## **Neuroprotection After Traumatic Brain Injury: Is There any Hope?**

Traumatic brain injury (TBI), whatever its cause, is already associated usually with disability and death worldwide.<sup>[1]</sup> The mechanism of injury in TBI includes primary and secondary injuries. The primary brain injury usually appears just when the trauma is occurred. Common mechanisms comprise direct impact, rapid acceleration/deceleration, penetrating injury, and shock waves. The damage that results include a combination of focal contusions and hematomas, as well as shearing of white matter tracts (diffuse axonal injury) along with cerebral edema and swelling.<sup>[2]</sup> While effective in managing the primary injury to the brain and the skull, these treatment modalities do not address the complex secondary cascades that occur at a cellular level following initial injury and greatly affect the ultimate neurologic outcome.<sup>[3]</sup> Neuroprotective agents that can limit the secondary tissue loss and/or improve behavioral outcomes have been identified in multiple animal models of acute brain injury. However, translation to the clinical setting has been largely disappointing.<sup>[4]</sup> More than 20 neuroprotective agents have been examined in experimental studies during the last 30 years<sup>[5]</sup> without evidence of significant outcome enhancement.<sup>[6]</sup> Some existing therapeutic interventions for neuroprotection are reperfusion strategies in ischemic stroke, prevention of secondary insults after TBI by, for example, decompressive craniectomy, maintaining optimal cerebral perfusion pressure, management of anemia in TBI cases, preserving brain perfusion in sepsis, and induced hypothermia. In recent years, some novel therapeutics have been introduced as neuroprotectors including infusion of mesenchymal stromal cells, remote ischemic conditioning (brief repeated cycles of peripheral vascular occlusion and deocclusion), the use of volatile anesthetic agents, metabolic therapy (i.e., sodium lactate infusion), sex hormones, for example, intravenous progesterone, and hyperoxia.<sup>[4]</sup> Nevertheless, to date, no neuroprotective agents or strategies have been shown to produce improved outcome significantly.

Among therapeutics being investigated, magnesium, cyclosporine, statins, and erythropoietin might have neurocytoprotective effects. Although during a large multicenter study on 606 patients with a TBI neurologic outcome at 6 months was not improved, mortality was nonsignificantly lower (11% vs. 16%) in patients who received erythropoietin.<sup>[7]</sup> Despite all the disappointments, there is still some hope. It will be achievable by a hybrid package of clinical measures including ensuring adequate oxygen delivery and avoiding excessive oxygen consumption<sup>[4]</sup>

using advanced neuromonitoring such as jugular venous oximetry, brain tissue oxygen tension monitoring, cerebral microdialysis, and thermal diffusion flowmetry<sup>[2]</sup> along with some therapeutic measures, and prevention and limitation of secondary insults in the early phases after the injury. We hope successes in the promising neuroprotective modalities in the future.

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