Original Paper

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Role of Apnea in Nonaccidental Head Injury

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Key Words
Apnea
Shaken baby syndrome
Impact injury
Child abuse
Diffuse brain swelling
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Subdural hemorrhage
Retinal hemorrhage

Abstract
We hypothesize that apnea induced by shaking or by shaking combined with impact plays a major role in the pathophysiology of nonaccidental head trauma and accounts for the poor outcome in this subgroup of patients. In a retrospective study of 28 children who suffered significant nonaccidental head injury, 57% had a history of apnea prior to hospitalization, 82% were intubated upon admission, and 71% had early seizures. For further evidence of ischemia and hypoxia, the first recorded blood pressure was <80 in 50% and the arterial pH <7.3 in 54%. Seventy-one percent had diffuse brain swelling which is characteristic of cerebral hypoxia and/or ischemia on the first CT scan. None of the children who had clinical evidence of cerebral hypoxia or ischemia had a good outcome. We conclude that trauma-induced apnea causes cerebral hypoxia and/or ischemia which is more fundamental to outcome than the mechanism of injury (shaken vs. shaken with impact), subdural hemorrhage, subarachnoid hemorrhage, diffuse axonal injury, parenchymal shear, or brain contusion.

Introduction

Severe nonaccidental head injuries in children have a poor prognosis [1]. Twenty years ago, Caffey [2] coined the term 'whiplash shaken baby syndrome' (SBS) to describe infants presenting with retinal hemorrhages, subdural or subarachnoid hemorrhages, and minimal or no signs of external trauma. The pathophysiology of the injury is not well understood because the injury is seldom witnessed, but shaking has been accepted as the most probable mechanism of injury [3]. Presumably, forceful, to-and-fro, shaking movements of the relatively large, poorly supported infant head cause intracranial and retinal hemorrhage by tearing the veins which bridge the subdural/subarachnoid spaces and the vascular attachments of the retina. Retinal hemorrhages are seldom seen in accidental head injury, and only with tremendous impact and rotational forces [4]. Duhaime et al. [5] provide convincing clinical and experimental evidence that sudden traumatic cranial impact plays a more pivotal role than shaking in the pathogenesis of SBS. In their study, vigorous shaking of a doll model could not reproduce the forces which result in subdural/subarachnoid hemorrhage in an animal model [6]. Only by striking the doll against an immobile surface could the injury forces be reproduced. Citing the lack of external signs of injury in SBS, other authors contend that severe head injuries can occur from shaking alone [7, 8, and L. Rorke, per. commun.].

Whether shaken alone or shaken with impact, abused children with severe head injury suffer high mortality and morbidity. Since a history of apnea prior to hospitalization has been common in our anecdotal experience and

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Table 1. Stratification of Glasgow Coma Scores

GCS	Shaken	Impact
3–8	5	7
9–12	3	5
13–15	5	3

Table 2. Clinical correlates and outcome

	Shaken	Impact
Skeletal fractures	8	10
Subarachnoid hemorrhage	7	10
Subdural hemorrhage	13	12
Cerebral contusion	2	4
Diffuse brain swelling	8	11
Intraventricular hemorrhage	1	3
Apnea[1]	8	8
Intubated on admission	10	13
Early seizure (with 24 h injury)	9	11
Retinal hemorrhage	11	10
Glasgow Coma Score (mean = median)	10	9
Outcome		
Good	5	4
Moderate	1	6
Severe or dead	7	5

[1] Abnormal or stopped breathing prior to hospitalization.

because early hypoxia-ischemia is predictive of a poor outcome in other head-injured patients [8], we hypothesized that trauma-induced apnea causes cerebral hypoxia and/or ischemia which is more fundamental to outcome than the mechanism of injury (shaken vs. shaken-impact), subdural hemorrhage (SDH), subarachnoid hemorrhage (SAH), diffuse axonal injury (DAI), parenchymal shear, brain contusion, or diffuse brain swelling (DBS).

Methods

A retrospective review of medical records and radiologic imaging studies was performed on 75 children admitted to the Children's Hospital with a presumptive diagnosis of child abuse. Twenty-eight children with a confirmed diagnosis of child abuse with central nervous system (CNS) injury were divided into two event groups: (1) *shaken-impact group* with physical signs of impact injury (in 1 infant occipital bruising was discovered only at autopsy) and/or a skull fracture and (2) *a shaken group* without evidence of direct trauma (craniofacial bruising or swelling) to the head and neck. The neuroimaging and clinical findings which focus on the role of apnea for these two groups were compared. Demographic information and medical background including age, sex, clinical presentation, hospital course, and outcome were reviewed. Postresuscitation Glasgow Coma Scores were modified for the examination of children [9]. In order to study the relationship between the comparison groups (shaken vs. shaken-impact) and specific radiographic and clinical parameters, two-way tables were constructed and independence was tested, using Fisher's exact test when the measure was categorical and a Cochran-Mantel-Haenszel test when the measure was ordinal. A significant relationship was defined as $p < 0.05$.

Results

Patient Population

Of the original 75 children studied, child abuse with significant head injury was confirmed in 28 children. Forty-seven were discarded because they lacked a central nervous injury, had insufficient records or imaging studies, or had pre-existing neurologic deficits. Twenty-one (75%) children were male; 7/28 (25%) were female. Fourteen (50%) were ≤ 3 months old; 25/28 (89%) were ≤ 6 months, and only 3 were >1 year. The mean age of infants in the shaken group and in the shaken-impact group was 4 and 6 months respectively.

Clinical Presentation and Course

Caretakers sought medical attention because of abnormal breathing or apnea in 16/28 (57%) children. Twenty-three (82%) children required intubation. Twenty (71%) children presented with a seizure, 5 of whom were in status epilepticus. Seven children had one or both pupils unreactive to light, and 22/28 (78%) had retinal hemorrhages. The mean Glasgow Coma Score was 10 in the shaken group vs. 9 in the shaken-impact group. Stratification of the Glasgow Coma Scores is presented in table 1. Fifteen children were transfused, and 5 underwent evacuation of an intracranial hemorrhage. No significant differences were found between the shaken and shaken-impact groups (table 2).

Radiographic Imagings

Diffuse parenchymal hypodensity was found on the first available CT scan in 20/28 (71%) children (day of admission in 16, day 1 in 3, day 4 in 1) (fig. 1, 2). Generalized atrophy was seen on subsequent scans which were done an average of 27 days (range 5–83) after the initial scan (fig. 1, 2). Radiographic skeletal survey revealed fractures in 18/28 (64%) children; skull or facial fractures were found in 8 (all in the shaken-impact group). Ribs

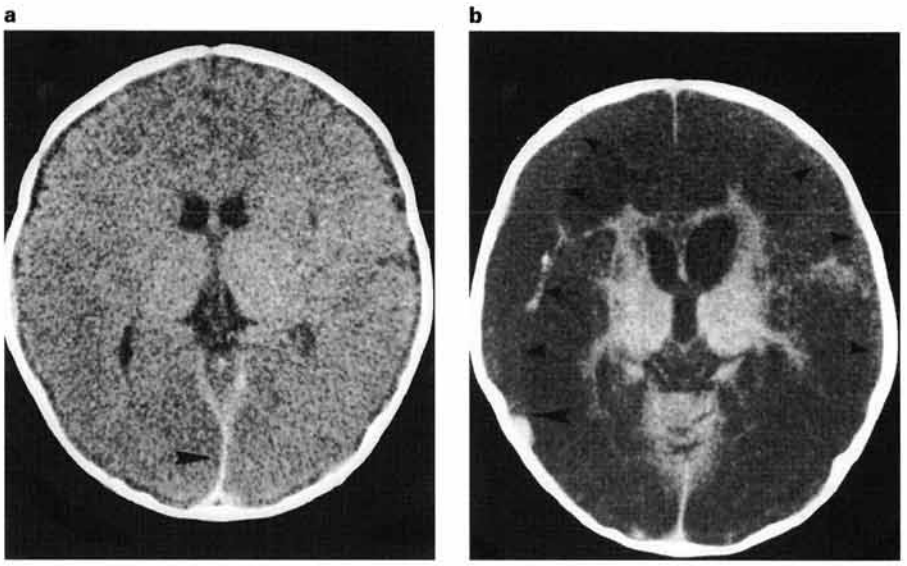

Fig. 1. **a** 4½-month-old male in shaken group. CT performed during the first 24 h reveals diffuse brain swelling characterized by patchy decreased attenuation and loss of gray/white differentiation with relative sparing of the basal ganglia. Tentorial and interhemispheric subdural hematomas (arrowhead). **b** 30 days later there is diffuse encephalomalacia, ventricular dilatation, and bilateral subdural collections, right much larger than left. Pia of the right and left hemispheres is demarcated (small arrowheads). Blood/CSF level in the right subdural hematoma (larger arrow). Poor outcome with seizures, quadriparesis, and arrested development.

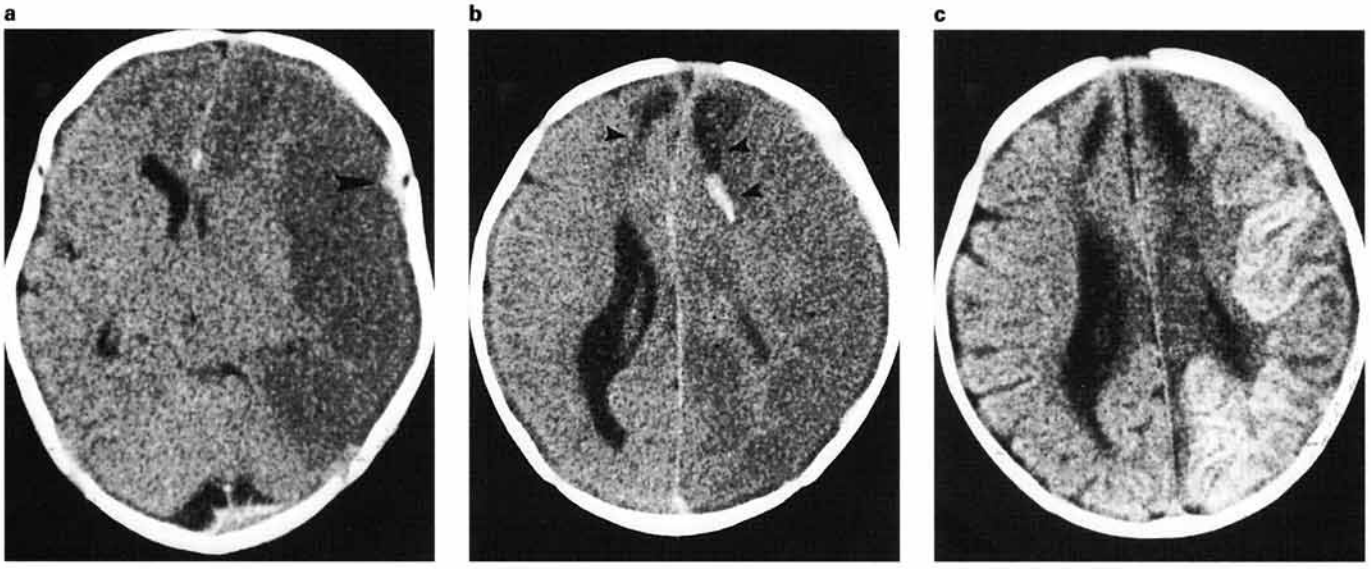

Fig. 2. **a** 2-month-old female in shaken group. Within 24 h of reported injury, CT shows unilateral swelling of the left hemisphere with transfalcine and transtentorial herniation. Left subudural hematoma (arrowhead). **b** Bifrontal gliding contusions with blood/CSF levels (arrowheads), unilateral brain swelling, and left hemispheric subdural hematoma. **c** 6 days later, increased gyral attenuation of left hemisphere, secondary to cortical petechial hemorrhage and luxury perfusion. Bifrontal gliding contusions, resolving diffuse brain swelling and subacute left subdural hematoma. Moderately disabled outcome (persistent seizures and hemiparesis).

were the predominant site of skeletal injury. Intracranial hemorrhage was found in all cases: 20 interhemispheric subdural, 17 subarachnoid, 17 cerebral convexity subdural, 7 tentorial subdural, and 4 intraventricular hemorrhages. Several children had hemorrhage in more than one location. Cerebral contusions (focal injury to brain surface) were seen in 6; contusional tears (linear hypodense defects) were found in 2 patients. Evidence of shear injury (petechial hemorrhages at the gray-white junction) was present in 4 children. No significant differences were found between the skeletal and CNS injuries of the shaken and shaken-impact groups (table 2).

Clinical Outcome

Twelve children (43%) were left with severe disability (7/28), death (4/28), or persistent vegetative state (1/28); 7 survived with moderate disability, and 9 had a good recovery. All 4 deaths occurred in the shaken-impact group; all were male children, abused by male perpetrators. The *shaken* group tended to have more severely disabled children whereas the *shaken-impact* group had more moderately disabled children (table 2). With one exception (moderate disability), children with the triad of apnea, seizures, and diffuse brain swelling died or were severely disabled. None of the children with Glasgow Coma Score ≤ 8 had a good outcome. None of the children with diffuse cerebral swelling had a good outcome.

Autopsy Findings

All 4 infants who died underwent postmortem examination, but the cervicomedullary junction was not examined in 1 infant. One infant had atlanto-occipital ligamentous disruption. Another had spinal cord contusion and laceration. Cervical and thoracic subdural hemorrhage was found in the third child. Occipital subperiosteal hemorrhage was found in 1 infant who otherwise would have been placed in the shaken group.

Discussion

An admitting history of apnea was a recurring theme: 'the baby wasn't breathing normal' or 'the baby stopped breathing so I shook it' or 'the baby stopped breathing and became stiff all over'. The veracity of these observations might be questioned if not for the stereotyped regularity with which they occurred. A majority of the children in this study had a history of apnea prior to hospitalization, and 82% were intubated upon admission to the hospital.

In addition to a history of apnea at home and the need for endotracheal intubation upon hospitalization, the first recorded systolic blood pressure was <80 in 14/28 (50%), and blood transfusion was given in 15/28 (54%). Since infant blood pressures are not always reliably obtained, and the first recorded blood pressure is only one measurement in a continuum of time between the injury and access to medical care, the magnitude of hypotension and possible ischemia which compounded cerebral hypoxia may be underestimated. The arterial pH at the time of the first encounter was <7.3 in 9/16 (56%) recorded arterial blood gases. Arterial pH is a measure of metabolic acidosis associated with hypoxia/ischemia but is heavily influenced by resuscitation. Since prehospital resuscitation had already been initiated, these values may also underestimate the true extent of initial hypotension and acidosis.

The high incidence of seizures (71%) in the study population lends further support to the central role that cerebral hypoxia plays in the poor outcome of children with SBS. Seizures are a common accompaniment of SBS as well as hypoxic-ischemic encephalopathy of neonates but relatively uncommon in accidental pediatric head injuries [7, 9–11].

The association between DBS and early hypoxia and hypotension is well established [12–14]. DBS was seen in 20/28 children to provide presumptive evidence of cerebral hypoxia/ischemia.

DAI is the classic white matter shearing injury. DBS with small parenchymal hemorrhages in the corpus callosum and/or gray-white matter junction is the CT 'signature'. Posttraumatic intraventricular hemorrhage has been implicated as an indirect manifestation of shear injury [9, 15]. Small, localized regions of subcortical edema attributed to DAI are too small to be seen on CT but can be seen on T_2-weighted MRI scans [16, 17]. CT clearly understimates the extent of injury which has been pathologically and experimentally substantiated by several authors [18–22]. Nonetheless, since only 6 children had CT evidence of DAI, the poor outcome in SBS cannot be solely attributed to DAI.

SDH and cerebral contusion have also been implicated in the pathophysiology of SBS. In this study, subdural hematomas were large enough to warrant evacuation in only 2/28 (7%). Unilateral cerebral edema subadjacent to hemorrhage, which might impune reactive vasospasm, was seen in only 2/17 (12%) children with hemispheric hemorrhages and is unlikely to account for the poor outcome [23]. Moreover, no clinical evidence of carotid or vertebral artery dissection was noted which could be another source of ischemia. Cerebral contusions were found in only 6/28 (21%) patients. Findings vary from one institution to another according to the bias of the data set [24], but none occur consistently enough to account for the poor outcome in SBS. The most consistent findings in our study were apnea, intracranial hemorrhage and DBS.

The pathophysiologic cascade of events which culminate in SBS is likely triggered by crying. Persistent crying has been previously linked to infant child abuse [25]. Crying provokes shaking or shaking with impact. The shaking stops when the perpetrator's frustration and anger dissipates or when the crying ends. The crying ends when the infant becomes apneic or loses consciousness. The duration of the hypoxic injury is proportional to the severity of the brain injury and is a major determinant of clinical out-

come [10–12]. Peroxidation of free fatty acids with formation of oxygen free radicals, uncoupling of oxidative phosphorylation, the accumulation of cytosolic free calcium ions, cytoxic excitatory amino acids, and cellular acidosis all contribute to cellular destruction [26–28]. Apnea results in a hypoxic-ischemic injury which is compounded by DBS, DAI, cerebral contusion, and SDH.

Further support for the role of apnea in SBS is provided by postmortem evidence of brainstem and cervical cord injury. SBS is largely limited to children less than 12 months old and this age-related vulnerability is at least in part due to the relatively large head, underdeveloped cervical musculature, and large subarachnoid space. Held by the chest and shoulders, the infant's head is whipped back and forth with or without impact, creating tremendous forces at the craniocervical junction. In a study of 13 abused children, no historic or physical evidence of trauma was found [7]. All of the children were shaken, as confessed by the perpetrator; 8 of the children died, and 6 were autopsied. Five of the 6 autopsied children had spinal epidural or subdural blood at the cervicomedullary junction; 4/6 children had ventral upper cervical cord contusions. In our study, all 3 infants who had complete autopsies had evidence of cervicomedullary injury.

Finally, the ability to breathe in response to a hypoxic challenge may be impaired or underdeveloped in infants [29, 30], and this susceptibility in the first year of life may make the infant more vulnerable to trauma-induced apnea.

Duhaime et al. [31] have clearly defined a significant role for impact in the pathophysiology of SBS. Experimental models of head injury have been described [32, 33] in which impact is followed by loss of consciousness and a variable period of apnea, depending on the severity of injury. Although *impact apnea* may play a part in the pathophysiology of nonaccidental head injury, no significant difference emerged between the shaken and shaken-impact groups. Duhaime et al. make the point that the lack of clinical signs of external trauma is often contradicted by postmortem evidence of scalp contusion and subperiosteal hemorrhage. Our criteria for inclusion in the shaken-impact group are strict, but some infants in the shaken group may have had subtle unrecognized impact injury as well. This point is underscored by the occult evidence of impact found at autopsy in 1 infant. In any event, apnea and DBS occurred with equal frequency in the shaken and in the shaken-impact groups.

Conclusion

Infants who suffer head injuries from child abuse have worse outcomes than those children with comparable Glasgow Coma Scores following accidental head injuries. A majority of the children in this study had clinical evidence of cerebral hypoxia or ischemia which included a history of apnea, the need for endotracheal intubation, an initial BP <80 mm Hg, the need for blood replacement transfusion, early posttraumatic seizures, and diffuse brain swelling. None of these children had a good outcome. A causal role for apnea in the SBS brings into focus the perpetrator's aggressive response to the crying child. The timing of the primary injury is closely linked to the onset of apnea.

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Editorial Comment

This is a particularly important paper in that it re-emphasizes several clinical and pathological observations which are not generally recognized, specifically the significance of hypoxic-ischemic events which determine the neurological outcome for some patients who have suffered nonaccidental injury. While pointing out the distinct differences between the shaken and the impact-shaken classes of patients, this paper stresses the difference in the pathogenesis of the two groups and the underlying importance of the hypoxic-ischemic event in the more severely affected shaken group of infants.