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REGULAR ARTICLE

Apparent diffusion coefficient values predict outcomes of abusive head trauma

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ABSTRACT

Aim: To evaluate the apparent diffusion coefficient (ADC) values for predicting the long-term neurodevelopmental outcomes of patients with abusive head trauma (AHT).

Methods: Apparent diffusion coefficient maps were retrospectively reviewed for 14 patients who presented with AHT at a mean age of 6.7 months (range 1–18 months), and the clinical outcomes of the survivors were based on the Glasgow Outcome Score.

Results: One of 14 infants died, and two were severely disabled. One had mild impairment and four had moderate disability. In the 4 days after admission, the ADC values in all brain regions were strongly associated with a poor neurodevelopmental outcome ($p < 0.05$): basal ganglia, thalamus, brain stem, corpus callosum, frontal white matter, central white matter, parietal white matter, frontal grey matter, parietal grey matter, cerebellar vermis, cerebellar cortex and mean total brain.

Conclusion: Apparent diffusion coefficient values during the acute phase of AHT were significantly associated with poor long-term neurodevelopmental outcomes.

INTRODUCTION

Child abuse is the most common cause of serious head injury in children of <1 year of age (1,2) and various types of abusive head trauma (AHT) are well recognized, and diagnosed in most countries (1). The most frequent form of AHT, referred to as shaken baby syndrome, occurs during the first year of life (2). Diagnosis of AHT is based on clinical and radiological findings and characteristic injuries are as follows: intracranial and retinal haemorrhages, rib fractures and metaphyseal corner fractures of long bones. However, retinal haemorrhages sometimes resolve within 24 h (3). The imaging abnormalities can be very extensive, but experience is required to detect subtle abnormalities at the early stage (4–7). Imaging of the central nervous system is particularly important as it can demonstrate subdural haematoma and/or subarachnoid haemorrhage, diffuse or focal cerebral oedema or cerebral contusions. Earlier studies established a correlation between acute neuroimaging findings on admission and the short-term and long-term outcomes of these patients (4,5,8).

Apparent diffusion coefficient (ADC) values can provide an objective measure of neonatal hypoxic-ischaemic brain injury or severe traumatic brain injury (TBI) (9,10). The aim of this study was to evaluate how useful ADC values are for predicting the long-term neurodevelopmental outcomes of patients with AHT.

MATERIALS AND METHODS

Study population

Between 1 April 2006 and 31 March 2012, 18 patients with AHT were identified at the Kanagawa Children's Medical Center. However, it is possible that further cases of AHT were misclassified as TBI or Sudden Infant Death Syndrome (SIDS) as AHT is not always easy to diagnose. We only included cases with a firm diagnosis of AHT in our study. Four of the children, we studied were female, 14 were male and they were aged between 1 and 18 months. The AHT diagnosis was based on clinical and physical findings, including ophthalmological, combined with diagnostic imaging examinations such as bone surveys, magnetic resonance imaging (MRI) and computed tomography

Key notes

- Radiological findings during the first month were significantly associated with the long-term outcomes of patients with abusive head trauma (AHT).
- Apparent diffusion coefficient (ADC) values can provide an objective measure of neonatal hypoxic-ischaemic brain injury or severe traumatic brain injury.
- ADC values during the acute phase of AHT were significantly associated with poor long-term neurodevelopmental outcomes.

(CT). All cases were evaluated and diagnosed as child abuse by the hospital's Child Abuse and Protection team, a multidisciplinary group that discusses cases of suspected child abuse and neglect. ADC maps were reviewed for 14 of the 18 patients. They were not reviewed in four patients: of these, one died, one had a severe disability (SD) and two made a good recovery (GR) (Table 1).

Neuroradiological assessments

All 18 children had clinical and initial radiological investigations on admission, including CT scans. In 11 cases, MRI scans were performed within 4 days of admission (acute period), and in a further five cases, they were carried out within 8 days to 1 month of admission. Diffusion-weighted imaging (DWI) and ADC maps were not obtained for two patients who were expected to make a GR. MRI scans could not be performed within a month on two patients who were very sick and required intensive care as they were expected to die or be severely disabled (Table 1). These four patients were excluded from the study.

Studies were performed using a circularly polarized head coil in a conventional 1.5 T whole-body imaging system or 3.0 T whole-body imaging system (Magnetom Avanto and Verio; Siemens Medical System, Erlangen, Germany), as shown Table 2. DWI was performed using a single-shot echo-planar technique (TR/TE = 4000/100 msec, 5 mm thick) in three encoding directions with four *b* values (0, 500, 1500, 2500 sec/mm^2) or two *b* values (1000, 2000 sec/mm^2). Circular regions of interest (ROIs) were drawn manually by one author (KT) over the following loci for calculation of ADC: basal ganglia (caudate and putamen; BG), thalamus, brain stem (BS), corpus callosum (CC), frontal white matter, central white matter, parietal white matter, frontal grey matter, parietal grey matter, cerebellar vermis and cerebellar cortex. ROI sizes were generally 1.0 and 0.5 cm^2 for CC. In this study, we only analysed ADC values and long-term outcome.

Table 1 The days to MRI, outcome and mean ADC

Case	Age (months)	Sex	Days to MRI	Outcome	Mean ADC ($\times 10^{-3}$ mm^2/sec)*
1	8	Male	2	GR	0.99
2	8	Female	1	GR	0.91
3	4	Male	1	GR	1.07
4	8	Male	2	GR	0.93
5	8	Male	14	MD	0.98
6	18	Male	2	MI	0.90
7	7	Male	25	MD	0.90
8	1	Male	19	SD	1.22
9	10	Male	4	MD	0.63
10	1	Male	8	GR	1.00
11	10	Female	2	Death	0.29
12	5	Male	3	GR	0.95
13	2	Male	1	MD	0.87
14	4	Female	4	SD	0.38
15	11	Male	3†	GR	Not performed
16	22	Female	6†	GR	Not performed
17	8	Male	44†	SD	Not performed
18	4	Male	Not performed	Death	Not performed

MRI = magnetic resonance imaging; ADC = apparent diffusion coefficient; GR = good recovery; MD = moderate disability; MI = Mild impairment; SD = severe disability.

*Mean ADC value of basal ganglia, thalamus, brain stem, corpus callosum, frontal white matter, central white matter, parietal white matter, frontal gray matter, parietal gray matter, cerebellar vermis and cerebellar hemisphere.

†Diffusion-weighted imaging and ADC maps were not performed.

Table 2 Magnetic resonance imaging systems

Vendor	Field strength (T)	Coil	Parallel imaging	Macimum gradient strength (mT/m)	Slew rate (T/m sec)
Siemens medical solutions	1.5	Quadrature detection	Yes	57	216
Siemens medical solutions	3	Quadrature detection	Yes	78	346

Outcome assessment

The Glasgow Outcome Scale was used to assess the overall developmental outcome at the last follow-up clinic visit. GR refers to a return to age-appropriate or preinjury levels of functioning. Mild impairment (MI) includes no significant disability or only minor changes. Moderate disability (MD) includes slight disability, such as unable to carry out some previous activities, but able to look after his/her own affairs without assistance. SD includes patients who are conscious, but disabled, and dependent on daily support. It includes a combination of moderately SD (unable to walk and attend to his/her own bodily needs without assistance) and SD (bedridden, incontinent and requiring constant nursing care and attention). Death refers to patients who died within 2 months of admission.

Statistical analysis

One-way analysis of variance was used to evaluate the relationship between radiological variables and poor neurodevelopmental outcomes. The Bartlett test was used to test for homogeneity of variance. The accepted level for statistical significance was $p < 0.05$.

RESULTS

The days to MRI, outcome and mean ADC values of all the brain regions of the 14 patients with AHT are summarized in Table 2. The mean age at injury was 6.7 months (range 1–18 months). The male-to-female ratio was 11:3 (11 boys and 3 girls). Thirteen of the 14 patients survived. The mean neurological follow-up time was 3 years (range 4 months–5 years). Three of the 14 patients (21%) had poor neurodevelopmental outcomes: one patient died and two had SD. Five patients had moderate developmental problems, four with MD and one with MI. Six patients were free of developmental problems at follow-up (GR). The follow-up

time for one patient was only 4 months, as she had an extremely poor outcome and needed mechanical ventilation for respiration and tube feeding. The follow-up time, without that one patient, exceeded 1 year 7 months.

Acute investigations (up to 4 days after admission) were performed in 10 children. Two of the 10 patients had poor neurodevelopmental outcomes: one died and one had SD. Three patients had moderate developmental problems, two with MD and one with MI. Five patients were free of developmental problems at follow-up (GR). They presented at a mean age of 7.7 months (range 2–18 months). ADC values for each anatomical region are shown in Table 3. Up to 4 days after admission, ADC values in all brain regions were strongly associated with poor neurodevelopmental outcomes: BG, thalamus, BS, CC, white matter, cerebral cortex, cerebellar vermis, cerebellar cortex, mean total brain ($p < 0.05$; especially BG, thalamus, BS, cerebral cortex, cerebellar vermis, cerebellar cortex), and mean total brain ($p < 0.001$). However, ADC in a few regions during the early phase (up to 1 month) was associated with a poor outcome ($p < 0.05$): BG, thalamus, BS and CC.

DISCUSSION

Different definitions for AHT are in use, making comparison of incidence rates reported by different institutions difficult. In British and Estonian studies, incidence rates of 14.2 and 40.0 per 100 000, respectively, were found in children under 1 year of age (11,12). In our study, 18 patients were identified during a period of 6 years, less than the number we would expect from the available epidemiological studies on AHT. However, not all abused infants need medical help and come in contact with our hospital and, as previously noted, some cases of AHT could be wrongly diagnosed as TBI or SIDS. Half of our study population (50%) had disabilities, which were severe (21%) or moderate (29%). This is consistent with key studies, in which 45–69% of children had a poor outcome (5,13,14).

Galloway et al. (10) analysed peripheral grey matter, peripheral white matter, deep white matter, deep grey matter and posterior fossa in TBI. The average total brain ADC value and ADC values in the peripheral white matter had the greatest ability to predict outcome. In our study, we referred to the results and analysed many such foci. Within 4 days of admission ADC values in the BG, BS, CC, white matter, grey matter and cerebellum were significantly associated with poor long-term outcomes in AHT. The variability of diffusion changes is often associated with time to imaging, the severity of injury, type of injury, injury location within the brain, tissue response to injury and the degree and severity of oedema (15). When abnormal ADC values in injured brain tissue were detected during the first week after the hypoxic-ischaemic event, they became higher before returning to normal values (9,16–20). ADC values alone in the BG and posterior limb of the internal capsule during the first days following hypoxic-ischaemic brain injury appear to be a sensitive marker for evaluating infants' early neurological outcomes. The lower the ADC value in these regions was between days 1 and 6, the worse the early neurological outcomes (21). In our study, one possibility is that ADC values became high at the time of imaging, as in the case of patient 8 (Table 1).

In AHT cases, multiple factors, all present in the setting of an immature, incompletely myelinated brain, are likely to be involved and include mechanical force resulting in haemorrhage, focal contusions or diffuse axonal injury; secondary hypoxic-ischaemic injury after apnoea, hypotension, strangulation, suffocation or seizures; vascular occlusion, from direct trauma leading to more focal infarctions and superimposed cytotoxic oedema. These combined factors account for the severe brain swelling and subsequent extensive tissue loss observed in infants who survive severe

Table 3 The means and standard divisions for ADC values for each anatomical region

	ADC <4 days ($\times 10^{-3}$ mm^2/sec)†					ADC <1 month ($\times 10^{-3}$ mm^2/sec)†				
	GR	MD	SD	χ^2	F	GR	MD	SD	χ^2	F
BG	0.91 (0.05)	0.80 (0.05)	0.42 (0.08)	0.16*	61.4***	0.91 (0.05)	0.84 (0.07)	0.58 (0.27)	4.3*	6.9*
Thalams	0.87 (0.04)	0.76 (0.03)	0.37 (0.02)	0.11*	145.7***	0.88 (0.06)	0.77 (0.07)	0.54 (0.30)	4.31*	6.08*
BS	0.87 (0.07)	0.79 (0.09)	0.31 (0.01)	0.92*	45.5***	0.87 (0.07)	0.79 (0.07)	0.49 (0.31)	4.02*	6.68*
CC	1.11 (0.15)	0.84 (0.21)	0.27 (0.13)	0.15*	19.1**	1.11 (0.15)	0.95 (0.27)	0.55 (0.48)	1.66*	4.1*
W (f)	1.08 (0.06)	0.79 (0.31)	0.38 (0.16)	2.86*	12.7**	1.08 (0.06)	0.92 (0.28)	0.79 (0.72)	6.32	0.7
W (c)	1.00 (0.13)	0.72 (0.37)	0.30 (0.14)	1.41*	8.3*	1.00 (0.13)	0.80 (0.28)	0.74 (0.77)	3.98*	0.65
W (p)	1.13 (0.11)	0.78 (0.46)	0.35 (0.15)	2.46*	7.61*	1.13 (0.11)	0.85 (0.35)	0.80 (0.80)	4.55*	0.9
C (f)	1.06 (0.09)	0.85 (0.03)	0.40 (0.03)	1.07*	63.2***	1.06 (0.09)	0.93 (0.11)	0.78 (0.44)	3.98*	1.83
C (p)	0.97 (0.06)	0.93 (0.12)	0.37 (0.03)	0.95*	51.7***	0.97 (0.06)	0.95 (0.09)	0.70 (0.58)	7.64	1.24
Ce (v)	0.82 (0.09)	0.66 (0.06)	0.31 (0.15)	0.41*	22.3***	0.82 (0.09)	0.68 (0.06)	0.52 (0.38)	4.77*	3.03
Ce (c)	0.85 (0.05)	0.75 (0.09)	0.31 (0.01)	1.29*	65.1***	0.85 (0.05)	0.79 (0.08)	0.56 (0.43)	6.77	2.49

ADC = apparent diffusion coefficient; GR = good recovery; MD = moderate disability; SD = severe disability; χ^2 = Bartlett test; F = one-way analysis of variance; BG = basal ganglia; BS = brain stem; CC = corpus callosum; W (f) = frontal white matter; W (c) = central white matter; W (p) = parietal white matter; C (f) = frontal cerebral cortex; C (p) = parietal cerebral cortex; Ce (v) = cerebellar vermis; Ce (c) = cerebellar cortex.

†Means (standard deviations).

***$p < 0.001$; **$p < 0.01$; *$p < 0.05$.

abuse-related head injury, with the particular pattern of injury dependent on the level of brain development. A key pathophysiological factor may be cerebral hypoperfusion. Cerebral hypoperfusion is associated with poor outcomes after severe head injury (22–24). BG lesions, which represent the results of hypoxia or hypoperfusion, were associated with poor outcomes (8). Contemporary neuropathological studies on injury mechanisms and structural changes in the brain following AHT are regarded as consistent with hypoxic-ischaemic injury (25). However, we found that brain ADC values in the acute phase showed a significant ability to predict outcomes not only in the BG but also in all brain regions.

This study has limitations. The potential concerns include the small sample size and the retrospective nature of the review. ADC values can be influenced by several imager-dependent factors, such as gradient systems, the coil system, pulse sequence design, imaging parameters and artefacts related to susceptibility effects or eddy currents. The difference between 1.5- and 3.0-T imagers from the same vendor was only 3–5% (26), even smaller than that previously reported (27). It is therefore suggested that at 1.5 or 3.0 T, the ADC value is generally a reproducible and reliable parameter. However, we must be aware of the presence of substantial interimager-intervendor variability of up to approximately 9% in the absolute ADC values (26).

Finally, in our series, the ADC values during the acute phase of AHT were significantly associated with long-term neurodevelopmental outcomes. This point needs to be explored further using detailed neuropsychological assessments in a larger series of AHT patients, preferably in prospective studies.

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