Central Nervous System Edema

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The concept of cerebral edema has been recognized for more than 2000 years, yet an understanding of the complex physiology of this condition has evolved only within the past 30 years.

Cerebral edema is frequently encountered in clinical practice in critically ill patients with acute brain injury from diverse origins and is a major cause of increased morbidity and death. The consequences of cerebral edema can be lethal and include cerebral ischemia from compromised regional or global cerebral blood flow and intracranial compartmental shifts due to intracranial pressure gradients that result in compression of vital brain structures

Despite the classification of edema into distinct forms as: vasogenic, cytotoxic, hydrocephalic and osmotic; This classification is highly simplistic, given that it pertains to complex pathophysiological and molecular mechanisms, but is valuable as a simple therapeutic guide for treatment of cerebral edema. Most brain insults involve a combination of these fundamental subtypes, although one can predominate depending on the type and duration of injury.

Cytotoxic edema results from swelling of the cellular elements (neurons, glia, and endothelial cells) because of substrate and energy failure, and affects both gray and white matter. This edema subtype is conventionally encountered in: cerebral ischemia, traumatic brain injury, infections, and metabolic disorders including kidney and liver failure.

Vasogenic edema that results from breakdown of the BBB due to increased vascular permeability, as commonly encountered in: hemorrhage, later stages of brain infarction, TBI, infections, seizures, trauma, tumors, radiation injury and hypertensive encephalopathy, predominantly affects white matter.

Interstitial edema, a consequence of impaired absorption of CSF, leads to increases in transependymal CSF flow, resulting in acute hydrocephalus. This edema subtype is not responsive to steroid administration, and to osmotherapy.

In osmotic edema there is an osmotic gradient between plasma and the extracellular fluid. Edema may occur with hypo-osmolar conditions including: improper administration of intravenous fluids, inappropriate antidiuretic hormone secretion, excessive hemodialysis of uremic patients and diabetic ketoacidosis.

Basic information about the types of edema is provided for better understanding of the expression pattern of some of the newer molecules implicated in the pathogenesis of brain edema. These molecules include the aquaporins (AQP), matrix metalloproteinases (MMPs) and growth factors such as vascular endothelial growth factors (VEGF) A and B and the angiopoietins. The potential of these agents in the treatment of edema is the subject of many reviews.

Neuroimaging by CT scans and magnetic resonance imaging can be particularly useful in confirming intracranial compartmental and midline shifts, herniation syndromes, ischemic brain injury, and exacerbation of cerebral edema (sulcal effacement and obliteration of basal cisterns).

Medical management of cerebral edema involves using a systematic and algorithmic approach, from general measures (optimal head and neck positioning for facilitating intracranial venous outflow, avoidance of dehydration and systemic hypotension, and maintenance of normothermia) to specific therapeutic interventions (controlled hyperventilation, administration of corticosteroids and diuretics, osmotherapy, and pharmacological cerebral metabolic suppression).

Traumatic insults to the spinal cord disrupt the functional integrity of the blood-spinal cord barrier (BSCB) and results into an increased transport of several substances from the vascular compartment to the spinal cord cellular microenvironment. Transport of macromolecules like proteins from the vascular compartment to the spinal cord microenvironment induces vasogenic edema

New pharmacotherapeutic agents that reduce trauma induced alterations in the BSCB and cell injury may strengthen the effects of endogenous neuroprotective agents and minimize the adverse influence of neurodestructive elements. Thus, drugs or agents that are capable to minimize trauma induced BSCB breakdown could be the promising therapeutic agents for the treatment of SCI in the future

Hence the significance of brain edema, which continues to be a major cause of mortality after diverse types of brain pathologies, the lack of effective treatment, remains a stimulus for continued interest and research into the pathogenesis of this condition

Research in the last decade has led to an appreciation of the complexity of brain edema pathogenesis and to the awareness that many molecules are involved in it. This suggests that effective treatment of brain edema cannot be achieved by a single agent, but will require the administration of a "magic bullet" containing a variety of agents released at different times during the course of edema in order to be successful

Current uncertainties and deficiencies must be resolved by continuing research, fueled by growing understanding of the pathophysiological processes responsible for the formation of the different forms of brain edema.

Probably in the days to come we can look forward to newer agents specifically acting on the various chemical mediators involved in the pathogenesis of cerebral edema

Many Thanks