SHORT REPORT

Post-traumatic epilepsy in children requiring inpatient rehabilitation following head injury

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Objective: To study the prevalence of, and identify possible risk factors for, the development of post-traumatic epilepsy in a cohort of children with severe head injury treated in an inpatient rehabilitation unit.
Methods: The hospital and community medical case notes of all children admitted prospectively to the unit and the records of the clinical EEG department over a seven year period were reviewed to identify those children who had developed late epilepsy after head injuries.
Results: 102 children received inpatient rehabilitation between 1 June 1991 and 28 February 1998. Follow up of these patients ranged from 18 months to over eight years. Nine patients (9%) developed post-traumatic epilepsy between eight months and over five years after the head injury. Three of the nine patients had experienced early tonic–clonic seizures in the first week after the injury. Other risk factors examined included the age of the patient, the cause of the head injury, initial Glasgow coma scale score, neuroimaging findings, and duration of ventilatory support. Only the presence of early seizures ($p = 0.002$) and possibly the Glasgow coma scale score ($p = 0.043$) were found to be specific risk factors for late late epilepsy.
Conclusions: Post-traumatic epilepsy appears to be uncommon, even in children with severe head injuries. Early seizures may indicate increased risk of developing late post-traumatic epilepsy in this study population.

Epilepsy is a well recognised though uncommon complication of traumatic brain injury in children. The true prevalence is difficult to determine because of the wide range of severity of head injuries and the heterogeneity of the paediatric populations previously reported. Thus there are inconsistencies about which specific risk factors have been linked to the development of late post-traumatic epilepsy. Our aim in this prospective study was to identify the prevalence of late post-traumatic epilepsy in a relatively homogeneous population of children with severe head injuries who had required inpatient rehabilitation.

METHODS

All children treated by a paediatric rehabilitation programme between 1 June 1991 and 28 February 1998 were followed up prospectively for the development of post-traumatic epilepsy. Data collection ended on 31 August 2000, with the follow up period ranging from two and a half years to nine years.

At this children's hospital all children who require admission after a head injury are admitted to either the paediatric intensive care unit (PICU) or to a general surgical or orthopaedic ward, depending on their injuries. The specific management of children with traumatic brain injury on the PICU is dependent on the individual child. There were no significant changes in the general or specific management of children with traumatic brain injury during the study period. Criteria for referral of children with a head injury to the head injury rehabilitation team include all children admitted to the PICU irrespective of the severity of their injury or their neurological status, and all children admitted to a surgical or orthopaedic ward who, 24 hours after admission, showed any neurological symptoms or signs. All children referred to the rehabilitation team were assessed within 48 hours by one consultant paediatric neurologist (REA), who subsequently decided whether the child required inpatient rehabilitation or could be discharged. All children who received inpatient rehabilitation did so for a minimum period of two weeks.

The only classification used to grade the severity of the head injury was the Glasgow coma scale (GCS).

The diagnosis of epilepsy was determined from a review of the medical case notes of all the children admitted with a head injury, the hospital's clinical electroencephalography (EEG) department, and the community child health departmental records. General practitioner records were not reviewed because it was considered unlikely that a GP would diagnose epilepsy in a child without first referring the child to a paediatrician or paediatric neurologist to confirm the diagnosis. The diagnosis of post-traumatic epilepsy was established on the basis of a witnessed account of a minimum of two or more unprovoked complex partial or tonic–clonic seizures.

Electroencephalography was undertaken in the waking state at the time of the clinical diagnosis of post-traumatic epilepsy, with a Schwartzer ED 24 channel machine using the international 10–20 electrode placement. EEGs were not undertaken routinely in those patients who did not develop post-traumatic epilepsy during the follow up period.

Magnetic resonance imaging (MRI) was undertaken using a 0.5 Tesla Philips Gyroscan NT-5 scanner, with axial and coronal views employing T1, T2, and FLAIR sequences.

RESULTS

In all, 262 children admitted to the hospital with a head injury were referred to the rehabilitation team during the period June 1991 to February 1998; this represented 26% of all children admitted with head injuries during that period. Of these 262 patients, 160 required no rehabilitation. To our knowledge, none of those 160 children had been diagnosed with epilepsy at the time of completion of data collection in August 2000, and with follow up periods ranging from 1.9 to 7.5 years. The children's head injury rehabilitation team treated and subsequently followed up 102 children aged 1.3 to 15.2 years during the study period. The follow up period of these children ranged from 19 months to seven years, with a median of approximately four years. Ninety (88%) of these 102 patients had been admitted to the PICU, 87 of whom had required mechanical ventilation.

At the termination of data collection (August 2000), nine children (9%) had developed post-traumatic epilepsy. Three other children had been diagnosed as having epilepsy before their admission, but only one (with childhood onset typical

Table 1 Demographic and seizure details of the nine patients who developed post-traumatic epilepsy

Patient	Age of patient at HI (years)	Time between HI and onset of PTE (years)	Seizure type	Neurological findings at onset of epilepsy
1 (M)	13.6	1.3	CP; SGTC	ST; dys; LD (mod)
2 (F)	6.5	0.7	CP	H; LD (mild)
3 (M)	9.9	5.1	CP; SGTC	H; LD (mod)
4 (F)	10.3	2.8	CP; SGTC	H
5 (F)	1.3	2.9	CP	N; (BD)*
6 (M)	13.2	2.8	CP; SGTC	N
7 (M)	12.3	5.2	SPS; CP	N; (BD)*
8 (M)	7.1	3.9	SPS; CP; SGTC	H; LD (mod); BD*
9 (M)	8.5	4.3	CP; SGTC	N; LD (mild)

*Behaviour difficulties: emotional lability, aggression, impulsivity and disinhibition.
BD, behaviour difficulties; CP, complex partial; dys; dysphasia; F, female; H, hemiplegia; HI, head injury; LD, learning difficulties; M, male; N, normal neurological examination; PTE, post-traumatic epilepsy; SGTC, secondarily generalised tonic–clonic; SPS, simple partial sensory; ST, spastic tetraplegia.

absence epilepsy) had been started on treatment before the head injury. These three children were excluded from further analysis. The first recognised post-traumatic seizure in the nine patients had occurred between eight months and over five years after the head injury (median 2.9, mean 3.2 years). Post-traumatic epilepsy was diagnosed between two and five months after the onset of seizures. The demographic features, age at diagnosis of post-traumatic epilepsy, and seizure type in the nine patients are shown in table 1. None of these patients had a family history of epilepsy.

Electroencephalography undertaken in the nine children at the time of diagnosis of post-traumatic epilepsy and before starting antiepileptic treatment showed focal abnormalities in six (spikes, sharp or slow waves), generalised slow wave activity in one, and no abnormality in the remaining two patients. Five of the nine patients have been seizure-free for at least 12 months on either carbamazepine or lamotrigine monotherapy; one patient on carbamazepine monotherapy and one on topiramate monotherapy showed a reduction in seizures but have not yet achieved a seizure-free period of six months. The parents of the remaining child declined treatment.

In the nine patients with post-traumatic epilepsy, MRI showed focal or multifocal areas of gliosis or infarction in four and three patients, respectively, and was normal in two.

The definition of early post-traumatic seizures is not consistent, with some studies defining this as a seizure occurring within the first week after the injury, while others exclude seizures that occur in the first hour after the injury. In our study, 10 children (10%) had a tonic–clonic seizure within the first week following the head injury, and two within "minutes" after the injury. Excluding these latter two patients, eight patients (8%) therefore experienced early post-traumatic seizures. Of these eight children, three (37%) subsequently developed post-traumatic epilepsy. Only one patient was observed to have experienced two seizures in the first week after the injury. Another child who had a tonic–clonic seizure in the first week after the head injury was already receiving sodium valproate for childhood absence epilepsy. The two patients who had seizures within "minutes" of their head injury had not developed post-traumatic epilepsy at the end of follow up.

Excluding the 10 children with definite early tonic–clonic seizures, 15 more patients were thought to have had possible epileptic seizures in the first week after the head injury. Three of these had episodes of "stiffening" which may have represented decerebrate posturing, and 12 had paroxysmal autonomic changes, manifested by sudden changes in blood pressure or heart rate, a reduction in arterial or transcutaneous oxygen saturation, episodes of skin flushing, or pupillary changes. No rhythmic clonic movements were seen to accompany any of these autonomic features, although five patients were receiving paralysing or sedating drugs at the time of the observed changes. Cerebral function monitoring was not available in this hospital's PICU. Thirteen of the 15 patients underwent 16 channel EEG recording, but in no case did this capture a clinical event. Non-specific abnormalities were seen in 10 of the 13 children. None of the 15 patients had developed post-traumatic epilepsy at the end of the study, and these patients have been excluded from further analysis.

The eight patients who had definite epileptic seizures in the first week after the head injury were treated with phenytoin for periods varying between five and 28 days. Eight of the 15 patients with possible seizures also received phenytoin for between three and 10 days. None of the nine patients with post-traumatic epilepsy was receiving an antiepileptic drug when epilepsy was diagnosed.

Statistical analysis

The effect of various factors on the likelihood of developing post-traumatic epilepsy was assessed univariately using Kaplan–Meier survival and log-rank tests. These factors included the child's sex and age (under nine *v* over nine years of age), the child's GCS score in the local accident and emergency department (3–8 *v* 9–14), whether the child had a seizure within the first week (an early seizure *v* no seizure), the duration of ventilatory support (0 days, 1–3 days, and over 3 days), and the results of the initial computed tomography of the head (definite abnormalities *v* no/equivocal abnormalities). The only factors found to be related to the development of post-traumatic epilepsy were the presence of early seizures ($p = 0.002$) and the GCS score ($p = 0.043$), though the latter was of marginal significance. A Cox proportionate hazards regression analysis was not undertaken because of the small number of patients in the study population.

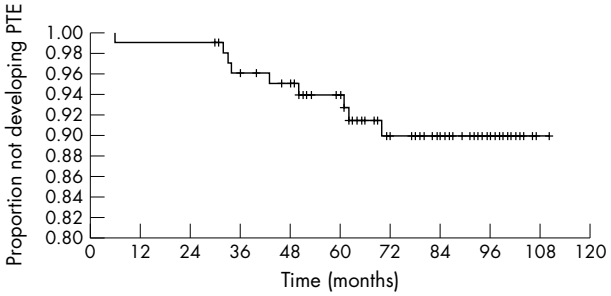

Figure 1 Cumulative proportion of children not developing post-traumatic epilepsy over 108 months. Dashes indicate censored cases. The number of children included at the various time intervals shown on the graph were as follows: 12 and 24 months, n=102; 36 months, n=94; 48 months, n=90; 60 months, n=78; 72 months, n=53; 84 months, n=35; 96 months, n=16; 108 months, n=1.

The effect of post-traumatic amnesia on the development of epilepsy was not assessed because of the relatively young age range of the study population and also because this specific information was rarely recorded. Similarly, the absence of EEG data in most of the children precluded an analysis of any correlation between early EEG findings and the risk of developing post-traumatic epilepsy.

The cumulative proportion of children who did not develop post-traumatic epilepsy over time is shown in fig 1.

DISCUSSION

Post-traumatic epilepsy is a well recognised though uncommon complication of head injury in children.[1 2] The precise incidence is unclear because reports vary depending on the demographics of the population studied, the severity of the injury, whether rehabilitation was required, and the length of follow up after the injury. Although over 25 years old, the largest study yet published reported an overall incidence of 5% in 1000 head injured children and adults, with the risk varying between 1% and 60%.[3] A more recent study of 318 children with "substantial" head injuries, aged one month to 17 years at the time of the injury, reported an incidence of 21%.[4]

The present survey was clearly highly selective, studying children who were referred to and treated by a head injury rehabilitation team. Of the 262 children initially referred to the team, only nine (3.5%, or 9% of the 102 children subsequently treated by the rehabilitation team) developed post-traumatic epilepsy. Although it is difficult and arguably even inappropriate to compare the results of this study with those of previous studies, as any comparisons are unlikely to be between similar populations, the overall rate of post-traumatic epilepsy in our study appears similar to that in previous paediatric studies, which reported overall rates of 9%[5] and 9.8%.[6] In addition, the 9.4% incidence of post-traumatic epilepsy in a population of 351 patients admitted to an adult head injury rehabilitation unit[7] is almost identical to the 9% of our 102 patients who were admitted to a paediatric brain injury rehabilitation unit. Other studies have reported both lower[8 9] and considerably higher rates of post-traumatic epilepsy,[4] discrepancies that could also be explained by the severity of the head injuries in the different study populations, the accuracy of the diagnosis of epilepsy (particularly in children with additional learning and behavioural problems), the extent of case ascertainment at follow up, and the duration of follow up.

The mean latency of the development of post-traumatic epilepsy in the nine children was 3.2 years, with two patients developing epilepsy over five years after their head injury. A longer period of follow up might allow more affected children to be identified, but most patients develop the condition by the end of the second year after their injury.

Approximately 8% of our patients experienced early seizures. This figure is higher than previous reports of 4.2%[8] and 4.8%,[9] but much lower than rates of between 9% and 19.8% reported in other studies.[2 5 6 10–12] There could be many reasons for such a discrepancy, including incorrect identification of seizures (versus decerebrate posturing or other involuntary movements), the possible inclusion of patients with less[8 9] or more[4] severe brain injuries than our own population, and patients whose seizures may have been diagnosed on purely electrophysiological and not clinical criteria. Unfortunately this information was not always available.[4] It is also possible that some of the studies reporting higher rates of early seizures may have included patients with immediate seizures, as reported in the study by Chiaretti *et al*,[10] where 10 of the 15 patients with early seizures (occurring in the first week after the injury) had experienced their seizures "within the first 24 hours."

The only specific risk factor that was clearly correlated with (and therefore could predict) the development of post-traumatic epilepsy was an early seizure occurring within the first week after the head injury. The GCS score on admission appeared to show a less marked correlation with post-traumatic epilepsy. The absence of any other risk factor may reflect the relatively small number of patients studied. Three of the nine children (33%) experienced early epileptic seizures within the first week after their head injury—similar to the 41% incidence of late post-traumatic epilepsy following early seizures in the study by Kieslich and Jacobi.[4] However, an earlier population based study showed no correlation between early and late seizures in children, although in adults with moderate or severe (but not mild) head injuries, early seizures were identified as a risk factor in predicting post-traumatic epilepsy.[12] Clearly, a larger study with a longer follow up period could confirm or refute our findings.

Finally, although it has not been possible to comment on the potential value of the EEG in predicting the development of post-traumatic epilepsy, because EEGs were not done routinely in these children following their head injury, one must question the value of undertaking "routine" EEGs in this situation. The heterogeneity of the study population (including the age of the patient and severity of head injury) and the variability in the timing of the EEG after the injury will both make the investigation less useful. An additional complicating factor may be the difficulty in successfully recording and interpreting EEGs in children who may be agitated and confused following their injury.

One would perhaps have expected that more patients would have developed post-traumatic epilepsy because of the severity of their head injuries. Such a trend may have been offset by the small number of children who suffered missile injuries, depressed skull fractures, or subdural haematomas requiring neurosurgical intervention—three of the most common risk factors associated with post-traumatic epilepsy.

An important finding in our study was the number of children who were considered to have experienced epileptic seizures while on the PICU, specifically on the basis of sudden changes in autonomic function without any accompanying abnormal movements. Although autonomic changes may reflect epileptic activity, particularly in the sedated or paralysed patient, there should be caution in ascribing such features to epileptic seizures in the non-sedated and non-paralysed patient. Unfortunately, none of these patients had an EEG recorded during one of the stiffening or "autonomic" episodes and therefore epileptic seizures cannot be wholly excluded. Finally, none of the 15 patients who were considered to have had epileptic seizures on the basis of either "stiffening" episodes or autonomic phenomena had been diagnosed with post-traumatic epilepsy at the end of the study. As far as we are aware this phenomenon has not been noted previously in studies of traumatic brain injury and epilepsy.

At least three of the children in this study were prescribed phenytoin because of decerebrate posturing; a further five children may also have been inappropriately treated with this drug on the basis of purely autonomic changes. A specific problem with using phenytoin in this situation is that it can cause acute dyskinesias,[13] which may further confuse the clinical picture and be misdiagnosed as epileptic seizures. There is no evidence that phenytoin (or any other antiepileptic drug) used prophylactically after head trauma prevents or reduces the risk of the development of late post-traumatic epilepsy,[14] although there is some evidence that prophylactic phenytoin may reduce early post-traumatic seizures.[6] There should therefore be a high threshold for using this drug in the first week after head trauma, and arguably it should only be used for immediate and repeated tonic–clonic seizures occurring within the first 24 to 48 hours.[6 14]

Conclusions

Post-traumatic epilepsy appeared to be an uncommon complication of severe head injuries in this highly selected

population. Although early seizures and possibly a low GCS score on admission (< 8) seemed to be specifically associated with an increased risk of developing late epilepsy, no other risk factors were identified.

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