Brain edema treatment

Standard clinical protocols for treating brain edema and intracranial hypertension after severe traumatic brain injury have remained remarkably similar over decades. Cerebral edema and intracranial hypertension are treated interchangeably when in fact intracranial pressure (ICP) is a proxy for cerebral edema but also other processes such as the extent of mass lesions, hydrocephalus, or cerebral blood volume. A complex interplay of multiple molecular mechanisms results in cerebral edema after severe TBI, and these are not measured or targeted by current clinically available tools. Addressing these underpinnings may be key to preventing or treating cerebral edema and improving outcome after severe TBI.

Jha et al. outlined an evolving precision medicine and translational approach towards cerebral edema and intracranial hypertension after severe TBI [1)].

Since brain edema presents a danger to the patient, treatment of cerebral contusion aims to prevent swelling. Measures to avoid swelling include prevention of hypotension, hyponatremia, and hypercapnia.

The early massive edema caused by severe cerebral contusion results in progressive intracranial pressure (ICP) elevation and clinical deterioration within 24-72 h post-trauma. Surgical excision of the necrotic brain tissue represents the only therapy, which can provide satisfactory control of the elevated ICP and clinical deterioration.

Contusions are likely to heal on their own without medical intervention.

Despite decades of research into the pathogenesis of cerebral edema, nonsurgical therapy for brain swelling has advanced very little after more than half a century. Recent advancements in our understanding of molecular water transport have generated interest in new targets for edema therapy.

see aquaporin 4

Monitoring of the patient's condition in the intensive care unit is a necessity. It is important to ensure proper positioning of the patient–the head should be tilted at 30 degrees in order to optimize the cerebral perfusion pressure and control of the increase in intracranial pressure. Hyperventilation should be applied. Controlled hypothermia decreases the rate of metabolism in the brain. Slightly positive fluid balance should be maintained using crystalloid or colloid (hypertonic-hyperoncotic) solutions, at the same time maintaining cerebral perfusion pressure exceeding 70 mmHg. The treatment includes administration of antihypertensive medications, nonsteroidal antiinflammatory drugs, and barbiturates. Steroids decrease the permeability of capillaries and the hemato-encephalic barrier, promoting the movement of Na(+)/K(+) ions and water through the main endothelial membrane, and therefore they are used in the treatment of vasogenic cerebral edema as well as edema caused by a cerebral tumor. Glutamate and N-methyl-D-aspartate receptor antagonists improve cerebral microcirculation and metabolism. Trometamol corrects cerebral acidosis. Extended cerebral edema is treated surgically via a bilateral decompressive craniotomy, sometimes including craniotomy of lateral and posterior fossae. The treatment of cerebral edema is complex, and positive

results may be expected only if the diagnosis and the provision of assistance are timely [2].

Mannitol is recommended as a first-line dehydration treatment to reduce brain edema and enable brain relaxation during neurosurgery. Research has indicated that mannitol enhanced brain relaxation in patients undergoing supratentorial tumor surgery; however, these results need further confirmation, and the optimal mannitol dose has not yet been established. We propose to examine whether different doses of 20% mannitol improve brain relaxation in a dose-dependent manner when administered at the time of incision. We will examine patients with preexisting mass effects and midline shift undergoing elective supratentorial brain tumor surgery.

Trial registration: The study is registered with the registry website http://www.chictr.org with the registration number ChiCTRTRC13003984 [3].

Evidence suggests low molecular weight heparin reduces brain edema and improves neurological recovery following stroke and traumatic brain injury (TBI), through blunting of cerebral leukocyte (LEU) recruitment. It remains unknown if unfractionated heparin (UFH) similarly affects brain inflammation and neurological recovery post TBI.

Prophylaxis was associated with decreased risk of pulmonary embolism and deep vein thrombosis, but no increase in risk of late neurosurgical intervention or death. Early prophylaxis may be safe and should be the goal for each patient in the context of appropriate risk stratification [4].

Unfractionated heparin (UFH) after TBI reduces LEU recruitment, microvascular permeability and brain edema to injured brain. Lower UFH doses concurrently improve neurological recovery while higher UFH may worsen functional recovery. Further study is needed to determine if this is due to increased bleeding from injured brain with higher UFH doses [5].

Mirroring Enoxaparin (ENX), HMGB1 signaling blockade reduces LEU recruitment, cerebrovascular permeability, and brain edema following TBI. ENX further reduced lung edema indicating a multifaceted effect beyond HMGB1 blockade. Further study is needed to determine how ENX may play a role in blunting HMGB1 signaling in brain injury patients [6].

1)
Jha RM, Kochanek PM. A Precision Medicine Approach to Cerebral Edema and Intracranial Hypertension after Severe Traumatic Brain Injury: Quo Vadis? Curr Neurol Neurosci Rep. 2018 Nov 7;18(12):105. doi: 10.1007/s11910-018-0912-9. Review. PubMed PMID: 30406315; PubMed Central PMCID: PMC6589108.
2)
Adukauskiene D, Bivainyte A, Radaviciūte E. [Cerebral edema and its treatment]. Medicina (Kaunas). 2007;43(2):170-6. Review. Lithuanian. PubMed PMID: 17329953.
3)
Peng Y, Liu X, Wang A, Han R. The effect of mannitol on intraoperative brain relaxation in patients undergoing supratentorial tumor surgery: study protocol for a randomized controlled trial. Trials. 2014 May 10;15(1):165. [Epub ahead of print] PubMed PMID: 24884731.
4)
Byrne JP, Mason SA, Gomez D, Hoeft C, Subacius H, Xiong W, Neal M, Pirouzmand F, Nathens AB. Timing of Pharmacologic Venous Thromboembolism Prophylaxis in Severe Traumatic Brain Injury: A Propensity-Matched Cohort Study. J Am Coll Surg. 2016 Jul 21. pii: S1072-7515(16)30651-2. doi:

10.1016/j.jamcollsurg.2016.06.382. [Epub ahead of print] PubMed PMID: 27453296.
5)

Nagata K, Kumasaka K, Browne KD, Li S, St-Pierre J, Cognetti J, Marks J, Johnson VE, Smith DH, Pascual JL. Unfractionated heparin after TBI reduces in vivo cerebrovascular inflammation, brain edema and accelerates cognitive recovery. J Trauma Acute Care Surg. 2016 Aug 16. [Epub ahead of print] PubMed PMID: 27533909.
6)

Li S, Eisenstadt R, Kumasaka K, Johnson VE, Marks J, Nagata K, Browne KD, Smith DH, Pascual JL. Does enoxaparin interfere with HMGB1 signaling after TBI? A potential mechanism for reduced cerebral edema and neurologic recovery. J Trauma Acute Care Surg. 2016 Mar;80(3):381-7; discussion 387-9. doi: 10.1097/TA.0000000000000935. PubMed PMID: 26670109.