Secondary brain injury treatment

Since impact damage cannot be influenced by the treating neurosurgeon, intense interest has focused on reducing secondary brain injury, which requires good general medical care and an understanding of intracranial pressure.

Intracranial pressure (ICP), variability in perfusion, and resulting ischemia are leading causes of secondary brain injury in patients treated in the neurointensive care unit. Continuous, accurate monitoring of cerebral blood flow (CBF) and ICP guide intervention and ultimately reduce morbidity and mortality. Currently, only invasive tools are used to monitor patients at high risk for intracranial hypertension.

Low oxygen delivery in hypotension, hypoxia, edema, intracranial hypertension, or changes in cerebral blood flow all account for the development of secondary injuries. Primary injuries are more or less complete, but secondary injuries could be prevented with adequate therapy. Understanding mechanisms of secondary injuries could help identify potentially beneficial therapies. Important elements of therapy are head position, normoglycemia, osmotherapy, normal body temperature, optimal blood pressure, and adequate oxygenation. barbiturate therapy. A neutral head and neck position is recommended to prevent intracranial hypertension. Hyperglycemia with less ATP leads to ischaemic acidosis, hypoglycemia enhances the decomposition of phospholipids and release of fatty acids, which makes the cellular damage worse. Normocapnia is recommended and adequate oxygenation (PaO2 higher than 90%). To prevent dehydration and electrolyte imbalance, serum electrolytes should be examined every 4-6 h as well as osmolarity. Moderate therapeutic hypothermia could be of benefit, and maintaining optimal blood pressure (MAP above 90 mmHg), especially in the first period after injury. As they have a lot of adverse effects, barbiturates are recommended only when conventional therapies show no effect. Patients should be hydrated well before the induction of barbiturates. In organized trauma centers and with adequate intensive care the mortality from traumatic brain injury decreased from 50% in 1970 to about 30% in 2006 [1)].

Traumatic brain injury (TBI) is accompanied by the overload of reactive oxygen species (ROS), which can result in secondary brain injury. Although procyanidins (PCs) have a powerful free radical scavenging capability and have been widely studied in the treatment of TBI, conventional systemic drug therapy cannot make the drug reach the targeted area in the early stage of TBI and will cause systemic side effects because of the presence of the blood-brain barrier (BBB). To address this issue, they designed and fabricated a ROS-scavenging functional hydrogel-loaded PC (GelMA-PPS/PC) to deliver the drug by responding to the traumatic microenvironment. In situ injection of the GelMA-PPS/PC hydrogel effectively avoided the BBB and was directly applied to the surface of brain tissue to target the traumatic area. Hydrophobic poly(propylene sulfide)60 (PPS60), a ROS quencher and H2O2-responsive substance, was covalently bound to GelMA and exposed in response to the trauma microenvironment. At the same time, the H2O2 response of PPS60 further caused the structure of the hydrogel to degrade and release the encapsulated PC. Then PC could regulate the oxidative stress response in the cells and synergistically deplete ROS to play a neurotrophic protective role. This work suggests a novel method for secondary brain injury treatment by inhibiting the oxidative stress

response after TBI [2].

A meta-analysis studied the effect of secondary brain injury targeted treatment on clinical outcome across the pathological entities.

Regarding specific medications, a statistically significant reduction of mortality and poor outcome was confirmed only for nimodipine for aSAH and dexamethasone for bacterial meningitis.

Results show that only a few selected secondary brain damage (SBD) directed medications are likely to reduce the rate of death and poor outcome following aneurysmal subarachnoid hemorrhage (aSAH), and bacterial meningitis, while no convincing evidence could be found for the usefulness of SBD directed medications in ischemic stroke, ICH and TBI. However, a subtle effect on good or excellent outcome might remain undetected. These results should lead to a new perspective of secondary reactions following cerebral injury. These processes should not be seen as suicide mechanisms that need to be fought. They should be rather seen as well orchestrated clean-up mechanisms, which may today be somewhat too active in a few very specific constellations, such as meningitis under antibiotic treatment and aSAH after surgical or endovascular exclusion of the aneurysm [3].

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Durić A, Omerbegović M, Ajanović M, Mahić Z, Alić M, Vanis-Vatrenjak S. Prevencija sekundarnih povreda mozga [Prevention of secondary brain injury]. Med Arh. 2006;60(2):120-3. Bosnian. PMID: 16528933.
2)
Huang X, Ye Y, Zhang J, Zhang X, Ma H, Zhang Y, Fu X, Tang J, Jiang N, Han Y, Liu H, Chen H. Reactive Oxygen Species Scavenging Functional Hydrogel Delivers Procyanidins for the Treatment of Traumatic Brain Injury in Mice. ACS Appl Mater Interfaces. 2022 Jul 14. doi: 10.1021/acsami.2c04930. Epub ahead of print. PMID: 35833273.
3)
Beez T, Steiger HJ, Etminan N. Pharmacological targeting of secondary brain damage following ischemic or hemorrhagic stroke, traumatic brain injury, and bacterial meningitis - a systematic review and meta-analysis. BMC Neurol. 2017 Dec 7;17(1):209. doi: 10.1186/s12883-017-0994-z. Review. PubMed PMID: 29212462; PubMed Central PMCID: PMC5719738.