



The Relationship between Acute Kidney Injury and Brain MRI Findings in Asphyxiated Newborns after Therapeutic Hypothermia

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Background

- Therapeutic hypothermia has become the standard of care for asphyxiated newborns.
- Recent studies evaluating Acute Kidney Injury (AKI) in neonates have begun to utilize a modified Acute Kidney Injury Network (AKIN) criteria in neonates
 - Premature newborns
 - Infants with congenital heart disease
 - Congenital Diaphragmatic hernia
- Utilizing this definition we have recently reported a 38% incidence of AKI in neonates treated with therapeutic hypothermia and its association with outcome
 - increased length of stay
 - Increased length of mechanical ventilation
- Perlman et al first examined the association of AKI with long-term neurologic outcomes in asphyxiated newborns prior to therapeutic hypothermia.
 - AKI defined by oliguria
 - Prior to regular imaging
- To date the impact of acute kidney injury (AKI) on brain MRI findings in asphyxiated newborns following therapeutic hypothermia has not been studied.

Objectives

- The aim of the study was to determine whether AKI during therapeutic hypothermia predicts the presence of subsequent brain MRI abnormalities related to hypoxia-ischemia.
- We hypothesized that hypoxic-ischemic lesion on brain MRI would differ between infants with AKI compared to those without AKI following cooling.

Methods

- Study Design: Single-center retrospective review of all newborns receiving therapeutic hypothermia from 2003-2010 (N=96).
- Therapeutic Hypothermia: According to Cool Cap and NICHD Neonatal Research Network protocols.
- Inclusion Criteria: A sentinel event
 - Cord pH, blood gas pH< 7.0, base deficit 16 on cord pH, APGAR < 5 at 10 minutes of life
 - AND: Evidence of moderate or severe encephalopathy or seizures
 - Exclusion Criteria:
 - Age > 6 hours, Chromosomal abnormality, Congenital Anomaly, Birth Weight < 1800 grams

- Brain Imaging: At 7-10 days of life all infants treated with therapeutic hypothermia receive a brain MRI
- Neuroradiologist were blinded
 - Mildly abnormal: Lesions either in basal nuclei, or cortex
 - Severely abnormal: Injuries involved the basal ganglia/thalamus and cortex

Acute Kidney Injury: during hospital course

- Modifications:
- SCr had to rise to over 0.5 mg/dL to qualify as AKI
 - Excluded urine output criteria
 - Stage 3 category a rise up to 2.5 mg/dL
 - To determine change in cr, values were compared to the lowest previous value.

Table 1: Modified Acute Kidney Injury Network Criteria

Stage	Criteria
0	No change in Cr
1	↑ SCr 0.3 mg/dL or ↑ SCr 150-200% from previous trough value
2	↑ SCr 200-300% from previous trough value
3	↑ SCr > 300% from previous trough value, SCr 2.5 mg/dL or dialysis

* Jetton et al. Current Opinion in Pediatrics (2011)

Results

- 88 of the 96 patients had MRI performed at a median of 8 days of life
 - 2 infants died prior to MRI
 - 6 infants had other imaging studies performed
- AKI was identified in 34 (39%) of neonate
 - Stage I: 15, Stage II: 7, and Stage III 12
- In hospital mortality was 7%
- Brain MRI abnormalities related to hypoxia-ischemia was present in 50/88 (59%) neonates
 - In 26 neonates brain MRI was “severely abnormal,” 14/34(41%) in AKI group vs 12/54, (22%) in those without AKI; p=0.091

Table 2: Patient Characteristics

Variable	Abnormal MRI		Odds Ratio	p- value
	Yes (N=50)	No (N=38)		
Acute Kidney Injury	25	9	3.2 (1.3,8.2)	0.012
Male Gender	26	25	0.6(0.2,1.3)	0.194
Receipt of chest compression	34	14	3.6 (1.5,8.8)	0.004
Clinical seizure	27	12	2.5 (1.05,6.1)	0.036
Intrapartum sentinel event	32	18	1.9 (0.8,4.6)	0.119
5-minute Apgar score of 0-3	37	26	1.3 (0.5,3.3)	0.565
Cord pH of <7	34	22	1.5 (0.6,3.7)	0.329
Base deficit >16 mmol/L	35	22	1.7 (0.7,4.1)	0.293
Need for ventilation for >10 min	49	35	4.2 (0.4,42.0)	0.189
Absent spontaneous movement	25	11	2.4 (1.0,6)	0.047

Table 3: MRI findings according to AKI Stage

Stage	N (88)	Normal MRI	Mild MRI Abnormality	Severe MRI Abnormality
0	54 (61%)	29	13	12
1	15 (17%)	0	7	8
2 and 3	19 (22%)	9	4	6

Results

Table 4: Multiple Logistic Regression* Factors Associated with Abnormal MRI

Covariates	Odds Ratio	95% Confidence Interval	p- value
Acute Kidney Injury	2.9	1.1, 7.6	0.032
Chest Compressions	3.3	1.3, 8.3	0.010

- * Stepwise Logistic with p variables < 0.2 in Univariate
- AKI, receipt of chest compression, clinical seizure, absent spontaneous movement, male gender, presence of an intrapartum sentinel event, and continued need for ventilation for more than 10 minutes for resuscitation

Conclusions

- This is the first report to evaluate the prognostic significance of AKI during the course of therapeutic hypothermia in neonates with birth asphyxia and its relationship to abnormal brain MRI
- We show that AKI is independently associated with the presence of hypoxic-ischemic lesions on post-cooling brain MRI at 7-10 days of life
- Those with AKI were 2.9 times more likely to have an abnormal MRI on multivariate analysis
- An interesting finding is that AKI did not predict “severe” brain abnormalities on MRI, which could be due to small sample size, insensitive definition of AKI, or protective effects of AKI on brain injury
- Our findings provide the clinician with a marker (AKI) during the course of therapeutic hypothermia that may help to stratify patients at risk for an adverse neurologic clinical outcome.

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