Abstract

Objective
Existing clinical decision rules (CDR) guide management for head injured children presenting ≤24 hours following injury, even though some may present >24 hours. We sought to determine the prevalence of traumatic brain injuries (TBI) presenting to emergency departments >24 hours and identify symptoms/signs to guide management.

Methods
Planned secondary analysis of the Australasian Paediatric Head Injury Rule Study concentrating on first presentations >24 hours following injury with GCS 14 and 15. We sought associations with predictors of TBI on computed tomography (TBI-on-CT) and clinically important traumatic brain injury (ciTBI).

Results
Of 19,765 eligible children, 981 (5.0%) presented >24 hours after injury, 465 (48.5%) resulting from falls <1 meter, 37 (3.8%) involved traffic incidents. Features associated significantly with presenting >24 hours in comparison with ≤24 hours were non-frontal scalp hematoma (20.8% vs 18.1%), headache (31.6% vs 19.9%), vomiting (30.0% vs 16.3%)) and assault with non-accidental injury concerns (1.4% vs 0.4%).

TBI-on-CT occurred in 37 (3.8%) including suspicion of depressed skull fracture (8 (0.8%)) and intracranial hemorrhage (31 (3.8%)). ciTBI occurred in 8 (0.8%) with 2 (0.2%) requiring neurosurgery with no deaths.

Suspicion of depressed skull fracture was associated with TBI-on-CT consistently with the only other significant factor being non-frontal scalp hematoma (OR 19.0, 8.2-43.9 95%CI) ciTBI was also associated with non-frontal scalp hematoma (OR 11.7, 2.4-58.6, 95%CI) and suspicion of depressed fracture (OR 19.7, 2.1-182.1 95%CI).

Conclusion
Delayed presentation following head injury, whilst infrequent, is significantly associated with TBI. Evaluation of delayed presentations must consider identified factors associated with this increased risk.

INTRODUCTION

Mild blunt head injuries in children is a common reason for presentation to emergency departments (EDs) worldwide (1). The majority of children present to hospital ≤24 hours after injury but there is a subset of children who present >24 hours after injury either with persistent or worsening head injury symptoms, symptoms of other injuries or as caregivers discover a scalp hematoma made more prominent with edema and liquefaction (2, 3).

The prevalence of traumatic brain injury (TBI) in children who sustain head injury (4-7) has been described in studies to derive clinical decision rules (CDRs) to guide the use of cranial CT scanning. Both the Pediatric Emergency Care Applied Research Network (PECARN) (4) and the Canadian Assessment of Tomography for Childhood Head Injury (CATCH) (5) CDRs specifically excluded children with head injury who presented > 24 hours after injury. The Children's Head Injury Algorithm for the Prediction of Important Clinical Events (CHALICE) (6) CDR had no exclusions except failure to consent but no data on the significance of delayed presentations has been published.

The most concerning complication of minor head injuries is the delayed or missed diagnosis of complicated skull fractures or intracranial injury, especially those that require intervention. Delayed hemorrhage may result from slow venous bleeding, blood dyscrasias and coagulation disorders (1). In adults, the available low-quality studies suggest delayed presentations have lower rates of intracranial injury (8-12) and yet account for 15% of cranial CTs undertaken. In addition, there is little evidence on how existing CDRs can be applied to this cohort of patients (9). In children <2 years old, retrospective studies have suggested that intracranial hemorrhage in delayed presentations occur at a similar rate to those presenting ≤24 hours after the head injury (3) although additional work-up for non-accidental injury may

still be required (2). A retrospective review of children presenting >6 hours post injury suggested that intracranial hemorrhage was rare in this cohort (1).

We aimed to determine the prevalence of Traumatic Brain Injury on CT scan (TBI-on-CT) and clinically important TBI (ciTBI) in children presenting >24 hours following a minor head injury. We also sought to determine which variables from previously published high quality CDRs (4-6) may increase the risk of these outcomes in order to assist clinicians to better identify those patients likely to require cranial CT scan or observation in hospital.

METHODS

Study design

This was a planned secondary analysis of the Australasian Paediatric Head Injury Rule Study (APHIRST) cohort (7), where all published rule-specific predictor and outcome variables for PECARN (4), CATCH (5) and CHALICE (6) CDRs were collected, with the primary outcome in the parent study of determining diagnostic accuracy (sensitivity, specificity, negative predictive value and positive predictive value) for each of the CDRs.

Treating clinicians enrolled patients presenting with a history of head injury and recorded prospective data on the ED presentation. There was no attempt to influence the clinician's management including undertaking a CT scan for the evaluation of the patients. Patients were enrolled by the treating ED clinician who then collected predictive clinical data prior to any neuroimaging on a paper-based CRF. The site research assistant recorded ED and hospital management data after the visit and conducted a telephone follow-up for patients who had not undergone neuroimaging (13).

The institutional ethics committees at each participating site approved the study. Informed verbal consent was obtained from parents/guardians, apart from instances of significant life threatening or fatal injuries, where participating ethics committees granted a waiver of consent. The trial protocol (13) was developed by the study investigators and was registered with the Australian New Zealand Clinical Trials Registry (ANZCTR) ACTRN12614000463673.

Setting

Ten paediatric EDs in Australia and New Zealand associated with the Paediatric Research in Emergency Department International Collaborative (PREDICT) research network (14) recruited patients in the study.

Population

Children younger than 18 years with head injury of any severity presenting to the participating EDs between April 2011 and November 2014.

Data Collection

In this planned sub-analysis, we compared the cohort of children who presented >24 hours post head injury with those that presented ≤24 hours. We excluded from the analysis children with GCS <14 as decision making regarding CT scanning and management is not controversial. Re-presentations for the same injury were also excluded to determine factors in a de novo presentation rather than deterioration following an earlier assessment.

We used the definition of TBI-on-CT of intracranial haemorrhage/contusion, cerebral oedema, traumatic infarction, diffuse axonal injury, shearing injury, sigmoid sinus

thrombosis, signs of brain herniation, midline shift, diastasis of the skull, pneumocephalus and depressed skull fracture. CiTBI was defined as death, intubation >24 hours, neurosurgery (intracranial pressure monitoring, craniotomy, haematoma evacuation, elevation of depressed skull fracture, dura repair, tissue debridement and lobectomy) or TBI-related hospital admission of 2 or more nights as per the PECARN study (15). We determined to describe the children presenting >24 hours of injury as clinicians report uncertainty in management decisions with these delayed presentations.

Outcomes

We report demographics including age, gender, vomiting, any loss of consciousness (LOC), headache, any amnesia, seizure, non-accidental injury (NAI) concern, altered mental state such as drowsiness and/or abnormal GCS, examination features suggestive of depressed skull fracture, abnormal neurological examination and the presence of a non-frontal scalp hematoma. NAI concern was determined by the treating clinician at the time of ED assessment who recorded this concern on the paper-based case report form (CRF) at the time of assessment.

Statistical Analysis

We tested associations between the delay in presentation and injury mechanisms; falls (<1, 1-1.5, 1.5-3 and >3 meters); road traffic incident (either as pedestrian, cyclist or occupant of a vehicle) and high-speed injury from a projectile or object, all of which have previously demonstrated to be predictors of increased risk of TBI (4). Low-impact mechanisms were defined as mechanisms not meeting the PECARN CDRs' definition of severe mechanisms; motor vehicle accident with patient ejection, death of another passenger, rollover; pedestrian

or cyclist without helmet struck by vehicle; falls >1 meter (<2 years) or >1.5 meters (>2 years) or being struck by high-impact object.

CRF data were subsequently entered into Epidata (The Epidata Association, Odense, Denmark (16)), and later REDCap hosted at Murdoch Childrens Research Institute (17), and analysed using Stata 13 (Statacorp, College Station, Texas, USA). Descriptive statistics were calculated for key variables with 95% confidence intervals (CI) where relevant. Comparisons of demographic and injury characteristics between those presenting ≤ and >24 hours were carried, and percentage differences (with 95% confidence intervals) presented. Associations between clinical predictors and outcomes between those presenting to ED ≤ and > 24 hours following a head injury were analysed by odds ratios and 95% CI. Multiple logistic regression analyses were undertaken, but as many predictors and outcomes were rarer in frequency, assumptions of cell sizes were violated. Exact methods for multiple logistic regressions were also explored but did not add information beyond bivariate analyses. Variables included in the bivariate analyses were determined through analysis of those with significant differences in those presenting >24 hours; vomiting, headache, known or suspected LOC at time of injury, any amnesia, suspicion of depressed skull fracture and non-frontal scalp hematoma.

RESULTS

The original study (7) included 20,137 head injury presentations. The present study excluded 352 cases with GCS <14, and a further 20 with unknown time to presentation (Figure 1). Of the 19,765 novel presentations of children enrolled in the APHIRST cohort study meeting our inclusion criteria, 981 (5.0%) presented >24 hours after injury, with 386 (39.4%) being female and 277 (28.3%) being <2 years (Table 1). Four hundred and sixty-five (48.5%, 45.3-

51.7 95% CI) resulted from falls <1 meter compared with 9,333 (50.8%, 50.1-51.5 95% CI) presenting ≤ 24 hours following a fall <1 meter. A road traffic incident occurred in 37 (3.8%, 2.6-5.0 95%CI) compared with 1038 (5.5%, 5.2-5.9 95% CI) presenting ≤24 hours. Head CTs were undertaken in 213 (21.7%, 95% CI 19.1-24.3%) children presenting >24 hours and 1606 (8.6%, 95%CI 8.2-9.0%) in children presenting ≤24 hours.

Those presenting >24 hours were significantly more likely than those presenting ≤24 hours to display the following features at any time between the injury and presentation (respectively): non-frontal scalp hematoma (20.8% vs 18.1%), headache (31.6% vs 19.9%), any vomiting (30.0% vs 16.3%) and assault with NAI concerns (1.4% vs 0.4%) (Table 1). Loss of consciousness (LOC) (13.5% vs 14.3%) and amnesia (6.3% vs 8.2%) were significantly more likely to occur in those presenting ≤24 hours after injury (Table 1).

Thirty-seven of 981 children had a TBI-on-CT as defined by PECARN (3.8%, 2.6–5.0 95% CI) with an odds ratio (OR) of 3.1 (2.2-4.4, 95% CI) when compared with presentations ≤24 hours after injury (Table 2). The commonest injuries were depressed skull fracture (8 (0.8%, 0.4-1.67 95% CI)) and intracranial hemorrhage/contusions (31 (3.2%, 2.2-4.5 95% CI)) (Table 3). CiTBI occurred in 8 children (0.8%, 0.4-1.6, 95% CI, OR 1.0 (0.5-2.0, 95% CI) with 2 (0.2%, 0.0-0.5 95% CI) requiring neurosurgical interventions. The clinical synopses of these 8 children with ciTBI are presented in Table 4 and highlight variables present in published CDRs at the time of the delayed presentation. There were no deaths or intubations >24 hours due to head injury in the delayed presentation cohort.

Bivariate analysis demonstrated significant variables associated with TBI-on-CT in delayed presentations with 30 children with non-frontal scalp hematoma being positive for TBI-on-

CT (OR 19.0, 8.2-43.9, 95% CI) (Table 5). All 8 cases with suspicion of depressed skull fracture were positive for TBI-on-CT and as such were not included in the bivariate analysis. No cases of children with amnesia were positive for TBI-on-CT. Suspicion of depressed fracture (OR 19.6, 0.0-143.5, 95% CI) and non-frontal scalp hematoma (OR 11.7, 2.4-58.6, 95% CI), were also significantly associated with ciTBI (Table 5). In children with LOC or amnesia there were no instances of ciTBI.

Limitations

In the original study CT scans were obtained on a minority of patients; it would have been unethical to obtain CT scans on patients the clinicians did not think required them. However, the benefit of this observational study, with extensive follow-up, allowed unexpected consequences of the head injury to be detected after discharge from hospital without CT scanning. In the parent study 5,203 of 29,433 (17.6%) were missed for inclusion. There is potential that delayed presentations were among those missed, resulting in selection bias, however, the size of the screened cohort and the inclusion of all Australasian tertiary paediatric centres as study sites makes it unlikely that serious adverse events in patients with delayed presentations were missed. Patients who presented with a head injury >24 hours who had isolated symptoms (such as vomiting or headache) may have been missed due to the treating clinician determining an alternate diagnosis, however, at every site the RAs reviewed these cases with the site investigator to determine if those patients constituted a missed recruitment. The decision to undertake CT scanning was a clinician decision with no information recorded to indicate why there was a higher CT rate in the delayed presentation, however, there is little guidance for clinicians as current CDRs do not address management in delayed presentations. The CT rate implies either that early presentations may be associated with minor mechanisms with minimal symptoms/signs or alternatively that clinicians have

greater suspicion of ciTBI in delayed presentations due to persistence of symptoms. We could not assess clustering of recruitment by ED clinicians at individual sites because the names of individual clinicians were not collected.

We report both TBI-on-CT and ciTBI as per the PECARN CDR outcomes which are well published and renowned methods determining the requirement for imaging head injured children. It is recognised that certain TBI-on-CT outcomes (such as an intracranial hemorrhage) while not necessarily requiring interventions as required for the definition of ciTBI, may still have significant implications for a child, particularly in relation to the advice on return to sport.

We focussed on the first presentation to the study EDs for the head injury and have not reported data on children representing to the ED after previous medical assessment as this implies an evolution of the head injury. We have concentrated in this study on assessing factors in children whose caregivers did not seek medical attention about the injury until >24 hours. As a consequence, we cannot determine if at the time of the injury there were predictor variables for neuro-imaging or admission present. Some children may have presented to other health care settings or non-study EDs prior to assessment at a study ED; these patients were included in this study if they had not had CT scans obtained elsewhere prior to arrival.

Finally, the patients reflect an Australian and New Zealand cohort with a bias towards tertiary children's hospitals where the neuroimaging rate is lower than reported from US studies (18). While it is possible that the data collection of CDR predictor variables influenced the CT ordering practice of the ED clinicians involved in the study, data on a large number of predictor variables were collected and for each data point a range of response options were

elicited, which would likely have limited influence on decision making of clinicians. In addition, based on a clinician survey prior to the study no specific head injury rules had been incorporated into clinical practice or practice guidelines in Australia and New Zealand (19).

DISCUSSION

In this large prospective observational study, we have demonstrated that 5% of children with minor head injuries present to ED >24 hours after the injury and have a significantly higher rate of CT scanning than children presenting ≤24 hours. Most of these head injuries occurred following low-impact falls (such as falls <1 meter) and the majority who sustained a ciTBI in this delayed presentation cohort were in this category. This indicates a need for vigilance in assessing and managing these patients in ED, as evidenced by the higher CT rate. Symptoms/signs more frequently present in delayed rather than early presentations were non-frontal scalp hematoma, headache, any vomiting and assault with NAI concerns. These features have face validity and are easily assessed prompting clinicians to raise their concern for TBI, which will assist the clinician to determine the need for further investigation or observation. The features significantly associated with TBI-on-CT and ciTBI (suspicion of depressed skull fracture and non-frontal scalp hematoma) have been identified for the first time and these results will guide clinicians to evaluating these suspicions promptly with a CT scan.

In this study we could not determine why the patients were delayed in presenting to ED and we were specifically not evaluating patients re-presenting to the ED due to evolution of symptoms of head injury. Symptoms that may prompt a child to be brought to ED >24 hours appear to be similar to those listed in head injury advice sheets provided to families presenting within 24 hours with a child with a head injury (20). These include features such

as persistent headache and vomiting. In this study the odds ratios for the presence of vomiting and headache in those with delayed presentations did not reach statistical significance. It reinforces that the clinician attempting to differentiate the likely risk of a significant head injury in a child with a reported minor head injury who has vomiting (that may or may not be associated with an intercurrent gastroenteritis) should evaluate these patients carefully for the significant factors of altered consciousness, suspicion of depressed fracture or presence of non-frontal scalp hematoma. We did not limit recruitment to a specified time-period from the injury and did not assess persistent headache in the setting of post-concussion syndrome in this study, however, headache was not significantly associated with TBI-on-CT or ciTBI.

In adult populations, delayed presentations in head injury has only been studied in a retrospective manner (9-11, 21). Although results from these cohort studies reveal co-morbidities and risks in the adult population the presence of significant injury is at best equal to or even slightly less than when presentation is not delayed. Unfortunately, in these studies the definition of delayed presentation is heterogeneous ranging from 4 hours to > 24 hours, and further hampers comparison with our prospective cohort of children.

Although clinicians reported their concern for NAI we did not, in this particular study, further evaluate if the clinician's NAI concerns were confirmed. One of the traditional historical associations with NAI relates to delay in presentation and this may contribute to the higher CT rate in our delayed cohort. This study expands on recent publications by Sellin et al and Gelernter et al on the delayed presentation in children <2 years concentrating on the detection of NAI (2, 3). Sellin demonstrated that isolated scalp swelling with non-focal examination findings had excellent prognosis and may not require radiology or neurosurgical interventions

(while still emphasizing the need for full evaluation of non-accidental injury). Gelernter also demonstrated similar rates of abnormal CT findings between presentations ≤ and >24 hours but their study specifically only included children who had already received CTs thus rendering this retrospective data less generalizable.

In this study we have described the variables associated with increased risk of significant injury when a child presents >24 hours after a head injury. The current published CDRs (4-6) were not designed to provide guidance on the application of the rules in children who present >24 hours after injury. There have been no other studies that have reported a prospective collection of outcomes in this cohort. Presenting >24 hours after injury with a GCS ≥14 does significantly increase the risk of a TBI-on-CT (OR 3.1), which may require neurosurgical management, prolonged hospitalization or intubation >24 hours. The presence of certain variables (including suspicion of depressed fracture and non-frontal scalp hematoma) have been demonstrated to increase the risk of TBI-on-CT and ciTBI in delayed presentations and clinicians should base their management decisions around CT scans use on these increased risks.

One of the strengths of this study is that this is the first large prospective cohort study in children to determine the rate and pattern of delayed presentations in head injury. The PECARN and CATCH rules do not address this and the CHALICE study outcomes for the delayed presentation cohort was not reported. The eight children who did develop ciTBI in our cohort all had CDR predictor variables at their delayed presentation. As such we have been able to report predictor variables that should be strongly considered in delayed presentations and should influence the need for imaging or prolonged observation.

Summary

Delayed presentation >24 hours after head injury in children, whilst infrequent, may be significantly associated with TBI. Factors associated with TBI include suspicion for depressed skull fracture and non-frontal scalp hematoma. Treating clinicians should evaluate and manage delayed presentations outside of the current head injury clinical decision rule parameters, as these rules have not been validated for this subset of patients.

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