Changes in NAA and Presence of Lactate on MRS Predict Outcome in Children with Nonaccidental Trauma

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Introduction: Traumatic brain injury (TBI) in children under 2 years of age is attributed to nonaccidental trauma (NAT) in about 24% to 32% of cases[1]. Outcome in victims of NAT is recognized to be worse possibly due to evidence that hypoxic-ischemic injury on MRI is more common in NAT victims compared to TBI from accidental trauma[2]. The more commonly used indicators of TBI severity include the Glasgow Coma Sale (GCS) score, duration of impaired consciousness and posttraumatic amnesia, presence of non-reactive pupils and brain imaging techniques. Unfortunately, these indicators of severity have not proved sufficiently accurate in predicting long-term outcome. Magnetic resonance spectroscopy (MRS) has been used to evaluate the extent of TBI in children and to predict outcomes from pediatric accidental TBI[3]. The results of these studies have suggested that decreased N-acetylaspartate (NAA) and the presence of lactate are correlated with poor outcome. In this study, we evaluated Magnetic Resonance Spectroscopy (MRS) findings in children with traumatic brain injury due to NAT to determine if metabolite changes predicted outcome.

Materials and Methods: A retrospective analysis of 109 children with confirmed NAT (mean age 8.2 ± 7.3 mo; range 1-32 mo) was performed with IRB approval from our institution. Proton single voxel (SVS)(STEAM; TR/TE=3000/20 msec) and/or MR spectroscopic imaging (MRSI) (PRESS;TR/TE=3000/144 msec) at 1.5T had been acquired in all children in the mid-occipital gray matter (OGM) and parietal white matter (PWM) or through the level of the corpus callosum, respectively, early after injury (mean 5d, range 1-30d). Quantitative metabolite levels and ratios from SVS for NAA, creatine/phosphocreatine (Cr), total choline (Cho), myo-inositol (Ins), glutamate/glutamine (Glx) and presence of lactate (Lac) were measured using LCModel. Regional and Total mean metabolite ratios were measured from MRSI data for NAA/Cr, NAA/Cho, Cho/Cre. Long term outcomes defined as $\geq$ 6 months were collected in 44/109 children (age 6 ± 5 mo; range 2 – 20 mo). We dichotomized patients into Good (normal, mild, moderate; n=33) and Poor (severe, vegetative or dead; n=11) outcome groups. Logistic regression models were constructed to identify spectroscopic and clinical variables that aided in predicting outcome only in those patients with long term outcomes.

Results and Discussion: A total of 44 patients (28 males, 16 females) had MRS studies and follow up medical visits more than 6 months after injury to determine outcome. Thirty three of these patients had good outcomes and 11 had poor outcomes. The age of children at the time of MRS was not significantly different between the two outcome groups (7± 5.4 mo vs 4.5± 5.3; p=0.02). The initial GCS score was 6 in the poor group compared to 11 in the good outcome group ($p \leq 0.001$). SVS MRS NAA/Cr and NAA/Cho ratios in OGM (p=0.02) and PWM ($p \leq 0.001$) were significantly lower in children with poor outcome and lactate was more likely to be present (>85%; p=0.001). MRSI Total mean NAA/Cre and total NAA/Cho ratios were significantly lower in children with poor outcome ($p \leq 0.02$) and lactate was more likely to be present in children with poor outcomes ($p < 0.002$). Regional MRSI data showed strong correlations between reduced NAA/Cr and NAA/Cho ratios (corpus callosum, frontal white matter) and poor outcomes ($p<0.01$). A logistic regression base model using age and initial GCS correctly predicted outcome in 84% of subjects (Table 1). The presence of retinal hemorrhages improved prediction of good outcomes. When tested with the base model, we found that the MRSI Total mean NAA/Cr ratio and presence of lactate improved prediction accuracy most compared to other MRS variables by improving prediction for poor outcomes. Table 1 compares results from logistic regression analyses.

Table 1. Prediction Models

	Variables Included	Good Outcome	Poor Outcome	Overall Outcome Prediction
Base Model	Age,Initial GCS	91%	64%	84%
Model #1	Base,Retinal Hemorrhages	94%	64%	86%
Model #2	Base,Ret hem.,Mean Total NAA/Cr ratio	94%	82%	91%
Model #3	Base, Lactate present, Mean Total NAA/Cr	94%	82%	91%
Model #4	Base, Retinal hem., Lactate present	100%	91%	98%
Model #5	Base,Ret hem., Lactate, Mean Total NAA/Cr	100%	100%	100%

Conclusions Reduced NAA (i.e. neuronal loss/dysfunction) and elevated lactate (altered energy metabolism) correlate with poor neurological outcomes in children with NAT. Elevated lactate may reflect primary or secondary hypoxic ischemic injury that can occur with NAT. MRSI data proved to be more predictive than single voxel MRS. Our data suggest that MRSI performed early after injury is helpful for long-term prognosis.

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