Increased expression of GLUT 1 in patients with acute liver failure

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Background: Acute liver failure (ALF) resulting in cerebral edema and intracranial pressure has been shown to cause disturbances in brain oxidative metabolites. Spectroscopic and gene expression studies in experimental ALF models reveal that altered brain oxidative glucose metabolism and lactate synthesis may be implicated in the cerebral complications of ALF. Glucose transporter 1 (GLUT 1), a facilitative glucose transporter that transports glucose across the blood brain barrier is required to sustain brain energy metabolism. We investigated to study the GLUT 1 expression in the brains of patients with acute liver failure.

Methods: In order to address this issue, dissected samples of cerebral cortex were obtained at autopsy from 8 patients with ALF due to either viral hepatitis or toxic liver injury and from 7 patients with no evidence of liver disease or other neurological disorders (control) matched for gender (ALF, 4 men; control, 4 men) and post-mortem delay intervals [ALF, median 245 minutes (range 180-415); control median 240 minutes (135-870)]. All ALF patients had high grade hepatic encephalopathy and, there was evidence of brain edema on autopsy in all. Expression of GLUT 1 mRNA was investigated by real-time PCR using appropriate molecular probes and protein expression was assessed using both immunoblotting (western) techniques as well as immunohistochemistry using commercially-available polyclonal antibodies.

Results: Expression of GLUT-1 at both the mRNA (7.8 folds; P=0.003) and protein levels (3.02±0.24 vs 2.44±0.55; P=0.020) was significantly increased in frontal cortex of ALF patients compared to control material respectively. Immunohistochemical analysis confirmed the increase of GLUT-1 immunoreactivity in endothelial cells in the frontal cortex of ALF compared to control cortex.

Conclusion: These results demonstrated that altered expression of GLUT 1 was involved in disturbances in the brain energy metabolism and could contribute to the pathophysiological mechanisms responsible for the neurological complications of ALF.

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