Diffusion Weighted Imaging of Brain in Fulminant Hepatic Failure

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Introduction: Nature of fulminant hepatic failure (FHF) associated cerebral edema (CE) (vasogenic or cytotoxic) in FHF is not known. In experimental model of FHF there is evidence of cytotoxic and vasogenic edema, but former seems to be the possible mechanism. Conventional magnetic resonance imaging (MRI) of brain is known to detect the cerebral edema in liver failure, however it is unable differentiate between these two types of CE. This is based on few imaging studies available in patients with FHF[6]. This study was done to find out distribution of CE in different areas of brain, nature of CE (cytotoxic or vasogenic) and its reversibility in survivors using diffusion weighted imaging (DWI) in patients with FHF.

Methods: Seven patients with FHF (4 male, median age 18 years,) and 13 controls (10 male, median age 27 years). The etiology of FHF was acute viral hepatitis in 4, drug induced hepatitis in 2 and unknown in 1. Cranial MRI was performed on a 1.5-T MR scanner. fast spin echo (FSE) T2-Weighted (T2-W) imaging along with DWI was performed in the axial plane by using a single shot EPI-SE pulse sequence with: TR/TE= 10.5 s/ 110 ms (minimum), FOV = 24×24 cm, NEX= 2, slice thickness =5 mm, interslice gap= 0.5 mm, matrix size of 128×128. Diffusion sensitizing gradients were applied sequentially along the three orthogonal directions with diffusion sensitivity of b =0 and 1000 s/mm^2 with ramp sampling on. An in-house software generate ADC maps from the DW images (b=0 and 1000 s/mm^2). Regions of interest (ROIs) of 2×2-pixel dimensions were drawn in 8 cortical areas (bilaterally in frontal, parietal and occipital cortical gray matter) and deep white matter (genu and splenium of corpus callosum, bilateral periventricular occipital, frontal and cingulum) and deep gray matter (caudate nucleus and putamen bilaterally) in a total of 12 locations (Fig 1a). Raised ICP was diagnosed in presence of decerebrate posturing alone or, when two out of four of the following criteria were met, i.e. hypertension (supine blood pressure > 150/90 mm hg), bradycardia (pulse rate <10/min for the expected pulse rate for the given body temperature), pupillary changes and neurogenic hyperventilation. One patient underwent live-related liver transplantation, 5 patients died (including the one who underwent liver transplantation) and 2 patients survived on conservative therapy and underwent repeat DW imaging as soon as possible after clinical stabilization (4 and 9 days after the initial imaging).

Results: Four of seven patients showed normal T2-W images (Fig 1b) and two of them had small old lacunar infarct in the periventricular white matter. Remaining one had multifocal hyperintensity on T2-W imaging. The results of ADC in patients with FHF are shown in table. Median ADC in all ROIs in both lobes was significantly lower (Fig 1c) in patients with FHF than in controls (table). One survivor patient who showed no improvement in ADC (Fig 1d) of any cortical and deep white matter areas on repeat study. MRI of this patient showed diffuse abnormality on initial study even on T2-W images and those persisted in the repeat MRI. However, this patient improved clinically with no gross residual sensory-motor deficit. The other patient showed significant improvement in the ADC in all cortical areas and deep gray, white matter and associated with complete clinical recovery (Fig 1e).

Table: ADC values in deep white and gray matter and cortical areas of patients with FHF (n=7) and controls (n=13). * Wilcoxon signed-rank test

ROI	ADC of patients, Median (range)	ADC of controls , Median (range)	p-value*
Genu of corpus callosum	75.6 (62.6-83.0)	84.3 (65.6-93.6)	0.001
Right occipital white matter	72.3 (62.3-82.0)	86.0 (76.3-97.6)	0.001
Left occipital white matter	76.3 (64.3-85.3)	82.6 (72.0-94.3)	0.001
Splenium of corpus callosum	77.6 (43.3-82.6)	88.3 (78.3-101.0)	0.001
Right cingulum white matter	74.0 (68.3-81.3)	82.3 (78.6-89.7)	0.001
Left cingulum white matter	81.6 (59.3-85.6)	85.6 (74.66-89.7)	0.001
Right caudate nucleus	69.0 (48.6-84.0)	77.6 (74.0-81.3)	0.001
Left caudate nucleus	68.3 (46.0-77.3)	72.3 (69.3-82.0)	0.001
Right lentiform nucleus	65.0 (52.0-78.3)	74.0 (70.3-82.0)	0.001
Left lentiform nucleus	65.3 (37.3-73.3)	80.0 (75.0-85.3)	0.001
Right frontal white matter	72.0 (61.0-87.3)	87.3 (78.3-95.00	0.001
Left frontal white matter	72.3 (57.3-81.0)	85.6 (84.6-95.0)	0.001
Right frontal cortex	57.8 (51.0-74.8)	86.6 (83.6-94.0)	0.001
Left frontal cortex	56.7 (53.4-73.6)	89.8 (77.8-98.2)	0.001
Right cingulate cortex	65.8 (51.2-76.0)	88.2 (82.6-94.0)	0.001
Left cingulate cortex	59.6 (50.6-76.4)	85.0 (79.0-88.4)	0.001
Right occipital cortex	60.2 (57.8-65.6)	88.0 (71.4-98.2)	0.001
Left occipital cortex	58.2 (46.8-70.3)	90.8 (80.2-96.2)	0.001
Right parietal cortex	59.8 (48.0-69.2)	89.2 (79.6-92.2)	0.001
Left parietal cortex	63.2 (52.1-70.2)	89.6 (78.6-93.4)	0.001

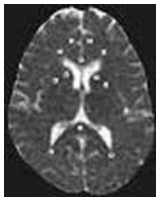
Fig 1a

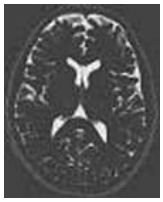
Fig 1b

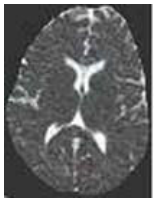
Fig 1c

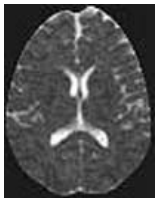
Fig 1d

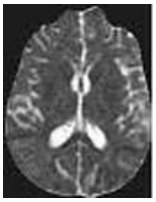
Fig 1e

Discussion: Significant reduction in ADC value in patients with FHF as compared to controls in different regions of brain indicative of global involvement of CE and mainly cytotoxic in nature. This suggests that the increase in brain water in patients with FHF is due to increase in intra-cellular water. We conclude that cerebral edema in patients with FHF is predominantly cytotoxic. The possible mechanism of CE is astrocyte swelling due to effects of ammonia metabolism. However other factors such as hypoxia and hypoglycemia may also be operative in FHF and contribute to astrocyte swelling.