Cerebral ischemia pathophysiology

Hypocapnia induces cerebral vasoconstriction leading to a decrease in cerebral blood flow, which might precipitate cerebral ischemia.

It is a well recognized and common cause of irreversible ischemic stroke.

The observation that brain cells are more resistant to ischemia than was previously assumed on the basis of clinical experience has stimulated considerable investigative work designed to determine those factors responsible for irreversible ischemic cell damage [1].

Knowledge regarding the pathophysiology of cerebral ischemia and brain trauma indicates that similar mechanisms contribute to loss of cellular integrity and tissue destruction.

Experimentally, injury to central neurons begins only with anoxic depolarization. This potentially reversible, spreading wave typically starts 2-5 min after the onset of severe ischemia, marking the onset of a toxic intraneuronal change that eventually results in irreversible injury.

To investigate this in the human brain, Dreier et al. from the Center for Stroke Research Berlin performed recordings with either subdural electrode strips (n=4) or intraparenchymal electrode arrays (n=5) in patients with devastating brain injury that resulted in activation of a Do Not Resuscitate-Comfort Care order followed by terminal extubation.

Withdrawal of life-sustaining therapies produced a decline in brain tissue partial pressure of oxygen(pti O2) and circulatory arrest. Silencing of spontaneous electrical activity developed simultaneously across regional electrode arrays in eight patients. This silencing, termed 'nonspreading depression', developed during the steep falling phase of pti O2 (intraparenchymal sensor, n=6) at 11 (7, 14) mmHg. Terminal spreading depolarization started to propagate between electrodes 3.9 (2.6, 6.3) min after onset of the final drop in perfusion and 13 to 266s after nonspreading depression. In one patient, terminal spreading depolarization induced the initial electrocerebral silence in a spreading depression pattern; circulatory arrest developed thereafter.

These results provide fundamental insight into the neurobiology of dying and have important implications for survivable cerebral ischemic insults [2].

Mechanisms of cell damage include excitotoxicity, oxidative stress, free radical production, apoptosis and inflammation. Genetic and gender factors have also been shown to be important mediators of pathomechanisms present in both injury settings. However, the fact that these injuries arise from different types of primary insults leads to diverse cellular vulnerability patterns as well as a spectrum of injury processes.

Blunt head trauma produces shear forces that result in primary membrane damage to neuronal cell bodies, white matter structures and vascular beds as well as secondary injury mechanisms. Severe cerebral ischemic insults lead to metabolic stress, ionic perturbations, and a complex cascade of biochemical and molecular events ultimately causing neuronal death. Similarities in the pathogenesis of these cerebral injuries may indicate that therapeutic strategies protective following ischemia may also be beneficial after trauma [3].

1)
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2)
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3)
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