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Early diagnosis and outcome prediction of neonatal hypoxic-ischemic encephalopathy with color Doppler ultrasound

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Abstract
Purpose: To describe the ultrasound presentation of the brain and cerebral hemodynamics in neonates with hypoxic-ischemic encephalopathy (HIE) by comparison with control subjects.
Material and methods: During June 2012 to April 2013, full term neonates who had clinical evidence of HIE were enrolled. Healthy newborns without HIE were used as a control group. Cerebral parenchyma, size of lateral ventricles and hemodynamic parameters of cerebral arteries were studied using two-dimensional duplex and color Doppler ultrasound. Neonates with moderate and severe HIE were followed-up with ultrasound for at least 3 months.
Results: A total of 158 consecutive neonates (82 boys and 76 girls), including 54 with mild HIE, 60 with moderate HIE and 44 with severe HIE were included. One hundred and twenty healthy newborns were randomly selected as a control group. Abnormal ultrasound findings of brain parenchyma were found in 25/54 (46.3%) neonates with mild HIE whereas they were found in 58/60 (96.7%) neonates with moderate HIE and 44/44 (100%) neonates with severe HIE. Almost all neonates with severe HIE had decreased cerebral artery blood flow velocity and increased resistance index of cerebral arteries. Of the 104 neonates with moderate or severe HIE, follow-up ultrasound examination revealed cystic parenchymal lesions in 12/104 (11.5%), progressive ventricular dilatation and brain atrophy in 12/104 (11.5%), mild ventricular dilatation in 15/104 (14.4%) and leukoencephalomalacia in 2/104 (1.9%) neonates.
Conclusion: Ultrasound features such as the size of lateral ventricles, altered brain parenchymal echogenicity and cerebral blood flow parameters are useful for the early diagnosis of HIE and help predict outcome.

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Neonatal hypoxic-ischemic encephalopathy (HIE) is caused by perinatal hypoxic brain injury. It is the main cause of neonatal mortality and neurological dysfunction [1]. Less severe HIE together with timely intervention could have a better prognosis, while severe HIE will leave permanent neurological sequelae [2]. Therefore, it is of major important to make an early diagnosis of HIE with a reliable imaging tool. Magnetic resonance imaging (MRI) of the brain is the most trustable imaging examination for the diagnosis of brain injury [3], but it is impossible to perform MRI immediately in acutely asphyxiated neonate.

Two-dimensional transcranial Doppler ultrasound (US) can provide detailed information on brain hemodynamics [4]. US can reflect the changes of cerebral blood flow after newborn asphyxia suffocation [5]. Moreover, US helps detect intracerebral lesions such as hydrocephalus, intraventricular hemorrhage, and infarction of the neonatal brain.

The goal of this study was to describe the ultrasound presentation of the brain and cerebral hemodynamics in neonates with hypoxic-ischemic encephalopathy (HIE) by comparison with control subjects.

Materials and methods

Patients

This study was approved by the Institutional Review Board of our institution and written consent was obtained from the parents of each child. During June 2012 to April 2013, full term neonates who met clinical evidence of HIE determined by clinical evaluation of consciousness, neuromuscular control, complex reflexes, autonomic function and presence of seizures were enrolled [6,7]. The control group consisted of healthy newborns without asphyxia and hypoxia history, who were randomly selected for transcranial US during the same time course at Guangzhou Women and Children Medical Center.

US examination

US examinations were performed with a SSA-660A scanner (Toshiba Medical Systems, Tokyo, Japan) that incorporated a 3.5-MHz curvilinear transducer and a 12-MHz linear array transducer, an EUB-7000HV scanner (Hitachi Medical Corporation, Tokyo, Japan) that incorporated a 2—5-MHz curvilinear transducer and a 6—13-MHz linear array transducer. Initial US examination was performed within 72 hours after birth by one radiologist with an experience of more than 10 years in neonatal cranial US. Neonates were kept in a quiet state with supine position. Firstly, the following items were assessed on sagittal and coronal planes through anterior fontanel:

- morphological structure of brain tissue;
- size and location of US abnormalities;
- size and shape of lateral ventricles;
- anterior cerebral artery (ACA) blood flow parameters using color Doppler flow image (CDFI), color Doppler energy (CDE) and pulsed wave Doppler (PWD).

We then scanned through temporal cross-section to display skull base arterial rings with CDFI and CDE, measured middle cerebral artery (MCA) blood flow parameters, detected bilateral lesions and recorded the focus lesion situation in dynamic images by using high-frequency probe through anterior fontanel and temporal cross-section. The blood flow parameters included resistance index (RI), systolic velocity (Vs) and diastolic velocity (Vd). RI was calculated with the following formula:

$$RI = \frac{Vs - Vd}{Vs}$$

All US examinations were performed under the same instrument settings, and each Doppler parameter was averaged on 3 to 4 cardiac cycles.

Imaging analysis

The US examinations of each neonate of the study group were reviewed in consensus by two radiologists with more than 10 years of experience in neonatal cranial US to determine the severity of HIE. These two radiologists were not involved in data acquisition. The severity of HIE for every neonate were classified into three categories as follows:

- mild: small hyperechoic foci of brain parenchyma echogenicity were predominantly located in the periventricular areas;
- moderate: more than two lobes of brain were diffusely hyperechoic, with obscure boundary of white-gray matter and narrowing lateral ventricle;
- severe: when diffuse parenchymal hyperechoic areas, and some with no echos, gray and white matter boundaries disappeared, while the lateral ventricle being compressed by intracranial hemorrhage [3—5].

For neonates who were classified into moderate and severe HIE on initial US examination, follow-up US examinations was performed three or four times a week and the follow-up was continued for at least 3 months [8].

Statistical analysis

Statistical analysis was performed with software (SPSS, version 16; SPSS, Chicago, IL, USA). Quantitative variables were expressed as mean ± standard deviation (SD) and ranges. Differences between the two groups were searched using Student *t*-test for quantitative variables and Chi^2 (χ^2) test for categorical variables. Significance was set at $P < 0.05$.

Results

Initial brain US

A total of 158 consecutive neonates (82 boys and 76 girls) with HIE, including 54 (54/158; 34.2%) with mild HIE, 60 (60/158; 38.0%) with moderate HIE and 44 (44/158; 27.8%) with severe HIE were enrolled. One hundred and twenty healthy newborns were randomly selected for transcranial US and served as a control group. No significant differences in gestational age, gender and body weight of the newborns were found between the two groups.

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