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Practical Aspects of Conducting a Prospective Statewide Incidence Study. The Incidence of Serious Inflicted Traumatic Brain Injury in North Carolina

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Abstract

The article describes practical problems encountered in setting up and maintaining an active statewide surveillance system for a low-frequency but high-impact injury, inflicted traumatic brain injury (iTBI). A system was designed to identify prospectively all children aged <2 years with a traumatic brain injury (TBI) admitted to any of the nine pediatric intensive care units (ICUs) in North Carolina in 2000 and 2001. Children who died prior to admission to hospital were identified from the records of the Office of the Chief Medical Examiner. The study design had strengths and weaknesses for ongoing surveillance. Strengths included a clear definition of a case, mechanisms to jury undecided cases, and a high level of quality control. Difficulties included appropriately addressing investigators' ethical and legal obligations in the study of child abuse, differing requirements of multiple institutional review boards (IRBs), and the time-intensive nature of the system. The described surveillance system produced high-quality data, but may not be practical for ongoing multi-year injury surveillance. Incorporation of iTBI into an existing surveillance system, such as a trauma database, may be a feasible solution to many of the problems encountered.

Over the past several years there has been an increase in state initiatives to prevent inflicted traumatic brain injury (iTBI) (<http://www.skippervigil.com>). One of the difficulties encountered with prevention initiatives is the lack of baseline data against which to measure the success of the programs in decreasing injury rates. As iTBI is a relatively uncommon event, a large population base is required to provide stable estimates of incidence. In general, hospital-based datasets do not code child abuse by external cause of injury codes (E-codes) adequately to reliably identify cases of iTBI.¹ Additionally, these data sets do not capture prehospital deaths. Furthermore, death records have been shown to misclassify deaths related to abuse.²

For these reasons, a prospective statewide incidence study of iTBI in North Carolina in the years 2000 and 2001 was conducted.³ At the time of this study, no population-based studies of iTBI existed in the United States. This type of study was desirable for a number of reasons: A population-based study has a denominator from which incidence can be calculated, it is more generalizable compared to single institution studies that may have a referral bias, and it allows the use of uniform definitions.

The North Carolina study was conducted over a 2-year time period both to increase the number of potential cases and to decrease the influence of temporality. Data also were collected on a

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head-injured comparison group who met the same study entrance criteria as the children with iTBI. The inclusion of a head-injury comparison group allowed the review of all cases of TBI in the state, which decreased the chance that cases would be missed secondary to misclassification at the hospital level and also provided a comparison group of similar-aged children.

Study Findings

The study found a total of 152 children with TBI who met entrance criteria. Of the 152 children, 80 (53%) incurred an iTBI. The rate of iTBI for children aged <2 years was 17.0 (95% CI=13.3–20.7) per 100,000 person-years. Rates of iTBI were higher in children in the first year of life compared to the second year of life, higher in boys than in girls, and higher in minority populations (Table 1). Factors that appeared to increase the risk of injury when compared to the general population of North Carolina included male gender, non-European American race/ethnicity, multiple birth, young maternal age, unmarried marital status, prenatal care starting after the first trimester, having a parent in the military, having extended family in the home, and being the first child in the family. Protective factors included having the father resident in the home and maternal education beyond high school. Using multivariate analysis, non-European American race/ethnicity, young maternal age, male child gender, and multiple birth remained the only significant risk factors.³

Significant changes in the rate ratio of iTBI were found in North Carolina associated with Hurricane Floyd (September 1999).⁴ In the most-affected 16 counties, defined by a hurricane-related death, damage to county infrastructure, or number of home buyouts, the rate ratio increased fivefold compared to the rest of the state in the first 6 months following the hurricane compared to the previous year, and then decreased to baseline levels. This probably did not have a large effect on overall state rates of TBI as only a small portion of the state was affected.

The work regarding iTBI included children hospitalized in an intensive care unit (ICU). A subsequent study of harsh child discipline conducted in North and South Carolina captured a broader range of parental behaviors in regards to shaking of children aged <2 years that did not necessarily lead to a recognized injury. Theodore et al.⁵ directly asked parents in a telephone survey about shaking children aged <2 years as a form of discipline. The incidence of shaking a child aged <2 years in the last year by parental self-report was 26 per 1000 children (95% CI=0–60). The authors estimated that for every child sustaining a life-threatening or fatal iTBI, 152 children may have been shaken by their caregivers and sustained subclinical brain trauma. These data are consistent with the finding that many children are found to have both old and new injuries when they are brought to medical attention.^{6,7} However, as shaking was assessed by only one question, these results should be viewed as intriguing rather than definitive.

Discussion

These studies were all performed in the southeastern U.S., which is homogenous compared to the country as a whole. It is possible that incident cases of iTBI could vary by geographic region, state levels of poverty, or different cultural attitudes toward child rearing in different regions of the country. Therefore, the results of these studies may not be generalizable to the U.S. as a whole. This study could be replicated in a different region over a longer time period to capture natural variations in rates over time; however, there are practical challenges that were encountered in the North Carolina studies that could be associated with study replication.

Challenges

Funding

A project of this scope requires external funding. Funding agencies had multiple concerns about the feasibility of the project including case ascertainment, credible case definitions, the likelihood of hospitals cooperating in a study of abusive injury, and the ability of gaining parental or caregiver participation for follow-up.

Case Definition

For study purposes, a case definition was required that could be applied consistently across hospitals and would allow for complete case capture. The case definition included North Carolina resident children with nonpenetrating intracranial injury (not fracture alone) hospitalized in an ICU or step-down unit or who died with a head injury and were aged <2 years. The intracranial injury had to be visible on radiographic imaging, at surgery, or on pathology. In order to ensure that all children met study criteria, a single pediatric radiologist who was blinded to the mechanism of injury, reviewed all of the neuro-imaging for study inclusion. A number of discrepancies were found between the readings by the study pediatric radiologist versus adult radiologists who may not have been as well versed in normal maturational changes in very young children. This case definition limited the study to children with moderate to severe injury. It was known that this would miss some children brought to medical attention who did not require monitored care and would miss all children not brought to medical attention; thus, the problem as a whole would be under-ascertained, but all of the children meeting this definition would be captured. A strict definition also allowed for the possibility that this study could be replicated or compared to other studies. For example, a study in the United Kingdom surveyed all pediatric providers.⁸ This type of study is more likely to capture less severe cases, but may be practical only in the setting of a smaller population base or socialized medicine. The UK study provided estimates for iTBI for children aged <1 year (24.6 per 100,000) that were within the confidence limits of the North Carolina study. The similarity in rates may reflect the difficulty in capturing children with lesser injury.

Inflicted Versus Non-Inflicted

Inflicted traumatic brain injury is a clinical diagnosis with no gold standard for comparison. Therefore, a mechanism was needed to decide injury type (inflicted versus non-inflicted injury). In most circumstances the child-protective team at the treating facility would be most likely to have complete information and be able to decide whether or not the case was inflicted or non-inflicted. In addition, the child-protective teams have access to the results of social work and police investigations. Therefore, the complete work-up by the child-protective team at each hospital was accepted as the study standard. The results of all medical and social investigations for each child were reviewed by the study investigators.

At the inception of the study, it was uncertain whether or not there would be head injury cases that were undecided or inadequately investigated. An example of an inadequately investigated case would be an unwitnessed TBI for which an inflicted injury was within the differential diagnosis of the investigators, but was not considered by the treating team. Therefore, a jury mechanism was set up to review all unwitnessed and undecided injury cases from each hospital and the Office of the Chief Medical Examiner (OCME). In instances where no decision was reached about a case by the treating team or an inadequate work-up had been performed, an abstract of the case was prepared by the project manager. The abstracts contained information about the reported mechanism of injury, the child's age, any pre-existing medical conditions, all imaging studies and ophthalmologic studies. The abstract excluded child race and ethnicity and information about the family to ensure that there was no bias. The abstract was then independently reviewed by the two primary investigators. If these two independent opinions

were not in agreement, the case was to be reviewed by an independent panel of five reviewers that included the two primary investigators. There were no cases of an unwitnessed TBI in which the intensive care physician did not either include the possibility of child abuse in the differential diagnosis (>90% documented child abuse among the differential diagnoses in the medical record) or specifically document the need for a child-protective team consult. There were two cases in which the two primary investigators both disagreed with the OCME. Both of these cases had been designated as undecided. As the two primary investigators agreed on the designation in these two cases (one inflicted, one non-inflicted), the cases did not go the five-member panel for review. There was no disagreement between the two primary investigators and decisions by hospital child-protective teams, so further review was never needed.

Data Sources

Data sources included all nine hospitals with a pediatric ICU in North Carolina. In order to ensure that no case of a North Carolina resident was missed, two hospitals outside of North Carolina were queried for admissions of North Carolina residents. Each hospital's ICU and step-down unit were called three times weekly by the project manager. It was a concern that children who were admitted only for an overnight stay could be missed. Thus, medical record searches were performed using the ICD-9-CM⁹ code for head injury and matched to the pediatric ICU log book for cases that may have been missed. Prehospital and emergency department deaths were captured through the North Carolina OCME. Unlike some state medical examiner systems, the North Carolina OCME receives cases from the entire state. In addition, the North Carolina OCME participates frequently in research projects and has established mechanisms for interacting with researchers and identifying records of interest. All injury deaths of children aged <2 years in the state and all deaths that were classified as undetermined or homicide were reviewed to ensure that no death caused by a TBI was missed.

In order to ensure that children meeting the study definition were likely to be hospitalized at one of the hospitals in the study, the North Carolina trauma database was queried for relevant ICD-9-CM codes for head injury. North Carolina gives trauma designations from Level One through Level Three so most hospitals caring for injured children have a trauma designation and participate in the registry. The registry provides information on a child's transfer to a higher level of care and identifies the hospital at which the child receives final treatment for injuries. This makes the trauma database a reasonable proxy for practice within the state. Data from the trauma registry confirmed that children evaluated and identified with a serious head injury in the emergency departments of hospitals contributing data to the trauma registry were transferred to the participating study centers. This provided reassurance that usual practice in North Carolina was to hospitalize young children with an acute head injury in a hospital that provided a monitored setting.

Getting Hospitals to Participate

There were nine hospitals in North Carolina with a pediatric ICU. These nine hospitals included private, public, and teaching hospitals. Each hospital had its own set of concerns about study participation. Many hospitals were unfamiliar with having researchers at all, and others were used to performing mainly pharmaceutical trials. This lack of experience and interest in clinical research on the part of some hospitals led to a variety of difficulties.

Each hospital's concerns were voiced via the hospital institutional review board (IRB). Each of the IRBs had different concerns and requirements. One of the most difficult concerns to address was hospital liability. Some hospitals were worried that they would place themselves at risk of legal action if investigators juried a case that was in disagreement with their doctors' decision. They wanted to know whether or not the study's "expert" opinion would be held

against them in court. As there was no direct advantage to any hospital for participating in the research, this possible downside made it difficult to get approval at several hospitals.

Ethics

Project staff, including the investigators and project managers, are mandated reporters for reasonable suspicion of child abuse in this state under the Child Abuse Prevention Treatment Act.¹⁰ The issue of mandated reporting by the investigators if there was disagreement with a hospital's disposition of a case and hospital liability was discussed with the State's Attorney General. The Attorney General stated that the state would not act on referrals from secondary information gained after a chart review as the primary team would have the most information about a case. However, the investigators were obliged to close the legal loop. A protocol was developed to handle this situation should it arise. The protocol was for the investigator to inform the specific hospital child-protective team if a case that they had not considered abuse was reviewed and determined to be an inflicted injury by the study team and request a letter back from them stating that they had received it and what action had been taken. If the hospital child-protective team declined to report the case and the study investigators still felt strongly that this was a possible case of child abuse, the investigators would file a mandated report to the Department of Child and Family Services (DCFS). Although it was doubtful that DCFS would act on a report based on secondary information, the case would be in the DCFS file if another incident occurred with that family. This protocol satisfied both the hospitals' and the investigators' ethical obligations, but the issue of potential liability delayed for months the IRB approval at some hospitals.

There were difficulties with differing interpretations of the risk and benefit of the research to the hospital, not only among hospital IRBs, but also within hospital IRBs. Large research hospitals often have multiple review boards to manage the large volume of protocols. Often the boards would interpret regulations differently each time the study came up for renewal. Over the 2-year study period, rules changed several times at a single institution, some of which allowed and some of which disallowed the research. The key to overcoming this was persistence, politeness, and maintaining accurate documentation of each interaction with the IRB. Hospitals were reluctant to allow research involving child abuse to be performed by investigators from outside of their community.

Getting Started and Keeping the Study Going

Each institution required an onsite primary investigator from its own hospital. There was no budget for the individual hospital-based primary investigators, and there was no financial or academic advantage for them to participate. Most of the hospital-based primary investigators were busy, clinical, pediatric ICU specialists. In order to gain participation it had to be ensured that each hospital-based primary investigator would not be inconvenienced. Therefore, all IRB forms, data collection, medical records requests, and chart reviews were performed by the research team from the University of North Carolina. The hospital-based primary investigators helped by ordering charts from medical records and asking for reports from hospital information systems. Additionally, some hospital-based primary investigators were engaged in the research effort because they thought that it was an important topic. The hospital-based primary investigators at times attended the IRB meetings, and their advocacy for the project was instrumental in having the research approved at their institution.

The key to the success of maintaining good relationships with the multiple ICUs was the project manager. The project manager for this study was a former pediatric ICU nurse who had additional training in research. She understood the ICU culture and language and was sensitive to the needs of the charge nurses and the individual hospital primary investigators. Each hospital was visited prior to beginning the study in order to meet the director of each ICU and

the nurse managers and to discuss with each unit the best method/timing of contacting them. During the study, an ICU charge nurse was contacted three times weekly by phone. The nurses were very helpful and were interested in participating. Each ICU was revisited at least once during the data acquisition portion of the study to discuss problems, provide updates, and remind people that the study was ongoing. Each site was given a binder with information about the study and consent forms. Each hospital primary investigator was sent a quarterly e-mail with summary statistics to encourage them to remember the study was still ongoing and to give feedback. These activities made the project very time-intensive for the project manager and primary investigator.

Weaknesses of this System for Injury Surveillance

There are a number of practical concerns about this protocol for ongoing injury surveillance. While the quality of the data in this study was high, the study was very time-intensive. The success of the study depended partially on donated effort of hospital-based primary investigators, medical records departments, and charge nurses. In order to maintain quality control, it also required the donated time of the study primary investigators and a pediatric radiologist, but it is unclear that this effort would be sustainable for a longer time period of continued injury surveillance outside of a research protocol. As changes within society appear to play a role in rates of iTBI, a longer period of surveillance would be desirable to ensure that rates obtained are not unduly influenced by a single societal stressor (e.g., closure of a large employer, natural disasters). Small numbers of cases even in a large U.S. state can lead to wide variations in measured rates from year to year.

It is likely that some cases that would have qualified for the study were missed. It is known that two children who were identified as they entered rehabilitation through a parallel project (Project ACCESS) for children with TBI in North Carolina were missed in the hospital.¹¹ There may have been children hospitalized in an ICU who had their neuro-imaging incorrectly read as negative for brain injury and were not enrolled because they did not meet study criteria. While it was possible to check the radiographs of children who were admitted to the ICU, it was not possible to identify children whose neuro-imaging was under-read and did not get admitted to a monitored unit. At least one case was admitted initially to a hospital ICU for the suspicion of TBI and had negative neuro-imaging. This same child was later admitted to a different hospital with positive neuro-imaging, but not admitted to the ICU as the injury was not acute and the child did not require intensive monitoring. Because the child was never admitted to an ICU with positive neuro-imaging, this child was ineligible for study inclusion.

Finally, this surveillance system may be more difficult to implement now. Some hospital systems started to interpret the Health Insurance Portability and Accountability Act (HIPAA) differently from the beginning of the study to the end. While the HIPAA guidelines do not prohibit this type of research, it is easier for risk-averse hospital systems to deny the research than to permit it.

Conclusion

The exact protocol used in the North Carolina study may not be advisable as an ongoing surveillance system. The main strengths of the system were a clear definition of a case, multiple sources of information, and ongoing quality checks in the form of investigator review of each case and review of all radiographs. The major weaknesses in the system for ongoing injury surveillance included fatigue of volunteers for the maintenance of such a time-intensive method of surveillance and that the entire system would fail if one hospital decided not to participate. A less time-intensive system of surveillance that could incorporate many elements of this study, could be financially feasible, and may be more acceptable to hospitals would be the incorporation of injury surveillance for iTBI into the existing trauma system. Trauma systems

maintain a database for both quality-control purposes and to maintain their trauma-level designation. Maintenance of a trauma designation is of importance to hospitals so these systems undergo quality checks and are already funded. Data for trauma databases are collected at the end of the hospitalization at which time a medical diagnosis of abuse often has been made. A surveillance system such as this would require that the trauma system be notified of all children with iTBI; however, some trauma services already participate in the care of any child with a brain injury in order to facilitate the need for potential surgical co-management, so the addition of an abuse flag or designation would not require many additional resources. As the trauma data sets have existing privacy protections and mechanisms for researchers to use the data, a single IRB application to the trauma system could be made rather than multiple IRB applications. A system as described above would neither incorporate all of the elements of quality control employed in the original study nor capture prehospital deaths, but it may be a low-cost surveillance system that is maintainable over multiple years that could establish trends in rates over time. This type of system could be used to monitor ongoing injury prevention efforts.

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Table 1Summary of North Carolina incidence study rates³

Characteristics	N/n	Incidence rate per 100,000 person-years (95% CI)
All children	80	17.0 (13.3–20.7)
Gender		
Boys	50	21.0 (15.1–26.2)
Girls	30	13.0 (8.4–17.7)
Race/ethnicity		
European American	32	9.5 (6.2–12.8)
African American	31	27.1 (17.5–36.6)
Other	17	95.7 (50.2–141.3)
Age (years)		
≤ 1 year	71	29.7 (22.9–36.7)
>1 year	9	3.8 (1.3–6.4)