC) will be identified. The ultimate goal of this study is to increase the utilization of evidenced-based care across the country.

**Grants Currently Funded within PNTC**


R01, NINDS – “Overcoming Membrane Transporters to Improve CNS Drug Therapy”; PI: Clark; Clinical PI: Bell - 2009 – 2014

R01, NINDS - “Implementation Science to Increase Implementation of Evidenced-Based Guidelines in Pediatric TBI”; PI: Vavilala, University of Washington, Site PI: Bell, 2010 – 2015


R01, NICHD - "Novel approaches to Screening for Inflicted Childhood Neurotrauma"; PI; Berger, 2009-2014

R01, NINDS – “Oxidative Lipidomics in Pediatric Traumatic Brain Injury”; PI: Bayir, 2008 – 2013

**Selected Papers from the PNTC**


Mehta A, Kochanek PM, Tyler-Kabara E, Adelson PD, Wisniewski S, Berger RP, Sidoni MD, Bell RL, Clark RSB and Bell MJ. “The Relationship Between Intracranial Pressure (ICP) and Cerebral Perfusion Pressure with Outcome in Young Children after Severe Traumatic Brain Injury”. Dev Neurosci 32(5-6): 413-9, 2010.


Au A, Carcillo JA, Clark RSB, Bell MJ. “Brain Injuries and Neurological System Failure are the Most Common Proximate Cause of Death in Children Admitted to a Pediatric Intensive Care Unit”. Pediatr Crit Care 2011 (in press).


Kochanek PM and Bell MJ. “Neurological Emergencies and Stabilization”. In Nelson’s Pediatrics 2011 (in press).


Advocacy Summary

Members of PNTC have been deeply involved national and international efforts to develop standards for children with TBI. In winter of 2011, the NIH developed working groups to standardize data collection methods for both clinical care and for biomarkers for studies in pediatric TBI. The results of these efforts were recently published in the Journal of Neurotrauma with the goal of standardizing basic data collection within clinical trials so that the trials can be rigorously compared. In addition, the Brain Trauma Foundation sponsored an effort to re-consider the published Guidelines for Medical Management of Severe TBI for Infants, Children and Adolescents (previously published in 2003). These new recommendations are to be published in the spring of 2011 and will set standards for caring for children with TBI.

Locally, a Community Advisory Board for the PNTC has been organized under the leadership of Mr. Mark Napodano (parent of one of our patients from 2008). He
is actively recruiting other family members to join this group and it is expected that they will advise us on how we can improve the care for the family of children with TBI. Lastly, members of the PNTC continue to work with the Sarah Jane Foundation, an effort started by Patrick Donohue in New York to advocate for funding for children with inflicted traumatic brain injury and other acquired brain disorders. Rachel Berger is leading the effort at the University of Pittsburgh and we have been named the Pennsylvania Lead Center for the Pediatric Acute Brain Injury Plan (PABI). We look forward to working with this national organization in increasing awareness of brain injuries in children across the US and in our community.

**Future Plans and Goals**

- We plan to continue to provide state-of-the-art care for children with TBI and incorporate new therapies and technologies into the Center. In order to determine the full effectiveness of these new interventions, a comprehensive program of neuropsychological testing of children who are not necessarily enrolled in clinical trials will need to be implemented.
- We plan to build a network of investigators within the US and in Europe in order to study the effectiveness of the medical therapies for intracranial hypertension and other care variables known to have important impact on outcomes. While 25 US sites have already agreed to join our consortium, a meeting is planned in Brussels in October 2011 where the collaboration will be extended to European sites in conjunction with an NIH and European Union initiative.
• We plan on expanding the educational opportunities within the PNTC by providing additional experience to NRSA-funded fellows in caring for children with severe TBI and establishing TBI-specific simulation experiences for trainees of all levels of experience.

• We plan on recruiting at least 10 parents/families to join the Community Advisory Board and develop a list of improvements that could be made to improve the experiences of families who have children that suffer TBI.

• A national meeting of the Pediatric Neurocritical Care Research Group, a group of 40 centers from across the country that specialize in treating children with brain injuries from trauma and other conditions, will be hosted by the Pediatric Critical Care Medicine Division, Department of Critical Care Medicine, University of Pittsburgh School of Medicine through generous support from the Children's Hospital of Pittsburgh of UPMC on October 22 and 23rd, 2011.