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Diffusion-weighted imaging in the evaluation of watershed hypoxic-ischemic brain injury in pediatric patients

Abstract  The purpose of our study was to determine the usefulness of echo-planar diffusion-weighted imaging (EPDI) in the evaluation of watershed hypoxic-ischemic brain injury in pediatric patients. Eighteen patients ranging in age from 3 weeks to 12 years were evaluated for evidence of ischemic/infarction changes on conventional MR and EPDI. Included in the study group were five patients with sickle cell disease, four with congenital heart disease, four with hypotensive episodes with various etiologies, three with sepsis, and two with encephalitis or meningitis. Patients were examined 2 h to 6 days after the initial insult, with follow-up studies in four patients at 1 to 62 days after the initial examination. After conventional MR imaging (T1, FSE T2, and FLAIR), diffusion-weighted MR imaging was performed using high-speed, single-shot EP techniques with TR 6000, TE 144, matrix 96 × 128, FOV 23.3 × 31 and five b values of 0, 160, 360, 640, and 1,000 s/mm². EPDI demonstrated abnormally increased signal in watershed ischemic/infarction zones in all initial cases. Apparent diffusion coefficients (ADC) were obtained in 59 lesions. When compared with radiographically normal (on EPDI) contralateral brain parenchyma, 45 demonstrated a relatively decreased ADC, while eight had normal (± 10%) and six had increased ADC. In four cases, signal abnormalities on EPDI were not seen or exceeded that seen with conventional MR imaging. In the remaining cases, signal abnormalities were obvious on EPDI and more subtle on conventional MR imaging. Follow-up studies demonstrated resolution of abnormal EPDI signal with persistent abnormalities on conventional imaging in some cases, while others revealed an increase in size or number of EPDI signal abnormalities, suggesting ongoing acute ischemic/infarctive changes. EPDI is a rapid, sensitive technique for detecting watershed ischemic/infarction changes in pediatric patients with hypoperfusion episodes, at times before such changes are apparent on conventional MR images and/or are clinically apparent.

Keywords  Pediatric brain · Echo-planar imaging · Diffusion imaging · Hypoxic-ischemic brain injury

Introduction
Watershed hypoxic-ischemic brain injury is the endpoint of a variety of medical conditions occurring in pediatric patients, including sickle cell disease, sepsis, congenital heart disease, and cardiovascular collapse. The common link in these disease processes is decreased perfusion to the brain, which may result from
decreased blood pressure and loss of vascular autoregulation [1, 2].

CT is relatively insensitive in detecting acute stroke and often appears normal in the first 24–48 h [3, 4]. Although conventional MR imaging (including T1- and T2-weighted imaging) is more sensitive than CT in detecting acute cerebral infarction [5], signal changes are not usually found before 8 h on T2-weighted images [6].

Diffusion-weighted MR imaging (DWI) measures the microscopic motion of water molecules and effectively detects small differences and changes in net translational movement of water. DWI has been extensively shown to be more sensitive than conventional MR imaging in the evaluation of acute ischemic changes in both animal models [7] and in the adult human population [8, 9]. Still others have concluded that DWI can be helpful in differentiating acute from chronic stroke [10]. In pediatric patients, although DWI has been utilized for the evaluation of myelination and normal brain development [11–15], there are relatively few published reports which evaluate the ability of DWI to detect acute stroke [16]. The purpose of this study is to determine the usefulness of echo-planar DWI in pediatric patients with suspected watershed hypoxic-ischemic brain injury.

Materials and methods

A total of 18 patients ranging in age from 3 weeks to 12 years was evaluated for evidence of ischemic changes on conventional MR and echo-planar diffusion-weighted imaging (EPDI). Included in the study group were five patients with sickle cell disease, four with congenital heart disease, four with hypotensive episodes with varying etiologies (lupus complicated by pericardial effusion, cardiovascular collapse during surgery, hypotensive episode during cardiac catheterization, and multisystem organ failure), three with sepsis, two with encephalitis or meningitis. This is summarized in Table 1. Patients were examined 2 h to 6 days after the initial ischemic event, and follow-up examinations were obtained in four patients at 1 to 62 days after the initial examination.

Imaging was performed using a standard head coil on a Siemens "Vision" 1.5 T whole body MR system. Conventional MR imaging included the following sequences: T1 (TR/TE 650/14), FSE T2 (TR/TE 6000/99), and FLAIR (TR/TE/TI 9000/119/2200). After conventional imaging sequences were obtained, diffusion-weighted MR imaging was performed using single-shot echo-planar sequences. For each slice, three sets of images were acquired, with five b values (0, 160, 360, 640, and 1,000 s/mm²) parallel to the Z, X, and Y gradients of the magnet. The sequence parameters were: TR 6000 s, TE 144 ms, matrix 96 × 128, FOV 23.3 × 31 cm. The diffusion images added approximately 1 min to the total examination time. The images were then processed off-line on a SUN SPARC workstation using software written specifically for this project using IDL (Research Systems CO). The diffusion-weighted images were first corrected for eddy current distortions as described by Haselgrove and Moore [17]. In order to distinguish the effects of diffusion and T2* on the diffusion-weighted images, we calculated maps of the apparent diffusion coefficients (ADC) in each of the three directions (X, Y, Z) using a least square fit of the ln (signal-intensity) against the b values (0, 1610, 260, 640, 1,000 s/mm²) for each pixel. Finally the trace image was calculated as the average of the three directional ADC images.

Regions of interest (ROI) were drawn on the diffusion ADC maps based on the areas of signal abnormality seen on the diffusion-weighted images. In each case, the areas of increased signal were identified in the same location within the brain parenchyma in the X, Y, and Z planes. The ADC values for the focal areas of abnormality were compared with those of contralateral normal-appearing brain parenchyma (i.e. areas without abnormal signal). When the abnormal signal was present bilaterally, the area was compared with ipsilateral normal-appearing brain parenchyma slightly above or below the lesion in question.

To ensure the accuracy of ADC measurements for the areas of abnormality, we also obtained ADC values in the CSF. The ADC for CSF, measured in the lateral ventricles, was approximately 300 × 10⁻³ mm²/s.

Results

A total of 22 MR examinations was obtained in the 18 patients. In each of these cases, EPDI demonstrated abnormally increased or decreased signal in watershed ischemic zones.

Fifty-nine lesions were identified on diffusion-weighted images in watershed regions, and ADC values were obtained in each of these lesions. Lesions which appeared hyperintense on the diffusion-weighted images appeared hypointense on the ADC maps. Conversely, hypointense lesions on diffusion-weighted images appeared hyperintense on the ADC maps.

When compared with radiographically normal (on EPDI) brain parenchyma, 45 lesions demonstrated a relatively decreased ADC (greater than 10% below normal, while eight had normal (within 10% of normal), and six had increased ADC values (greater than 10% above normal). A scatter plot of the relationship between percent of normal ADC (degree of increase or decrease in the ADC) and the time to imaging (time between onset of symptoms and time of the MR imaging examination) is shown in Fig. 1. In several cases, the time interval between onset of symptoms and the MR imaging could only be estimated to within 1 day due to the uncertainty of, and difficulty in, obtaining clinical history, which was particularly difficult in our pediatric population. Given the relatively small number of patients and lesions in our study, as well as the uncertainties in clinical history, rigorous statistical analysis was not possible. Nevertheless, there was a preponderance of lesions with relatively decreased ADCs in our study. Of the 51 lesions examined within 6 days of symptom onset, 42 (82%) had decreased ADCs, while six (12%) were normal and three (6%) had increased ADCs.

Lesions which had ADC values within 10% of normal appeared iso- to slightly hyperintense. All of the lesions were considerably more conspicuous on the diffusion-weighted images than on the ADC maps.