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Diffuse brain swelling in severely head-injured children

A report from the NIH Traumatic Coma Data Bank

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✓ In this study, data were prospectively collected from 753 patients (111 children and 642 adults) with severe head injury and examined for evidence of diffuse brain swelling and its association with outcome. Diffuse brain swelling occurred approximately twice as often in children (aged 16 years or younger) as in adults. A high mortality rate (53%) was found in these children, which was three times that of the children without diffuse brain swelling (16%). Adults with diffuse brain swelling had a mortality rate (46%) similar to that of children, but only slightly higher than that for adults without diffuse brain swelling (39%). When the diagnosis of diffuse brain swelling was expanded to include patients with diffuse brain swelling plus small parenchymal hemorrhages (< 15 cu cm), these mortality rates were virtually unchanged.

Key Words • **brain injury** • **head injury** • **Traumatic Coma Data Bank** • **brain swelling** • **children**

Computerized tomography (CT) has allowed the identification of diffuse brain swelling in patients with traumatic brain injury. This pathological condition is diagnosed by a decrease in the cerebrospinal fluid spaces: compressed or obliterated mesencephalic cisterns and/or small ventricles in the absence of other intracranial pathology.[1–3,5,8,10,12]

Diffuse brain swelling has been reported to be commonly associated with severe head injury in children, where it is said to be a frequent cause of delayed neurological deterioration and where it is associated with a favorable outcome. These features are said to distinguish diffuse brain swelling in children from that found in adults. In addition, it has been reported that patients with diffuse brain swelling should be distinguished from those with diffuse brain swelling plus small parenchymal hemorrhages (the CT "signature" of diffuse axonal injury) who are said to have a worse prognosis.[3]

The National Institutes of Health (NIH) Traumatic Coma Data Bank (TCDB) includes data on 1030 severely head-injured patients. It is well suited for investigating these differences since it is a large data set, with regard to both the number of patients and the spectrum of information included. These data were collected in a prospective fashion at four centers under similar conditions, and the information included was coded according to predetermined definitions. Adults and children with severe head injury were admitted to all four centers in approximately the same ratios.

Clinical Material and Methods

Patient Population

During the period of patient accrual (January, 1984, to September, 1987), 1030 patients with severe head injury were entered into the TCDB. These patients were defined as having a severe head injury on the basis of a Glasgow Coma Scale[11] (GCS) score of 8 or less after acute nonsurgical resuscitation, or deterioration to that level within 48 hours of impact. Of the 1030 cases, patients were excluded from the present analysis for the following reasons: 1) they were dead on arrival at the TCDB hospital (137 cases); 2) they had sustained a gunshot wound to the head (114 cases); or 3) they did not undergo CT (26 cases). Of this latter group, most were diagnosed as brain-dead in the emergency room. Patients with gunshot wounds were excluded because it was believed that these injuries differ from other types of head injury with regard to both pathophysiology and outcome. These analyses, then, encompassed the remaining 753 patients (111 children and 642 adults).

Study Groups

The 753 patients were assigned to three groups based on CT criteria only. Group I (diffuse brain swelling with or without small parenchymal hemorrhages) included patients displaying the following criteria on CT scans: 1) compressed or obliterated mesencephalic cisterns; 2) small or normal ventricles; 3) no midline shift greater than 3 mm; and 4) no intraparenchymal hemorrhages larger than 15 ml. There were 138 patients (111 adults and 27 children) in this group.

Group II (diffuse brain swelling) is a subset of Group I and identical to it except that those patients with small parenchymal hemorrhages (< 15 ml) were also excluded. This group consisted of 75 patients (56 adults and 19 children), which is smaller than the group examined in a previously published report[4] due to different selection criteria. To be included in the present study, all patients in both groups had to have both abnormal mesencephalic cisterns and small or normal ventricles. In contrast, only one of these criteria was required for inclusion in the previous report.

The third group (Group III, termed "other") included those patients who did not fit into either Group I or Group II, and consisted of 564 patients (488 adults and 76 children). Data were missing for 51 patients (43 adults and eight children).

Only data from the initial CT scans, made as soon as possible after admission to the TCDB hospital, were considered in forming these study groups since later CT scans were obtained only when a patient's condition specifically required this information. Therefore, data from the initial CT scan were considered less biased than data from later CT scans.

The study groups were further subdivided according to age: children (16 years of age or younger) and adults. These groups were analyzed for their association with variables that included the GCS score, neurological deterioration, intracranial pressure (ICP), presence of early (preadmission) hypotension and hypoxia, and period of survival.

Glasgow Coma Scale Score

Two GCS scores were used in these analyses. The initial GCS score was the first coded after impact, either at the injury site, during transportation from the scene, at a referring hospital's emergency room, or at the emergency room of the TCDB hospital, whichever was earliest. Initial GCS scores were available for 137 patients (110 adults and 27 children) in Group I, for 74 patients (55 adults and 19 children) in Group II and for 563 patients (487 adults and 76 children) in Group III. The second GCS score was obtained after admission to the TCDB hospital and after nonsurgical resuscitation. Second GCS scores were available for 133 patients (107 adults and 26 children) in Group I, for 72 patients (53 adults and 19 children) in Group II, and for 518 patients (448 adults and 70 children) in Group III.

Intracranial Pressure

Two ICP variables were examined: 1) the percentage of time that ICP was greater than 20 mm Hg during the first 72 hours after injury, and 2) the highest ICP recorded within the first 72 hours. Of these, the percentage of time that ICP was greater than 20 mm Hg was found in a separate analysis to be the most important variable in the ICP record at the TCDB (A Marmarou, unpublished data). Intracranial pressure was measured in 116 patients (92 adults and 24 children) in Group I, in 64 patients (47 adults and 17 children) in Group II, and in 487 patients (417 adults and 70 children) in Group III.

Systemic Parameters

The association of early systemic insults, hypoxia, and hypotension (as observed before admission to the TCDB emergency room) with diffuse brain swelling was also examined. Early definite hypoxia was defined as a PaO_2 of less than 60 torr. Hypoxia data were available for 70 patients (61 adults and nine children) in Group I, for 44 patients (38 adults and six children) in Group II, and for 291 patients (253 adults and 38 children) in Group III. Early hypotension was defined as a systolic blood pressure of less than 90 mm Hg in adults and less than 80 mm Hg in children. Hypotension data were available for 126 patients (103 adults and 23 children) in Group I, for 68 patients (51 adults and 17 children) in Group II, and for 497 patients (430 adults and 67 children) in Group III.

Data Analysis

The mortality rate for the various groups was calculated based on the entire 3-year follow-up period. The differences in mortality rates were analyzed using chi-squared tests. Since the follow-up duration was variable and extended over a long period, the mortality probabilities were also tested by life-table analysis. Differences in survival curves were assessed with log rank tests.

Results

Frequency of Diffuse Brain Swelling

The cohort studied consisted of 753 patients (642 adults and 111 children). There were 138 patients in Group I (diffuse brain swelling with or without small parenchymal hemorrhages), including 111 adults (17%) and 27 children (24%), and 75 patients in Group II (diffuse brain swelling without small parenchymal hemorrhages), including 56 adults (9%) and 19 children (17%). When the specific ages of children with diffuse brain swelling were considered: in Group I, five patients were 0 to 3 years old, five were 4 to 7 years old, three were 8 to 11 years old, and 14 were 12 to 16 years old; in Group II, four patients were 0 to 3 years old, five were 4 to 7 years old, one was between 8 and 11 years old, and nine were 12 to 16 years old. Group III included 18 patients aged 0 to 3 years, nine aged 4 to 7 years, 16 aged 8 to 11 years, and 33 aged 12 to 16 years.

Glasgow Coma Scale Score and Delayed Neurological Deterioration

A comparison of patients' initial and postresuscitation GCS scores showed a slight improvement following resuscitation. Among patients with diffuse brain swelling, with or without small parenchymal hemorrhages, only seven adults and one child deteriorated within 48 hours from a GCS score of greater than 8 to 8 or less. Approximately one-half of these scores were recorded at the scene of injury; the remainder were recorded at locations fairly evenly distributed among other sites. The average time from impact to admission to the TCDB hospital was 2.2 hours in children and 3.1 hours in adults.

Intracranial Pressure

In children, the mean percentage of time that ICP was greater than 20 mm Hg was higher for the group with diffuse brain swelling (Group II) than for the remainder of the pediatric cohort (30% vs. 18%). The observed mean percentage of time of elevated ICP was slightly lower in adults (24%) than in children with diffuse brain swelling, and was comparable to the value for the rest of the adult cohort (22%). None of the differences is statistically significant and all of the confidence intervals overlap. The mean highest ICP was virtually identical in all of the subgroups, ranging only from 30 to 35 mm Hg.

Hypoxia and Hypotension

More patients with diffuse brain swelling had early hypoxia (61%) than did those without diffuse brain swelling (34%). The relationship between early hypotension and diffuse brain swelling was similar to that of early hypoxia (57% vs. 35%). For both systemic events, the addition of parenchymal hemorrhages did not substantially alter the relative occurrences and no difference could be found between the pediatric and the adult cohorts.

Mortality Rate

The mortality rates for the various subgroups for the total duration of the study (3 years) are shown in Fig. 1. Ten (53%) of the 19 children with diffuse brain swelling (Group II) died, as compared to 12 (16%) of the 76 children without diffuse brain swelling. Twenty-six (46%) of the 56 adult patients with diffuse brain swelling (Group II) died, as compared to 190 (39%) of the 488 adult patients without diffuse brain swelling. When these diagnostic groups were expanded to include small parenchymal hemorrhages, the mortality rates in children and adults were identical (44%).

When Groups I and III are considered together, adult patients had a significantly higher risk of dying than children ($p < 0.003$). However, no significant differences in mortality rate were found between children and adults in either Group I or Group II.

Because these figures included all causes of death within the follow-up period to a maximum of 3 years, analysis was performed to evaluate the time frame in which these patients died. It was found that 11 (92%) of the 12 Group I children who died, did so within 6 days, as compared to 36 (73%) of the 49 adult deaths in Group I. In Group III, the deaths occurring within 6 days were comparable for adults and children (67%).

The 6-day survival probabilities for patients with diffuse brain swelling with or without parenchymal hemorrhage (Group I) versus all other patients are outlined in Fig. 2. This life-table analysis indicated a nearly 50% mortality rate in children with diffuse brain swelling at 6 days as compared to 15% in all other children and 30% for adults in Group I. The overall chance of survival for children with diffuse brain swelling versus other children was significantly worse ($p = 0.005$).

Discussion

Appearance of Diffuse Brain Swelling on CT

The CT criteria for diffuse brain swelling have been defined in several reports.[1–3,5,8,10,12] The most important factors are generally thought to be compressed or obliterated mesencephalic cisterns and small ventricles. The mesencephalic cisterns are usually well imaged in children,[12] therefore compression or obliteration of these cisterns on CT scans warrants a conclusion of brain swelling. Unfortunately, the evaluation of ventricular size represents a problem, particularly in the pediatric population. Snoek, *et al.*,[9] warned that until clear, defined criteria for minimum ventricular size in normal children are set, caution is needed when interpreting "small" ventricles. Our previous analysis,[4] as well as that of Teasdale, *et al.*,[10] indicated that lateral ventricular size is not an accurate predictor of raised ICP. For this reason, we decided to include both "small" and "normal" ventricles in our definition of diffuse brain swelling, thereby excluding only cases with ventricular enlargement. Despite this decision, only three of the 19 children with diffuse brain swelling in this cohort were coded as not having small ventricles.

We defined two groups of patients with diffuse brain swelling for our study, according to the presence or absence of small intraparenchymal hemorrhages (< 15 cu cm). Small parenchymal hemorrhages are thought to be associated with diffuse axonal injury[13] and have also been shown to be of major predictive importance in the outcome of pediatric patients with diffuse brain swelling.[3,5] However, in our series, the addition of small

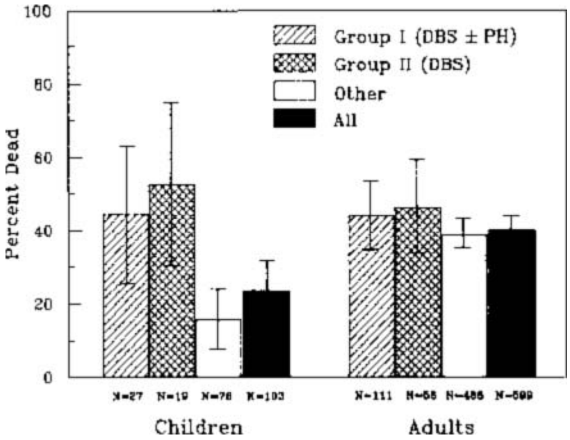

FIG. 1. Graph showing mortality rates in traumatic brain-injured patients with diffuse brain swelling (DBS), diffuse brain swelling with or without small parenchymal hemorrhage (DBS ± PH), and without either ("other"). *Bars* indicate upper and lower 95% confidence limits. Confidence intervals that do not overlap indicate a significant difference at the p = 0.05 level.

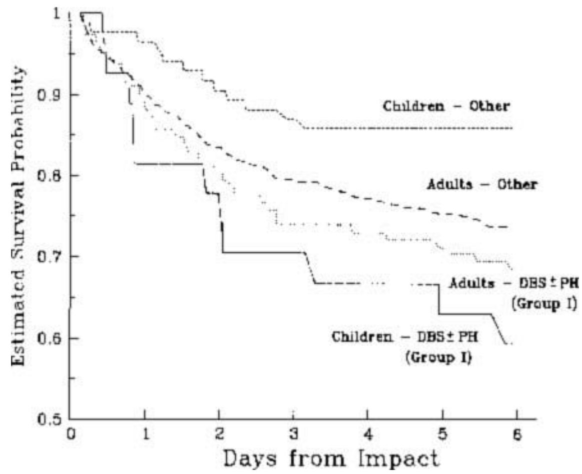

FIG. 2. Life-table analysis for survival of patients with diffuse brain swelling with or without small parenchymal hemorrhage (DBS ± PH) versus all other patients, considering adults and children separately.

parenchymal hemorrhages to the definition of diffuse brain swelling did not alter the frequency of any of the variables that we considered.

Frequency of Diffuse Brain Swelling

Diffuse brain swelling has been reported to be the most common initial CT scan finding in severely head-injured children.[2,12] While Kobayashi, *et al.*,[8] reported an incidence of 16% in severely head-injured patients of all ages, 44% of severely head-injured children fulfilled the criteria for diffuse brain swelling in the study of Berger, *et al.*[1] Bruce, *et al.*,[2] reported an incidence of 29% in their series of pediatric patients with diffuse brain swelling. However, in that report the indicative CT pattern was seen in only 15% of those patients with GCS scores greater than 8, while it was present in 41% of those with lower GCS scores. In contrast to our findings, Bruce, *et al.*, stated that diffuse brain swelling is rarely seen in adults and, when it occurs, it frequently involves only one hemisphere.

Although in our patients, diffuse brain swelling was found to be twice as common in children as in adults (17% vs. 9%), it clearly was not unique to our pediatric cohort, even though our reported frequency for children is lower than that reported in some other series of pediatric cases.

Delayed Neurological Deterioration

In other studies, the diagnosis of diffuse brain swelling in children was associated in some patients with delayed deterioration of neurological status.[1,2,9,12] It has been suggested that, while delayed deterioration in adults is most frequently associated with focal mass lesion, delayed deterioration in children is associated with diffuse brain swelling.[2] In one study, 50% of children who died following head injury were conscious on admission.[6]

In our study, the mean GCS score slightly improved following nonsurgical resuscitation in patients with diffuse brain swelling in both the pediatric and adult groups. However, to evaluate deterioration in greater detail, we found that only one child and seven adults actually deteriorated from a GCS score of greater than 8 to 8 or less. It is possible that deterioration had taken place between the time of impact and the time of the first GCS score. However, approximately 50% of our patients had their first GCS score recorded at the scene of injury, thereby mitigating this concern. Although initial evaluations were obtained in the emergency rooms of other institutions, while the patient was in transit, or in the TCDB hospital, the average time that elapsed from impact to admission to the TCDB hospital was 2.2 hours for the pediatric group and 3.1 hours for the adult group. If deterioration took place in these patients, it must have happened very soon after injury. Likewise, in the expanded group with parenchymal hemorrhages, deterioration was uncommon. We concluded therefore that neurological deterioration, at least during the time of observation, was not a feature in either children or adults with diffuse brain swelling with or without small parenchymal hemorrhages.

Intracranial Pressure

Contradictory findings regarding ICP in children with diffuse brain swelling have been reported.[2,3,12] We have previously reported that compressed or absent mesencephalic cisterns following severe head injury is an important predictor of elevated ICP.[4] Therefore, it was not surprising to find that intracranial hypertension is a feature in both children and adults with diffuse brain swelling. In the present study, we evaluated abnormal

ICP according to two definitions. First, using the more conventional definition of the highest ICP, we found that intracranial hypertension was present to the same degree in both adults and children with diffuse brain swelling and that the addition of patients with small parenchymal hemorrhages did not appear to make a difference in this regard. Second, we considered the percentage of time during the first 72 hours that ICP was greater than 20 mm Hg, as this proved to be the most salient ICP measure in the NIH TCDB data when many features of the ICP record were examined in statistical models (A Marmarou, unpublished data). Our results indicate that abnormal ICP is an important feature in both children and adults with diffuse brain swelling, whether defined with or without small parenchymal hemorrhages.

Hypoxia and Hypotension

In a previous report, we showed a strong association between diffuse brain swelling and either hypoxia or early hypotension.[4] In this study, we found that hypotension was one and one-half times as common, and that proven hypoxia was twice as common, in patients with diffuse brain swelling as compared to the remainder of the patients in the cohort. There were no differences between children and adults, or whether small parenchymal hemorrhages were or were not included in the diagnostic groups. We conclude, then, that these systemic events (hypoxia and hypotension) may play an important role in the pathogenesis of diffuse brain swelling.

Mortality Rates

The literature, with one exception,[7] indicates that children with diffuse brain swelling carry a favorable prognosis.[1-3] Bruce, *et al.*,[2] reported a 12% mortality rate in children with diffuse brain swelling and GCS scores less than 8. Likewise, in a small series of severely head-injured children with diffuse brain swelling, Berger, *et al.*,[1] found that 75% had satisfactory outcomes, with only one death. In a series described by Cordobes, *et al.*,[3] all seven children with diffuse brain swelling were found to have favorable outcomes.

Perhaps the most striking finding in our study is the high mortality rate (53%) among children with diffuse brain swelling. This rate is appreciably higher than in most previously reported studies, but is in agreement with the study of Humphreys, *et al.*,[7] who found a mortality rate of 39% in their series of severely head-injured children with diffuse brain swelling. The addition of patients with diffuse brain swelling plus small parenchymal hemorrhages did not appreciably alter these results. A significant observation was that, of the children with diffuse brain swelling who died, 90% did so within 6 days of the accident.

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References

1. Berger MS, Pitts LH, Lovely M, et al: Outcome from severe head injury in children and adolescents. **J Neurosurg 62:**194–199, 1985
2. Bruce DA, Alavi A, Bilaniuk L, et al: Diffuse cerebral swelling following head injuries in children: the syndrome of "malignant brain edema." **J Neurosurg 54:**170–178, 1981
3. Cordobes F, Lobato RD, Rivas JJ, et al: Post-traumatic diffuse brain swelling: isolated or associated with cerebral axonal injury. Clinical course and intracranial pressure in 18 children. **Childs Nerv Syst 3:**235–238, 1987
4. Eisenberg HM, Gary HE Jr, Aldrich EF, et al: Initial CT findings in 753 patients with severe head injury. A report from the NIH Traumatic Coma Data Bank. **J Neurosurg 73:**688–698, 1990
5. Graham DI, Ford I, Adams JH, et al: Fatal head injury in children. **J Clin Pathol 42:**18–22, 1989
6. Hendrick EB, Harwood-Nash DCF, Hudson AR: Head injuries in children: a survey of 4465 consecutive cases at the Hospital for Sick Children, Toronto, Canada. **Clin Neurosurg 11:**46–65, 1964
7. Humphreys RP, Jaimovich R, Hendrick EB, et al: Severe head injuries in children, in Humphreys RP (ed): **Concepts in Pediatric Neurosurgery 4.** Basel: S Karger, 1983, pp 230–242
8. Kobayashi S, Nakazawa S, Yano M, et al: The value of intracranial pressure (ICP) measurement in acute severe head injury showing diffuse cerebral swelling, in Ishii S, Nagai H, Brock M (eds): **Intracranial Pressure V.** Berlin: Springer-Verlag, 1983, pp 527–531
9. Snoek JW, Minderhoud JM, Wilmink JT: Delayed deterioration following mild head injury in children. **Brain 107:**15–36, 1984
10. Teasdale E, Cardoso E, Galbraith S, et al: CT scan in severe diffuse head injury: physiological and clinical correlations. **J Neurol Neurosurg Psychiatry 47:**600–603, 1984
11. Teasdale G, Jennett B: Assessment of coma and impaired consciousness. A practical scale. **Lancet 2:**81–84, 1974
12. Zimmerman RA, Bilaniuk LT, Bruce D, et al: Computed tomography of pediatric head trauma: acute general cerebral swelling. **Radiology 126:**403–408, 1978
13. Zimmerman RA, Bilaniuk LT, Gennarelli T: Computed tomography of shearing injuries of the cerebral white matter. **Radiology 127:**393–396, 1979

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The TCDB Manual of Operations, which includes the TCDB data forms, is available from the National Technical Information Service (NTIS), United States Department of Commerce, 5285 Port Royal Road, Springfield, Virginia 22161 (NTIS Accession No. PB87 228060/AS).

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