

Posttraumatic epilepsy after traumatic brain injury and prophylactic administration of antiepileptic drugs

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More than 50 million people endure traumatic brain injuries (TBI) each year in the world. TBI impacts lead to many negative outcomes including various disabilities, neurologic deficits, and even deaths for all ages in all countries,² which make TBI a chronic health condition and a global healthcare burden.³ In the United States, approximately 1.5 million people suffer from TBI, 280 000 hospitalizations and 50 000 deaths annually during 1997-2007.4,5 Approximately one-third of adults hospitalized with TBI still need assistance with daily activities one year after their discharge. Estimated lifetime costs of TBI in America totaled approximately \$56.3 billion in 1995.4 During 2007–2008 in Taiwan, a total of 99 391 patients were admitted with TBI, 48 792 (49.1%) of which had moderate-to-severe head injury.⁵ The most common group of people (30.1%, 29930/99391) with TBI are motorcycle riders or passengers. The in-hospital mortality rate for patients with severe TBI (Abbreviated Injury Score head of 4, 5, 6) was up to 12.3% during 2007–2008 despite the enforcement of motorcycle helmet use law in 1997 in Taiwan.⁵ Furthermore, Taiwan also institute the new trauma care hospital classification system in 2009.5

Posttraumatic epilepsy (PTE) after head injuries is a recognized complication of TBI.^{1,6} The risk factors based on initial clinical radiological findings of patients with TBI developing PTE included men, a history of alcohol abuse, posttraumatic amnesia, focal neurologic signs, and loss of consciousness at initial TBI, skull fracture, midline shift, brain contusion, subdural hemorrhage, epidural hemorrhage, and intracranial hemorrhage.⁷ Prior studies with various research designs showed the severity of TBI as the greatest predictor of PTE.⁸ The Glasgow Coma Scale (GCS) is often used as an assessment tool for severity of TBI.⁹ The cumulative incidence rates of PTE over the past 30 years encompass 2% patients with mild TBI, 4% patients with moderate TBI, and over 15% with severe.¹⁰

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PTE has three subtypes: immediate epilepsy (occurring within 24 h), early PTE (occurring between 24 h and 7 d after TBI), and late PTE (occurring after 7 d). Increasing computed tomography findings identify PTE outcomes 3–5 years following TBI: specially, 75% of patients with hemorrhagic contusions and related extracerebral hematoma had late PTE; only 16.7% of patients presenting intracerebral hemorrhage alone without extracerebral hematoma developed late seizures. A recent pilot study further reported that lesions in the temporal lobe rather than overall injury severity were associated with the highest risk of PTE. Brain blood barrier abnormalities predicting delayed, long-lasting seizures near the injured tissue are detectable on dynamic contrast-enhanced magnetic resonance imaging, gadolinium-enhanced T1, and T2-weighted fluid attenuated inversion recovery.

Because PTE following TBI has a significant negative impact on patients regarding physical safety and life quality,8 the prophylactic use of antiepileptic drugs (AED) in patients with TBI seems an option for clinicians. A previous randomized study reported that prophylactic AED administration (Phenytoin) decreased the early PTE rate of TBI patients from 14.2% to 3.6% (p<0.001) but has no effect on late PTE.¹² Liou's study with a propensity score analysis published in the current issue of the Journal of the Chinese Medical Association reported that AED prophylaxis was ineffective in preventing PTE (p=0.566), which is compatible with a previous Cochrane systemic review.¹⁴ Controlling the potential confounders made Liou's results more reliable than prior studies. This finding has clinical implications, and the authors conclude that clinicians should reevaluate the benefit of routine prophylactic AED in caring patients with TBI.

Increasing studies support that there is a causal relationship between PTE induction propagation and TBI-associated neuroinflammation, characterized by the activation of microglia and astrocytes, and the massive release of proinflammatory cytokines and chemokines.¹⁵ It has potential in the future to develop immune-based biomakers for PTE prediction and immune-targeted therapies for PTE prevention.¹⁵

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