Clinical Article

Traumatic Brain Injury in Children under Age 24 Months: Analysis of Demographic Data, Risk Factors, and Outcomes of Post-traumatic Seizure

Sang-Youl Yoon, M.D., Yeon-Ju Choi, M.D., Seong-Hyun Park, M.D., Ph.D., Jeong-Hyun Hwang, M.D., Ph.D., Sung Kyoo Hwang, M.D., Ph.D.
Department of Neurosurgery, Kyungpook National University Hospital, Daegu, Korea

Objective: Traumatic brain injury (TBI) in children under age 24 months has characteristic features because the brain at this age is rapidly growing and sutures are opened. Moreover, children this age are completely dependent on their parents. We analyzed the demographic data and risk factors for outcomes in TBI patients in this age group to elucidate their clinical characteristics.

Methods: We retrospectively reviewed the medical records and radiological films of children under 24 months who were admitted to Kyungpook National University Hospital from January 2004 to December 2013 for TBI. Specifically, we analyzed age, cause of injury, initial Glasgow coma scale (GCS) score, radiological diagnosis, seizure, hydrocephalus, subdural hygroma, and Glasgow outcome scale (GOS) score, and we divided outcomes into good (GOS 4–5) or poor (GOS 1–3). We identified the risk factors for post-traumatic seizure (PTS) and outcomes using univariate and multivariate analyses.

Results: The total number of patients was 60, 39 males and 21 females. Most common age group was between 0 to 5 months, and the median age was 6 months. Falls were the most common cause of injury (n=29, 48.3%); among them, 15 were falls from household furniture such as beds and chairs. Ten patients (16.7%) developed PTS, nine in one week; thirty-seven patients (61.7%) had skull fractures. Forty-eight patients had initial GCS scores of 13–15, 8 had scores of 12–8, and 4 had scored 3–7. The diagnoses were as follows: 26 acute subdural hematomas, 8 acute epidural hematomas, 7 focal contusional hemorrhages, 13 subdural hygromas, and 4 traumatic intracerebral hematomas larger than 2 cm in diameter. Among them, two patients underwent craniotomy for hematoma removal. Four patients were victims of child abuse, and all of them had PTS. Fifty-five patients improved to good-to-moderate disability. Child abuse, acute subdural hematoma, and subdural hygroma were risk factors for PTS in univariate analyses. Multivariate analysis found that the salient risk factor for a poor outcome was initial GCS on admission.

Conclusion: The most common cause of traumatic head injury in individuals aged less than 24 months was falls, especially from household furniture. Child abuse, moderate to severe TBI, acute subdural hematoma, and subdural hygroma were risk factors for PTS. Most of the patients recovered with good outcomes, and the risk factor for a poor outcome was initial mental status.

Key Words: Craniocerebral trauma · Infants · Demography · Risk factors · Seizures · Glasgow outcome scale.

Received: July 19, 2016 • Revised: December 15, 2016 • Accepted: March 14, 2017
Address for reprints: Sung Kyoo Hwang, M.D., Ph.D.
Department of Neurosurgery, Kyungpook National University Hospital, 130 Dongdeok-ro, Jung-gu, Daegu 41944, Korea
Tel.: +82-53-200-5654, Fax.: +82-53-423-0504, E-mail: shwang@knu.ac.kr

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (http://creativecommons.org/licenses/by-nc/4.0) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.
INTRODUCTION

Traumatic brain injury (TBI) is one of the most important causes of disability and death in children. The incidence of infantile injury is little reported and unclear, but it has been reported to be ~124 per 1000 children. TBI in children under age 24 months has characteristic features that differ from those other age groups. Children this age are completely dependent on their caretakers; additionally, because their skulls are thin, sutures are opened and the brain is not fully matured, their brain is more vulnerable to external forces. As a result, it is conceivable that pathophysiology and recovery process may be different from those of adults. The incidence of post-traumatic seizure (PTS) is reported to be ~10 to 20% among children with TBI. Many authors have reported a higher incidence of PTS in young children than in other age groups. PTS is a major cause of poor outcomes.

Most reports on pediatric TBI include children of wide age ranges, and few articles focus on the characteristic features of TBI in this infantile age group. Therefore, we conducted this study to elucidate the demographic characteristics and risk factors of PTS and TBI outcomes in very young children.

MATERIALS AND METHODS

We retrospectively reviewed patients under age 24 months who were admitted to Kyungpook National University Hospital from January 2004 to December 2013 for TBI using their medical records and radiological findings. Specifically, we analyzed them for age, cause of injury, initial Glasgow coma scale (GCS) score, radiological diagnosis, development of seizure, hydrocephalus, and Glasgow outcome scale (GOS) score. The radiologic data we analyzed were skull fracture, acute subdural or epidural hematoma, subdural hygroma, traumatic intracerebral hematoma (defined as larger than 2 cm in diameter), focal contusional hemorrhage (defined as smaller than 2 cm), and diffuse axonal injury without significant hemorrhage.

We divided initial GCS scored into three groups: mild (GCS 13–15), moderate (GCS 8–12), or severe (GCS 3–7) head injury, and we divided outcomes into either good (GOS 4–5, good outcome or moderate disability) or poor (GOS 1–3, severe disability or death). We also statistically analyzed the risk factors for PTS and good or poor outcomes; we evaluated the children’s outcomes at the time of discharge from the hospital or at their last follow-up visits, which varied from one week to two years. The follow-up periods varied so markedly because most of the neurologically intact patients were not followed up for long periods, whereas patients with worse deficits stayed in the hospital or visited regularly for years.

Statistical methods

We calculated significance probability using the chi-squared test; if the result was significant and the expected frequencies were less than five in more than 25% of the cells, we calculated p values using Fisher’s exact test. We used multiple logistic regression analysis to test the partial effects of the variables that were significant in the univariate analysis and calculated the C-statistics. We conducted the statistical analyses using SAS software (SAS 9.4; SAS Institute Inc., Cary, NC, USA) and considered p values <0.05 to indicate statistical significance.

RESULTS

The total number of patients was 60, 39 males and 21 females; most common age group was between 0 and 5 months (26 cases, 43.3%), followed by 22 patients who were age 6–11 months; additionally, twelve patients were aged between 12 to 23 months. The mean age was 7.5 months and the median was six (Table 1). Regarding the etiology, falls were the most common cause of injuries at 29 (48.3%). Among these, 15 were falls from household furniture such as beds and chairs, comprising 25.0% of all cases. On admission, 48 patients (80.0%) had GCS scores of 13 to 15, 8 (13.3%) had scores of 8 to 12, and 4 (6.7%) had scores of 3 to 7 (Table 3).

Skull fracture was found in 37 patients (61.7%) and was the...
most common radiological finding. The intracranial diagnoses on computed tomography (CT) and magnetic resonance imaging (MRI) were as follows: 26 acute subdural hematomas, 8 acute epidural hematomas, 13 subdural hygromas, 7 focal contusional hemorrhages, and 4 traumatic intracerebral hematomas.

No patients had diffuse axonal injury without significant hemorrhage (Table 4). Two patients underwent craniotomy to remove hematomas, and 10 patients (16.7%) developed PTS; in nine of those ten, the PTS developed within one week after injury, and six of these patients showed generalized seizure. Two patients (3.3%) developed post-traumatic hydrocephalus, one of whom underwent ventriculo-peritoneal shunt. Four patients, 6.4% of all patients had been victims of child abuse; all of them had had PTS and poor outcomes. Regarding GOS scores, 55 patients showed good outcomes and 5 showed poor outcomes (Table 5).

### Risk analysis

We conducted risk analysis regarding PTS and poor outcomes. According to univariate analyses, child abuse, subdural hygroma, acute subdural hematoma, and GOS score were related to a higher incidence of PTS (Table 6). Multivariate analysis revealed that subdural hygroma was a significant risk factor for seizure development ($p=0.018$, odds ratio [OR]=6.7, 95% confidence interval [CI]=1.4–32.1), and patient outcomes were significantly related to traumatic intracerebral hematoma and initial GCS score on univariate analysis (Table 7). Multivariate analysis revealed that only initial GCS score was significantly related to outcomes ($p=0.002$, OR=26.5, 95% CI=3.2–216.2, c-statistics=0.97).

### DISCUSSION

TBI in children is one of the main causes of disability and death. There are few reports of TBI in children aged less than 24 months, and studies most involve children of all age ranges. However, children under age 24 months are completely dependent on caretakers, and it is conceivable that the etiology and mechanisms of TBI in these patients could differ from those in other age groups. The thin skull in these very young children is susceptible to fracture; moreover, because their brains grow rapidly, brain injury can result in serious permanent damage.

The incidence of TBI in children in this age range is unclear, but it has been reported to be ~124 per 1000 children. Quayle et al. reported a clinical observational study con-
ducted in the United States through the Pediatric Emergency Care Applied Research Network. Among their cohort of 43399 patients, most were children aged one and two, and the most common injury mechanism was falls from heights, comprising 54%, followed by falling down stairs and falling to the ground from standing, walking, or running. Fakharian et al.\(^\text{10}\) also reported that falling was the most common cause of injury, and more than 65% of the injuries in that study had occurred at home. However, those authors stated that traffic accidents were an increasingly common cause of injury. In our series, the most common cause of TBI in this age group was falls, and approximately half of them were from household furniture such as beds and chairs. With this in mind, special care should be taken with infants, and safety regarding household furniture cannot be overemphasized. Injuries from falling from household objects were usually mild. Fall from low heights rarely cause significant brain injury, with the exception of epidural hematoma\(^\text{8}\). Kim et al.\(^\text{18}\) reported clinical features of TBI in children aged less than 24 months, and the most common mode of injury was stairs followed by in-car accidents. The incidence of injury due to child abuse was 2.9%.

A number of authors have reported on non-accidental causes of TBI in this age group\(^\text{8,9,28}\). Duhaime et al.\(^\text{8}\) reported that ~24% of head injuries in children aged less than two years were presumed inflicted, and 32% were suspicious for abuse, neglect, or social or family problems on careful interviewing by trauma social workers and ophthalmic evaluation. Children under age two years had worse outcomes than any other age groups. In our series, 4 of 60 cases (6.7%) were due to child abuse. Concern about child abuse is increasing in Korea, but the incidence is still considered low.

We diagnosed child abuse based on history taken from caretakers or related persons and general physical examination. It is true that special consideration should be paid to diagnose non-accidental head injury in this age group, but this is problematic; subdural hematoma and retinal hemorrhage can suggest non-accidental injury, but not decisively so. Thus, careful history taking and whole body examinations are important, as is the role of the injury coordinator. It was not conclusive from our series that child abuse had resulted in poorer outcomes than other causes of injury due to the small number of abused patients. However, many papers have reported poor outcomes from abuse\(^\text{8}\). We pro-

| Diagnosis                      | Number of patients | Number of seizures | p-value |
|--------------------------------|--------------------|--------------------|---------|
| Cause of injury                |                    |                    |         |
| Abuse                          | 4                  | 4                  |         |
| Traffic accident                | 12                 | 1                  | 0.003\(^\dagger\) |
| Fall                           | 29                 | 2                  | 0.000\(^\dagger\) |
| Others                         | 15                 | 3                  | 0.009\(^\dagger\) |
| Subdural hygroma               | 13                 | 6                  | 0.004   |
| Acute subdural hematoma        | 26                 | 8                  | 0.015   |
| Acute epidural hematoma        | 8                  | 0                  | 0.330   |
| Skull fracture                 | 37                 | 4                  | 0.161   |
| Hydrocephalus                  | 2                  | 1                  | 0.308   |
| Glasgow outcome (poor)\(^a\)  | 5                  | 0                  | 0.578   |
| Glasgow coma scale             |                    |                    |         |
| 13–15                          | 48                 | 5                  |         |
| 8–12                           | 12                 | 4                  | 0.042\(^\dagger\) |
| 3–7                            | 4                  | 1                  |         |

\(^a\)Factors with p-values larger than 0.5 were not included in the table.
\(^\dagger\)Comparison between abuse and each other causes by Fisher’s exact test.
\(^\text{8}\)Poor’ meant severe disability or death, \(^\text{8}\)Incidence was high in moderately to severely injured patients compared with the mild TBI group. TBI : traumatic brain injury

| Diagnosis                      | Number of patients | Number of poor outcomes | p-value |
|--------------------------------|--------------------|-------------------------|---------|
| Focal contusional hemorrhage   |                    | 7                       | 5       | 0.099   |
| Traumatic ICH                  | 4                  | 2                       | 0.032   |
| Acute subdural hematoma        | 26                 | 25                      | 0.377   |
| Hydrocephalus                  | 2                  | 1                       | 0.161   |
| Glasgow coma scale score       |                    |                         | 0.000   |
| 13–15                          | 48                 | 0                       |         |
| 8–12                           | 8                  | 2                       |         |
| 3–7                            | 4                  | 3                       |         |
| Age                            |                    |                         | 0.088   |
| 0–5                            | 26                 | 1                       |         |
| 6–11                           | 22                 | 1                       |         |
| 12–17                          | 6                  | 2                       |         |
| 18–23                          | 6                  | 1                       |         |

\(^a\)Factors with p-values larger than 0.5 were not included in the table.
ICH : intracerebral hematoma
pose two reasons for the poor outcome in abused children; one is that most of the child abuse patients without mental deterioration did not visit the hospital, and the other is that rotational forces caused their injuries.

Skull fracture was one of the most common features of head injury in our series, comprising 37 of 60 patients; it was associated with relatively mild TBI with good prognoses. It is conceivable that a thin skull is associated with susceptibility to skull fracture. A number of authors reported that the incidence of neurosurgical intervention in children with isolated skull fracture and no neurological deficit was so low that the patients could be discharged after initial evaluation. However, considering that PTS can result in devastating outcomes and that young children have a high incidence of these seizures, we recommend that patients with skull fracture be closely observed after admission. We routinely take brain CT scan in patients who visit our emergency room after head injury if they are not completely normal or if their parents want us to take CT scans in spite of our warning about possible radiation hazard.

Post-traumatic epilepsy (PTE) develops in 10–20% of children with TBI. PTS can result in worse outcomes due to secondary brain injury from increased intracranial pressure, hypoxia, and increased metabolic requirements. A number of authors report that children have a higher incidence of PTS than adults. In particular, very young children are more prone to developing PTS. Kieslich and Jacobi reported an increased incidence of early and late seizure (43.8%) in children under age two, who showed greater susceptibility to PTS. Several authors have also reported that subclinical epilepsy developed in a considerable number of patients. Arndt et al. monitored continuous EEG in pediatric head injury to detect subclinical early PTS and found seizures of any type in 43.7% of their cohort; additionally, 42.9% of the patients in that study, 6.9% of the total population, had subclinical seizures. Penetrating injury, subdural hematoma, and intracerebral hematoma showed a higher incidence than other types of injury. Liesemer et al. reported that age below two years, a GCS score below 8, and non-accidental trauma were risk factors for early PTS. In our study, the incidence of seizure was 16.7%, and risk factors were abuse, subdural hygroma, subdural hematoma, and GCS score. Severe TBI is a risk factor for a higher incidence of PTS. Our study also showed a higher rate of seizure development in moderate-to-severe than in mild TBI; however, there was no difference between moderate and severe injuries. Subdural hygroma was related to a high incidence of PTS in univariate and multivariate analyses in our series. The reason for the high frequency of PTS in subdural hygroma is unclear because there have been no similar reports regarding any relationship between PTS and subdural hygroma; its clinical courses and significance are usually neglected in studies of TBI. It is conceivable that subdural hygroma that develops as a result of minor laceration of the arachnoid membrane is associated with cortical injury; however, additional studies are needed to clarify this relationship. The incidence also varies according to the etiology of trauma; many authors have reported a higher incidence of PTS in non-accidental injury. Our series also showed a higher incidence of PTS in abused children, despite their small number. Subdural hematoma has been reported to be a risk factor for PTS. Considering the high incidence of seizure in infantile TBI, an aggressive approach is needed to prevent early seizure in TBI in infants. Role of antiepileptic drug (AED) in pediatric PTE is not definitely determined. However, many authors report the effectiveness of AED to prevent early seizure. We routinely prescribed the preventive AED to patients admitted in our hospital; however, the duration was variable.

It is well-known that patient outcome is related to GCS on admission. In our series, initial GCS and intracerebral hematoma were significant risk factors on univariate analysis. However, multivariate analysis found that intracerebral hematoma did not contribute to the predictability of poor outcomes. We believe that we need more data to determine the importance of intracerebral hemorrhage as an independent risk factor.

One of the limitations of our study was the small number of patients despite our institution being a tertiary referral hospital with an active pediatric neurosurgical division. Although a high proportion of pediatric TBI patients are under age 24 months, the number of patients in our study was insufficient for reliable analysis. We believe that a cooperative inter-hospital study is required to provide a good reference database for managing and protecting against TBI in very young children. Second limitation was the wide range in follow-up periods; neurologically intact patients were followed for a short time, but patients with disability could be followed for years. Another limitation was diagnosis of subdural hygroma. It is not uncommon that some infant has wide subarachnoid space.
which reveals similar findings in CT scan and can be differentiated by MRI. However, we did not take MRI routinely and diagnosed the subdural hygroma when the subdural space was definitely wide initially or widened at the follow up CT scan.

CONCLUSION

We assessed the demographic data and risk factors for PTS and outcomes in TBI in children aged less than two years. Falls were the most common cause of injury, especially falls scan. We assessed the demographic data and risk factors for PTS, and injury severity and intracerebral hematoma were risk factors for poor prognoses.

References

1. Annegers JF, Coan SP: The risks of epilepsy after traumatic brain injury. Seizure 9: 453-457, 2000
2. Annegers JF, Grabow JD, Groover RV, Laws ER Jr, Elveback LR, Kurland LT: Seizures after head trauma: a population study. Neurology 30(7 Pt 1): 683-689, 1980
3. Annegers JF, Hauser WA, Coan SP, Rocca WA: A population-based study of seizures after traumatic brain injuries. N Engl J Med 338: 20-24, 1998
4. Arndt DH, Lerner JT, Matsumoto JH, Madikians A, Yudovin S, Valino H, et al.: Subclinical early posttraumatic seizures detected by continuous EEG monitoring in a consecutive pediatric cohort. Epilepsia 54: 1780-1788, 2013
5. Chang BS, Lowenstein DH: Quality Standards Subcommittee of the American Academy of Neurology: Practice parameter: antiepileptic drug prophylaxis in severe traumatic brain injury: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 60: 10-16, 2003
6. Chiaretti A, De Benedictis R, Polidori G, Piastra M, Iannelli A, Di Rocco C: Early post-traumatic seizures in children with head injury. Childs Nerv Syst 16: 862-866, 2000
7. Desai BT, Whitman S, Coonley-Hoganson R, Coleman TE, Gabriel G, Dell J: Seizures and civilian head injuries. Epilepsia 24: 289-296, 1983
8. Duhaime AC, Alarion AJ, Lewander WJ, Schut L, Sutton LN, Seidl TS, et al.: Head injury in very young children: mechanisms, injury types, and ophthalmologic findings in 100 hospitalized patients younger than 2 years of age. Pediatrics 90(2 Pt 1): 179-185, 1992
9. Duhaime AC, Christian CW, Rorke LB, Zimmerman RA: Nonaccidental head injury in infants—the "shaken-baby syndrome". N Engl J Med 338: 1822-1829, 1998
10. Fakharian E, Mohammadzadeh M, Behdad S, Babamohammadi A, Mirzadeh AS, Mohammadzadeh J: A seven-year study on head injuries in infants, Iran—the changing pattern. Chin J Traumatol 17: 153-156, 2014
11. Formisano R, Barba C, Buzzi MG, Newcomb-Fernandez J, Meninni-Ippolito F, Zafonte R, et al.: The impact of prophylactic treatment on post-traumatic epilepsy after severe traumatic brain injury. Brain Inj 21: 499-504, 2007
12. Greenses DS, Schutzman SA: Infants with isolated skull fracture: what are their clinical characteristics, and do they require hospitalization? Ann Emerg Med 30: 253-259, 1997
13. Hahn YS, Chyung C, Barthel MJ, Bailes J, Flannery AM, McLone DG: Head injuries in children under 36 months of age. Demography and outcome. Childs Nerv Syst 4: 34-40, 1988
14. Hahn YS, Fuchs S, Flannery AM, Barthel MJ, McLone DG: Factors influencing posttraumatic seizures in children. Neurosurgery 22: 864-867, 1988
15. Keenan HT, Runyan DK, Marshall SW, Nocera MA, Merten DF: A population-based comparison of clinical and outcome characteristics of young children with serious inflicted and noninflicted traumatic brain injury. Pediatrics 114: 623-639, 2004
16. Kieslich M, Jacobi G: Incidence and risk factors of post-traumatic epilepsy in childhood. Lancet 345: 187, 1995
17. Kieslich M, Marquardt G, Galow G, Lorenz R, Jacobit G: Neurological and mental outcome after severe head injury in childhood: a long-term follow-up of 318 children. Disabil Rehabil 23: 665-669, 2001
18. Kim JK, Park JY, Cho TH, Kwon TH, Lim DJ, Chung YK, et al.: Clinical features and prognostic factors of head injury in less than two-year-old children. J Korean Neurosurg Soc 27: 625-631, 1998
19. Kochanek PM, Carney N, Adelson PD, Ashwal S, Bell MJ, Bratton S, et al.: Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents—second edition. Pediatr Crit Care Med 13 Suppl 1: S1-582, 2012
20. Liesemer K, Bratton SL, Zebrack CM, Brockmeyer D, Statler KD: Early post-traumatic seizures in moderate to severe pediatric traumatic brain injury: rates, risk factors, and clinical features. J Neurotrauma 28: 755-762, 2011
21. Ma CY, Xue YJ, Li M, Zhang Y, Li GZ: Sodium valproate for prevention of early posttraumatic seizures. Chin J Traumatol 13: 293-296, 2010
22. Mannix R, Monuteaux MC, Schutzman SA, Meehan WP 3rd, Nigrovic LE, Neuman MI: Isolated skull fractures: trends in management in US pediatric emergency departments. Ann Emerg Med 62: 327-331, 2013
23. Ostahowski PJ, Kannan N, Wainwright MS, Qui O, Mink RB, Groner Jl, et al.: Variation in seizure prophylaxis in severe pediatric traumatic brain injury: rates, risk factors, and clinical features. J Neurotrauma 28: 755-762, 2011
24. Park JT, Chugani HT: Post-traumatic epilepsy in children-experience from a tertiary referral center. Pediatr Neurol 52: 174-181, 2015
25. Powell EC, Atabaki SM, Wootton-Gorges S, Wisner D, Mahajan P, Glass T, et al.: Isolated linear skull fractures in children with blunt head trauma. Pediatrics 135: e851-e857, 2015
26. Quayle KS, Powell EC, Mahajan P, Hoyle JD Jr, Nadel FM, Badawy MK, et al. : Epidemiology of blunt head trauma in children in U.S. emergency departments. *N Engl J Med* 371 : 1945-1947, 2014
27. Ratan SK, Kulshreshtha R, Pandey RM : Predictors of posttraumatic convulsions in head-injured children. *Pediatr Neurosurg* 30 : 127-131, 1999
28. Rhine T, Wade SL, Makoroff KL, Cassedy A, Michaud LJ : Clinical predictors of outcome following inflicted traumatic brain injury in children. *J Trauma Acute Care Surg* 73(4 Suppl 3) : S248-S253, 2012
29. Rollins MD, Barnhart DC, Greenberg RA, Scaife ER, Holsti M, Meyers RL, et al. : Neurologically intact children with an isolated skull fracture may be safely discharged after brief observation. *J Pediatr Surg* 46 : 1342-1346, 2011