Quantification of Cerebral Blood Flow (CBF) in Acute-on Chronic Liver Failure (ACLF) patients with 3D Pseudo continuous Arterial Spin Labeling

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Introduction: Acute-on-chronic liver (ACLF) failure develops in patients with previously well-compensated chronic liver disease following an acute precipitating event (1). Alteration in cerebral blood flow (CBF) is well reported in acute liver failure (ALF) patients (2). There are various imaging techniques that can potentially be used to study the CBF changes such as positron emission tomography (PET), arterial spin labeling (ASL) and contrast-enhanced perfusion MR (CEMRI) (3). A number of studies have reported CBF measurement with ASL, both in normal subjects (4) and in various cerebrovascular and psychiatric diseases (5). It is known that the cerebral autoregulation may be defective in patients of liver failure (6), and raised ICP is often seen in ALF patients (6). There is increasing evidence that increased CBF may be responsible for elevated intracranial pressure (ICP) in ALF (6, 7). However studies in patients with ALF have shown wide variations in the measured values of CBF (7). It has been reported that the increased blood ammonia and proinflammatory cytokines may be involved in the alteration in CBF in ALF patients by modulating the autoregulation (8). There are reports of CBF alteration in patients of HE which is implicated in the pathogenesis of HE and in the development of cerebral edema (2). Both ammonia and cytokines are known to be increased in ACLF and are known to suggest synergistic role in pathogenesis of HE (8). The aim of this study was to quantify the CBF changes in ACLF patients in both gray and white matter by using non-invasive 3D pseudocontineous ASL technique.

Material and methods: Eleven patients with ACLF (mean age 34±11years), and 10 controls were included in this study. The study protocol was approved by the institutional ethics committee and written informed consent obtained by caregiver. ACLF was diagnosed when there was evidence of acute hepatitis, defined as an abrupt rise (over < 4 weeks) in serum bilirubin to ≥10 mg% and ALT to ≥5 times of normal (≥200 IU/L), developing in a patient with clinical, biochemical or ultrasonographic evidence of liver cirrhosis. Conventional MRI, 3D pseudo-continuous arterial spin labeling (PC ASL) was recorded in all patients as well as in controls. ASL was performed using following parameters (Frequency=512/Phage=8/NEX=3/no. of slice=46/FOV=24/slice thickness=3 mm/Band width=62.50) using 3T MRI (Signa HDXT, GE Healthcare, USA). Total time required for whole imaging was 15 minutes. ASL derived CBF were compared by independent t test between controls and patients. Statistical analysis was performed by using SPSS 16.

Results: On ASL, ACLF patients showed significantly increased CBF (Figure 1) in 7 regions [temporal lobe (TL) p=0.05, parietal lobe (PL, p=0.05), anterior cingulate gyrus (ACG, p=0.01), caudate nuclei (CN, p=0.01), putamen (PUT, p=0.01), globus pallidus (GP, p=0.01), and thalamus (THAL, p=0.01)] out of 10 regions in gray matter (Table 1); however it did not show any significant change in any of white matter regions [frontal white matter (FWM), occipital white matter (OWM), genu, splenium (SPL), anterior limb of internal capsule (ALIC), and posterior limb of internal capsule (PLIC)] (Table 2) as compared to controls.

Regions	Groups		p-Value
	Controls	Patients	
FGM	36.80±13.48	45.69±3.21	0.15
TGM	46.10±5.57	66.25±16.28	0.05
PGM	44.63±9.79	62.05±14.07	0.05
OGM	45.73±12.25	56.89±21.13	0.33
ACG	38.43±6.09	54.86±8.96	0.01
PCG	53.00±8.76	72.14±24.36	0.13
CN	39.87±3.55	55.68±5.15	0.01
PUT	35.39±5.84	64.48±8.94	0.01
GP	32.35±5.64	57.30±7.15	0.01
THAL	35.95±3.36	62.46±5.19	0.01

Table 1: Summary of CBF (ml/100g/min) values of different gray matter regions of ACLF patients and controls.

Regions	Groups		p-Value
	Control	Patients	
FWM	8.73±3.27	11.00±2.43	0.25
OWM	8.67±5.89	9.71±2.54	0.72
Genu	11.00±3.27	12.35±5.38	0.64
SPL	22.11±6.83	15.92±8.64	0.24
ALIC	20.80±9.37	26.13±9.07	0.38
PLIC	17.65±3.51	19.18±8.85	0.73

Table 2: Summary of CBF (ml/100g/min) values of different white matter regions of ACLF patients and controls.

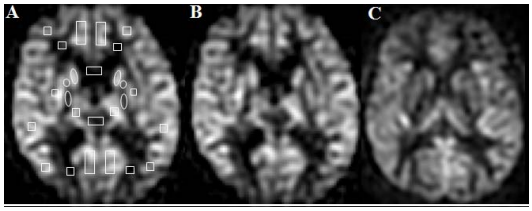

Figure 1: (A) Showing ROIs placement in gray and white matter. CBF image of patient (B) showing increased signal in grey matter regions as compare to control (C).

Discussion: In this study we observed significantly increased CBF in these patients in gray matter as compared to controls, however no significant changes were observed in any region of the brain in white matter as compared to controls. It is well established that patients of HE have significantly altered CBF, however the report of increasing or decreeing the CBF in patients of HE is inconsistent (9). It has been reported that ammonia is mainly responsible for the changes in CBF in these patients (8). The extraction of ammonia in brain varies in different brain regions and it may determine the variations in the CBF in different brain regions in these patients (8). The extraction of ammonia in the brain is carried out by the astrocytic cells, and most of astrocytic cells are present in the gray matter as compared to white matter that may be responsible for significantly increased CBF in gray matter as compared to white matter in our study. It is reported that there is significant linear correlation between TNF-α and CBF indicating that these proinflammatory cytokines are also involved in the alteration of CBF in HE (10). Our study suggest that ASL, a noncontrast enhanced technique demonstrates the CBF changes in ACLF and may be useful in the initial and follow up study of these patients.

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