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Comparison of the efficacy of diffusion-weighted magnetic resonance imaging and conventional magnetic resonance imaging in determining the prognosis in newborns with hypoxic ischemic encephalopathy

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Summary

Aim: The aim of the study was to compare the conventional brain MR imaging and diffusion-weighted MR imaging performed during the first 48 postnatal hours in their relevance to predict the long-term neurodevelopmental outcome in patients with hypoxic ischemic encephalopathy Sarnat Stage II.

Material and Method: Medical records of 69 patients with HIE between January 2006 and January 2010 were studied retrospectively. Twenty-one patients whose data were consistent with Sarnat Stage II and for whom conventional MRI and diffusion-weighted MRI had been performed in the first 48 postnatal hours were included the study. Neurodevelopmental assessment of these patients was based on Ankara Developmental Screening Inventory (AGTE-GG). Patients whose overall developmental age was 30% below, within the 20-30% range and above 20% the chronologic age were classified as poor, moderate and good prognosis, respectively.

Results: Based on the results of the AGTE-GG, 11 (52.3%) out of 21 patients included in the study had good and 10 (47.7%) had poor prognoses. In terms of the predictivity for long-term prognosis, the conventional brain MRI had an OR value of 6.22 (0.94-41.3), while the same value for the diffusion-weighted MRI was 4.8 (0.68-33.9). The positive predictivity, negative predictivity, sensitivity and specificity of the conventional brain MRI were 61.5, 75, 80 and 54%, respectively, whilst the same values for the diffusion MRI were 70, 72.7, 70 and 72.7%, respectively.

Conclusions: No statistically significant difference was noted between the two imaging methods in terms of the predictive value for long-term neurologic prognosis ($p>0.05$). The present study showed that both the conventional brain MRI and diffusion MRI may be used for long-term neurologic prognosis in patients with stage II HIE, with neither of the methods being superior to the other. (*Turk Arch Ped* 2011; 46: 283-6)

Key words: Diffusion-weighted MR imaging, hypoxic ischemic encephalopathy, conventional brain MR imaging, Sarnat stage 2, prognosis

Introduction

Prenatal, perinatal and postnatal factors are involved in the etiology of hypoxic ischemic encephalopathy (HIE). It is observed with a rate of 1-6/1000 in term infants and is a severe cause of morbidity and mortality (1,2). While the disease has a fatal prognosis with a rate of 10-15%, cerebral palsy is observed in 10-15% of the patients and blindness, deafness, cognitive and behavioral problems are observed in 40% of the patients (3,4).

Hypoxic ischemic encephalopathy is defined as three stages according to electroencephalographic (EEG) findings (5). Although the long-term prognosis of patients with Sarnat and

Sarnat stage 1 is excellent, it is known that the morbidity and mortality rates of the patients with stage 3 are high. The prognosis of the patients with moderate encephalopathy (Sarnat stage 2) is not clear. While cerebral palsy develops in some patients, the development is within normal limits in some patients (6). Prediction of long-term outcomes in patients with HIE is important in terms of early treatment decision and informing the family about the prognosis. Since the long-term outcomes of the patients with Sarnat stage 2 is not clear, reliable indicators are needed to indicate the prognosis. Many clinical variables have been proposed determining the prognosis, but very few has been used successfully (7).

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The aim of this study was to investigate if the conventional brain MR imaging and diffusion-weighted MR imaging performed during the first 48 postnatal hours are significant in predicting the long-term neurodevelopmental outcome in patients with hypoxic ischemic encephalopathy Sarnat stage II and to compare the efficiency of these two methods.

Material and Method

The file records of 69 patients who were followed up in the Neonatal Intensive Care Unit of Akdeniz University Medical Faculty between January 2006 and January 2010 with a diagnosis of HIE were examined retrospectively. For a diagnosis of hypoxic ischemic encephalopathy the four criteria defined were looked for (89):

1. At least one of the following:
 - (a) An APGAR score of <5 at the 5th minute,
 - (b) Metabolic acidosis (base excess > -16 mEq/L in the chord blood or arterial blood taken in one hour after birth).
 - (c) Absence of respiration for ≥5 minutes,
 - (d) Cesarean section because of fetal distress.
2. Requirement of ventilation at the time of delivery.
3. Lethargia/stupor, hypotonia, absence of sucking reflex or poor sucking reflex, abnormal reflex findings.
4. At least one other organ involvement in addition to encephalopathy.

The staging of HIE was determined according to Sarnat and Sarnat (5). Infants with a gestational age <35 weeks and patients with additional diseases including significant congenital anomaly, dysmorphic syndrome, metabolic disease and sepsis were not included in the study. Among 69 infants who fulfilled the defined criteria and diagnosed as HIE, the files of 21 patients whose clinic state was compatible with Sarnat and Sarnat Stage 2 and who were undergone Diffusion-Weighted Magnetic Resonance Imaging and Conventional Magnetic Resonance Imaging in the first two days were examined. Gender, gestational age, birth weight, birth place and mode of delivery, APGAR scores, parity, clinical properties, laboratory results and hospitalization times of the patients determined were recorded from the files. The gestational weeks of the patients were determined according to the New Ballard Score system. APGAR values of the patients born in external centers were accepted as stated in the epicrisis sent.

Patients who were found to have an appearance compatible with hypoxia in the sequences of axial T1 A, T2 A and FLAIR were determined as CBMRI(+). Patients who were found to have diffusion limitation in favor of hypoxia on echoplanar imaging (EPI) and in the apparent diffusion coefficient (ADC) sequences in the diffusion weighted brain MR imaging were considered as DWBI(+).

The neurodevelopmental evaluation of 21 subjects defined as Sarnat and Sarnat stage 2 was performed by the attendant specialist psychologist in the Department of Pediatrics using Ankara Developmental Screening Inventory (ADSI). The mean

age of the patients at the time of the test was 2.6±1.2 years (the youngest 12 months old and the oldest 4.5 years old). The patients were evaluated in terms of language-cognitive development (LC), fine motor (FM) development, gross motor (GM) development and social ability-self care (SASC) development and their general development (GD) was determined. Patients with a general development age younger than 30% of the chronological age were considered to have poor prognosis in terms of development. Patients with a general development age younger than 20-30% of the chronological age were considered to have borderline prognosis and patients with a general development age older than 20% of the chronological age were considered to have good prognosis.

Results

10 of our patients (47.7%) included in the study were born in an external center and 11 (52.3%) were born in our hospital. 8 patients were born by normal spontaneous vaginal delivery (38%) and 13 patients were born by cesarean section (62%). The general properties of the patients are shown in Table 1.

Placenta and chord pathology was found in 4 patients (19%), premature rupture of membranes was found in 5 patients (23.8%), preeclampsia was found in 2 patients (9.5%), intrauterine growth retardation was found in 2 patients (9.5%), fetal distress was found in 15 patients (71%) and flow disturbance in the fetal umbilical artery on Doppler ultrasonography was found in 10 patients (47%).

According to Ankara Developmental Screening Inventory, 9 of 21 patients had poor prognosis in terms of language-cognitive development (LC), fine motor (FM) development and social ability-self care (SASC) development and gross motor (GM) development was found to be poor in 8 patients. According to ADSI-GD 11 (52.3%) of 21 patients in Sarnat stage 2 were

Table 1. Characteristics of the patients

Gender (Female/Male)	11/10
Birth place (Hospital/external center)	10/11
Mode of delivery (normal vaginal/cesarean section)	8/13
Gestational age at the time of birth*	38±1
Birth weight (g)*	3415±566
Apgar 1*	3±1
Apgar 5*	5±1
pH*	7.18±0.11
Bicarbonate*	7.81±3.44
Base excess*	-14±3
pCO ₂ mmHg*	44±18
Ventilation time (days)*	7±3
Full feeding time (days)*	8±4

* Ort.±SS

evaluated to have good prognosis and 10 (47.7%) were evaluated to have poor prognosis (Table 2).

Diffusion weighted brain magnetic resonance imaging was found to be normal in 8 of the patients (72.7%) who showed a good prognosis and conventional brain magnetic resonance imaging was found to be normal in 6 (54.5%) of the patients who showed a good prognosis. In the group with a poor prognosis, findings compatible with hypoxia were found in 7 patients (70%) on DWBMR and in 8 patients (80%) on CBMRI (Table 2). The positive predictive value of CBMRI was found to be 61.5% and the negative predictive value of CBMRI was found to be 75%. The positive predictive value of DWBMR was found to be 70% and the negative predictive value of CBMRI was found to be 72.7%. The sensitivity and the negative predictive value of CBMRI were found to be better and the specificity and the positive predictive value of DWBMR were found to be better. However, no statistical difference was found between the two imaging methods in terms of indicating long-term neurologic prognosis ($p > 0.05$). [CBMRI OR: 6.22 (0.94-41.3), DWBMR OR: 4.8 (0.68-33.9)] (Table 3,4).

Discussion

Since the long-term outcomes of the patients in Sarnat and Sarnat stage 2 are unclear, reliable markers are needed to indicate the prognosis (5,7). With CBMRI brain lesions developed in infants with HIE can be determined at an early time (14). Therefore, imaging is recommended on the 2-8th days (10-12).

In many studies, the relation between different imaging techniques and long-term prognosis was investigated and different results were reported. In some studies, the value of conventional cranial MRI in indicating the long-term neurologic prognosis in patients with a diagnosis of HIE was investigated. According to the results of all these studies the sensitivity of CBMRI in determining the long-term neurologic prognosis was found to be 38-100%, the specificity was found to be 43-100%, the positive predictive value was found to be 75-100% and the negative predictive value was found to be 67-82% (13-16). In contrast to all these, Van Schie et al. (17) reported that involvement of basal ganglia, thalamus, cortex and posterior limb of the internal capsule on MR imaging was not related to motor development at one year of age in patients with a diagnosis of HIE. In our study, the sensitivity of CBMRI findings in determining the long-term prognosis was found to be 80%, the specificity was found to be 54%, the predictive value was found to be 64,5% and the negative predictive value was found to be 75% independent of the findings of involvement in terms of hypoxia which was compatible with the literature.

It is thought that the value of CBMRI in determining the long-term neurologic prognosis is limited (18). Although a normal appearance was found in the T2 and T2 weighted sequences on CBMRI performed on the first few days after birth, severe neurologic defects were reported to be observed in clinical evaluation of the patients (19,20).

Recently, it has been reported that the lesion can be determined with MR spectroscopy and DWBMR in the early period before T1 and T2 weighted CBMR finding appears and the value of MR spectroscopy and DWBMR might be higher in terms of determining the prognosis (21,22,23). Diffusion weighted brain MR imaging is the MRI technique used for evaluation of brain ischemia in the first 10 days after birth (20,21). While conventional brain MR imaging can show a normal result in the first 48 hours in patients with a diagnosis of HIE, the size and severity of the lesion can be determined in the first 24 hours with DWBMR and ADC imaging (21). Studies performed showed that diffusion limitation found on DWBMR in the early period after birth in patients with a diagnosis of HIE was related to poor neurologic prognosis (24,25). However, it was reported that normal ADC findings on imaging performed in the first week of life did not mean that the tissue was normal and ADC value might be observed to be slightly increased or normal in patients with moderate white matter and basal ganglion damage (26). These values were similar to our CBMRI results.

Our study found that the sensitivity of DWBMR in determining long-term neurologic prognosis was 70%, the specificity was 72.7%, the positive predictive value was 70% and the negative predictive value was 72.7%. These results are

Table 2. ADSI results of the patients with Sarnat stage 2 HIE

	ADSI Language cognitive	ADSI Fine motor	ADSI Gross motor	ADSI Social ability Self-care	ADSI General development
Good prognosis	10	9	10	12	11
Borderline development	2	3	3	-	-
Poor prognosis	9	9	8	9	10

ADSI : Ankara developmental screening inventory

Table 3. The relation between cranial MR and involvement on DWBMR and ADSI-GD in patients with Sarnat and Sarnat stage 2

ADSI GD	CBMRI (-) n=8	CBMRI (+) n=13	DWI(-) n=11	DWIG(+) n=10
Good prognosis n=11	6 54.5%	5 45.5%	8 72.7%	3 27.3%
Poor prognosis n=10	2 20.0%	8 80.0%	3 30.0%	7 70.0%

ADSI GD: Ankara developmental screening inventory general development, CBMRI: Conventional brain MR imaging, DWBMR: Diffusion weighted brain MR imaging

Table 4. Diagnostic accuracy rates of CBMRI and DWBMR in terms of determining the prognosis in patients with Sarnat and Sarnat stage 2 HIE

	Specificity	Sensitivity	Positive prediction	Negative prediction
DWBMR	%72.7	%70	%70	%72.7
CBMRI	%54	%80	%61.5	%75

similar to our CBMRI results. While involvement in favor of HIE on CBMRI was found in our patient in Sarnat and Sarnat stage 1 who was found to have a poor prognosis according to ADSI-GD, no involvement was found on DWBMRI. However, no involvement was found on CBMRI, although involvement was found on DWBMRI in our 2 patients who were defined to have a poor prognosis. While no involvement in favour of HIE was found on neither DWBMRI nor CBMRI in our 5 patients who were defined to have a good prognosis according to ADSI-GD, involvement was found on both DWBMRI and CBMRI in our 7 patients who were defined to have a poor prognosis. These results suggest that both imaging methods have a similar prediction level about long-term neurologic prognosis in patients with a diagnosis of Sarnat and Sarnat stage 2 HIE who show poor prognosis especially according to ADSI-GD. However, no statistically significant superiority was found for either imaging method in our study.

The limitations of this study which examined HIE in newborns included limited number of subjects, absence of a control group, absence of apparent diffusion coefficient measurements and selection of a b value of 1000 s/mm² instead of 750 s/mm².

CBMRI and DWBMRI give important information about brain damage in newborns with a diagnosis of hypoxic ischemic encephalopathy. Although recent studies stated that DWBMRI was superior to CBMRI in terms of indicating long-term neurologic prognosis, our results do not support this view. Although the number of patients in our study group was inadequate, it was shown that DWBMRI was not superior to CBMRI in terms of indicating long-term neurologic prognosis in patients with a diagnosis of stage 2 HIE. We believe that it is adequate to use CBMRI which has a wider area of usage instead of DWBMRI which is expensive and not available in all centers in evaluation of newborns with a diagnosis of stage 2 HIE and in predicting the long-term prognosis.

Conflict of interest: none declared.

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