Traumatic Brain Injury Advances

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KEYWORDS

• Traumatic brain injury • Antiseizure prophylaxis • Hyperosmolar therapy
• Targeted temperature modulation • Intracranial pressure monitoring
• Decompressive craniectomy

KEY POINTS

- Antiseizure prophylaxis is beneficial only in the first 7 days after injury.
- Hyperosmolar therapy, with mannitol or hypertonic saline, can be used to control intracranial hypertension.
- Prevention of hyperthermia can prevent secondary brain injury. However, benefits of hypothermia are unclear.
- Intracranial pressure monitoring can aid in therapy.
- Decompressive craniectomy has not shown long-term benefits.

INTRODUCTION

Traumatic brain injury (TBI) continues to be a significant cause of mortality, morbidity, and economic burden globally.[1] Research on TBI over the last century has shown that a hallmark of treatment of TBI is prevention of secondary insults. Studies have shown that even brief episodes of hypoperfusion and hypoxemia can cause secondary injury and lead to worse short-term and long-term outcomes.[1–3] In order to improve medical care and patient outcomes, it is important to be knowledgeable of current literature regarding treatment of patients with TBI.

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PHARMACOLOGIC THERAPY

Posttraumatic Seizures Prophylaxis

Seizures in the acutely injured brain can increase intracranial pressure (ICP) and alter oxygen delivery to the brain.[1,4,5] In an attempt to prevent secondary brain injury, many investigators have studied the benefit of prophylaxis for posttraumatic seizures. A randomized, double-blind, placebo-controlled trial, published by Temkin and colleagues[6] in 1990, studied the role of phenytoin in prevention of early and late posttraumatic seizures. The trial included 404 patients, randomized to phenytoin or placebo treatment arms, for a treatment time of 12 months and a follow-up time of 24 months. The results showed a statistically significant difference in the rate of early posttraumatic seizures in the phenytoin group (3.6%) compared with the placebo group (14.2%).[6] There was no significant difference in the rate of posttraumatic seizures between the two groups from day 8 to end of follow-up. Overall, treatment with phenytoin was shown to be effective in decreasing the rate of posttraumatic seizures in the first 7 days of injury, but had no significant role in prevention of posttraumatic seizures after the first week of injury.[6] Notably, inclusion criteria allowed for a wide range of severity of TBI. Therefore, the difference in the benefit of treatment with phenytoin compared with placebo stratified by severity of TBI remains unclear.

As discussed by Temkin and colleagues,[6] treatment with phenytoin has some disadvantages; including several side effects and the need to monitor serum drug levels.[7] In the past decade, studies that compare the effectiveness of phenytoin with levetiracetam in prevention of early posttraumatic seizure prophylaxis have been conducted in an effort to provide an alternative pharmacologic therapy.[5,8] Zafar and colleagues[8] conducted a meta-analysis to compare the efficacies of phenytoin and levetiracetam in posttraumatic seizure prophylaxis. Eight studies comparing the 2 drugs were included in the meta-analysis: 2 randomized controlled trials (RCTs) and 6 observational studies. The meta-analysis showed no significant difference in the odds of seizures when comparing treatment with phenytoin and levetiracetam.[8]

Since publication of the Zafar and colleagues[8] study, a large multicenter prospective study comparing the efficacy of treatment with phenytoin with that of levetiracetam was completed by Inaba and colleagues.[9] This study, which included 813 patients, found no significant difference in rates of early posttraumatic seizures among patients treated with phenytoin compared with patients treated with levetiracetam.

The current Brain Trauma Foundation Guidelines recommend treatment with anticonvulsants within 7 days of injury.[1,10] Because this recommendation is based on the level II evidence outlined earlier, larger RCTs comparing efficacy of phenytoin with that of levetiracetam are needed to further delineate these recommendations. In addition, the importance of the severity of TBI and the use of anticonvulsants remains unclear, an important aspect to consider, because the long-term disadvantages related to seizure prophylaxis are poorly understood.[7]

Hyperosmolar Therapy

Hyperosmolar therapy is used to decrease high ICP in an effort to maintain cerebral blood flow and prevent secondary brain injury. The 2 most common pharmacologic interventions are mannitol and hypertonic saline. Mannitol increases cerebral blood flow by plasma expansion, decreasing the blood viscosity via deformed erythrocytes, and promotes osmotic diuresis.[1,11] Hypertonic saline promotes mobilization of water across the blood-brain barrier, and improved blood flow via plasma volume expansion.[1] Debate regarding the efficacy of these treatment modalities for increased ICP continues.