J. H. Lee<sup>1</sup>, K.-S. Kim<sup>2</sup>, C. H. Yoon<sup>3</sup>, S. M. Lim<sup>3</sup>, S.-T. Kim<sup>1</sup>, T.-H. Lim<sup>3</sup>

NMR Laboratory<sup>3</sup>, Asan Institute for Life Sciences, Department of Pediatrics & Division of Neonatology<sup>2</sup>, and Diagnostic Radiology<sup>3</sup>, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

### Introduction

Although the effective therapeutic strategy for hypoxic ischemic injury after birth asphyxia has not been known, early diagnosis is very important for developing the therapeutic method. However, imaging techniques and clinical evaluations are sometimes misleading for newborn infants less than 7 days old. In this study, we evaluated <sup>1</sup>H MR spectroscopy for detection of early abnormal changes in the brain of hypoxic ischemic injury after birth asphyxia in newborn infants, and the sensitivity over MR imaging was evaluated in a series of follow up examinations over 2-15 months.

#### Patients

Fullterm newborn infants with severe hypoxic ischemic encephalopathy with Sanat stage II (N=8) and Sanat stage III (N=8) were examined at their postconceptional age (PCA=gestational age+ postnatal age) of  $40.3\pm$  0.7 weeks. For 12 infants, the initial MRI and MRS were performed within 1 week after birth, and for the rest 4 infants, the exams were performed 2-3 weeks after birth. For those who developed abnormal neurologic sequlae at the PCA of 8 months by clinical evaluations were subjected to the follow-up MRI and MRS examinations. For 16 infants, total 26 exams were performed: 8 of 16 infants were examined for the initial exam, 6 infants for the 2<sup>nd</sup> follow – up exams, and 2 infants for 2<sup>nd</sup> and 3<sup>nd</sup> follow-up exams.

#### Materials and Methods

All MR imaging and localized *in vivo* <sup>1</sup>H MR spectroscopy were performed on a GE 1.5T SIGNA system equipped with shielded gradients (General Electric Medical System, Milwaukee, USA). Spectroscopy was performed following a routine brain MRI exam including T1- and T2- weighted images, and T1-weighted images were used for localization. Image guided STEAM-spectra were obtained from the parietal white matter region with TE of 30 msec, TR of 3.0 sec, and 36 AVG with PROton Brain Exam (PROBE) (General Electric Medical System, Milwaukee, USA). Volumes of the voxels were 7~9 ml and 3pulse CHESS sequence was used for suppression of the H<sub>2</sub>0 signal. All spectroscopic raw data were processed according to Kreis *et al.* (1), and the values of the [NAA/ Cr] and [Lac/ NAA] were evaluated for all infants. All MR images were evaluated by two radiologists to delineate the lesions of focal ischemia and diffuse atrophy, the abnormalities in basal ganglia, and *etc.* (Table 1)

The neurological outcomes were evaluated at the PCA of 8 months by pediatric neurologists.

## **Results and Discussion**

*Clinical Evaluations:* Four of 16 infants showed normal neurological developments when examined at their PCA of 8 months, and therefore, they were excluded for further evaluations. The rest 12 infants showed abnormal neurological developments such as cerebral palsy or developmental delay (n=9) or death (n=3).

*MRI Results:* Of the total 26 examinations, 22 examinations were evaluated excluding 4 initial examinations for 4 infants who showed normal developmental outcomes. Table 1 summarizes the results of MRI in times when the examinations were performed. When MRI was performed within 1 week, 8 of 10 showed normal MRI findings and 2 showed mild brain edema. When MRI was performed after 1 week, 11 of 12 showed abnormal MRI findings. Five of 6 infants showed abnormal MRI findings at the 2<sup>nd</sup> MRI examinations although their initial MRI findings at the 3<sup>rd</sup> MRI examinations although their 1<sup>st</sup>

and 2<sup>nd</sup> MRI findings were normal.

*MRS Results:* The plots in Figure 1 show that the [NAA/Cr] ratios for infants with abnormal developmental outcomes are similar to those with normal outcomes when examined within 1 week: and their [NAA/Cr] ratios decreased after 2 weeks. However, the elevated [Lac/NAA] ratios for infants with abnormal developmental outcomes were observed when examined within 1 week.

#### Conclusions

The results of MRI performed within 1 week after birth for infants with hypoxic ischemic encephalopathy do not seem to be useful for diagnosis of the disease. However, the [Lac/NAA] ratios in the <sup>1</sup>H MR spectrum observed within 1 week after birth seems to be very useful for diagnosis of the early abnormal changes in the brain of hypoxic ischemic encephalopathy, and thus, the elevated [Lac/NAA] ratios can be used as an early predictor for prognosis as previously reported (2). In addition, <sup>1</sup>H MRS has a potential to be used as a very practical way to evaluate new therapeutic strategies for hypoxic ischemic injury of newborn infants.

# Table 1. The MRI findings in the Follow-up Exams (n=22),

Date	<7 d	7-13 d	2 w 2 m	15 m
MRI Finding				
Normal	8	1		
Brain edema	2			
Abn. Cortical Signal		2		
Basal ganglia lesion		2	1	
Cerebral infarction		1	2	
Diffuse atrophy			1	1
Encephalo-malacia			1	







Figure 2. <sup>1</sup>H MR spectra from the parietal white matter for an infant with hypoxic ischemic injury (Sanat stage III) for the 1<sup>st</sup> exam at the PCA of 41 weeks and the 2<sup>nd</sup> exam after 1 week. For the 1<sup>st</sup> exam, MRI was normal, but for the 2<sup>nd</sup> exam, MRI was abnormal.

## References

- 1. Kreis, R., Ross, B.D., Farrow, N.A., Radiology 182, 19, 1992.
- 2. Kim, K.-S., Pi, S.-Y., Kim, E.A., 6th ISMRM, 95,1998.