

## Antiepileptic Drug Use in Traumatic Brain Injury:

### Indications, Duration of Therapy, and Criteria for Discontinuation

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#### Abstract

Traumatic brain injury (TBI) is a major cause of neurological morbidity worldwide and is frequently associated with post-traumatic seizures. The prophylactic administration of antiepileptic drugs (AEDs) has become standard practice in patients with moderate to severe head injury to prevent early seizures. Evidence indicates that AEDs reduce the incidence of seizures occurring within the first week following injury but do not significantly decrease the risk of late post-traumatic epilepsy. This article reviews the pathophysiology of post-traumatic seizures, indications for AED prophylaxis, commonly used medications, and evidence-based recommendations regarding duration of therapy and criteria for discontinuation.

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#### Introduction

Traumatic brain injury remains a leading cause of mortality and disability globally. Post-traumatic seizures are among the most important neurological complications associated with TBI and can worsen clinical outcomes by increasing cerebral metabolic demand, intracranial pressure, and risk of secondary brain injury.

Post-traumatic seizures are broadly classified into **early seizures** and **late seizures** based on the time of occurrence following injury. Preventing early seizures is a major goal of acute TBI management, and prophylactic antiepileptic therapy is commonly implemented in neurosurgical practice.

Commonly used agents include Phenytoin, Levetiracetam, and occasionally Sodium Valproate.

Despite widespread use, the appropriate duration of prophylaxis and indications for long-term therapy remain areas of clinical discussion.

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#### Classification of Post-Traumatic Seizures

##### Early Post-Traumatic Seizures

Early seizures occur within **7 days of injury** and are primarily related to acute cortical irritation resulting from intracranial bleeding, brain edema, or direct cortical damage.

Intracranial lesions such as Acute Subdural Hematoma and Epidural Hematoma are frequently associated with early seizures.

Early seizures are clinically significant because they may lead to secondary neuronal injury through increased intracranial pressure, metabolic stress, and transient hypoxia.

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### **Late Post-Traumatic Seizures**

Late seizures occur **after 7 days** following injury and are usually associated with structural changes in the brain, including gliosis, cortical scarring, and encephalomalacia.

These seizures may evolve into chronic epilepsy known as Post-Traumatic Epilepsy.

Unlike early seizures, prophylactic AED therapy has not been shown to significantly prevent the development of late epilepsy.

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### **Indications for Antiepileptic Prophylaxis**

AED prophylaxis is recommended in patients with **moderate to severe traumatic brain injury** and in those with known risk factors for seizures.

Common indications include:

- Severe TBI (Glasgow Coma Scale < 8)
- Cortical brain contusions
- Intracranial hematomas
- Depressed skull fractures
- Penetrating brain injuries
- Patients undergoing neurosurgical procedures
- Cortical involvement on neuroimaging

These patients demonstrate a significantly increased risk of early seizures, and prophylactic therapy is justified.

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### **Choice of Antiepileptic Drugs**

Historically, phenytoin has been the most widely used agent for seizure prophylaxis in TBI. However, levetiracetam has increasingly gained popularity because of its favorable side-effect profile, minimal drug interactions, and ease of administration without the need for serum level monitoring.

Multiple studies have demonstrated comparable efficacy between levetiracetam and phenytoin in preventing early seizures following traumatic brain injury.

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### **Duration of Therapy**

Current clinical evidence supports **limiting prophylactic AED therapy to seven days following traumatic brain injury.**

Clinical trials have shown that while AEDs effectively reduce early seizures, prolonged administration does not significantly reduce the incidence of late post-traumatic epilepsy.

Therefore, routine continuation of AEDs beyond one week in seizure-free patients is generally not recommended.

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### **Criteria for Discontinuation**

Antiepileptic therapy may be discontinued after the first week in patients who meet the following criteria:

- No clinical seizures during the acute period
- Stable neurological condition
- Absence of significant cortical injury on imaging
- No epileptiform abnormalities on electroencephalography

In such cases, continued AED therapy may expose patients to adverse effects without clear benefit.

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### **Indications for Long-Term AED Therapy**

Long-term therapy should be considered in patients with persistent seizure risk factors, including:

1. Documented post-traumatic seizures
2. Extensive cortical contusions or scarring
3. Penetrating brain injuries

4. Retained intracranial foreign bodies
5. Abnormal electroencephalographic findings
6. Structural brain lesions such as Intracerebral Hemorrhage

These patients have a higher likelihood of developing recurrent seizures and may benefit from prolonged treatment.

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### **Discontinuation Strategy**

Abrupt discontinuation of antiepileptic medication should be avoided. Gradual tapering is recommended to minimize the risk of withdrawal seizures. Follow-up neurological assessment and, when indicated, EEG evaluation should guide clinical decision-making.

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### **Conclusion**

Post-traumatic seizures remain a significant complication of traumatic brain injury. Short-term prophylactic use of antiepileptic drugs effectively reduces the incidence of early seizures in high-risk patients. However, evidence does not support routine continuation beyond seven days in seizure-free individuals without additional risk factors.

Long-term therapy should be reserved for patients with documented seizures or persistent epileptogenic structural abnormalities. Careful patient selection and evidence-based discontinuation strategies are essential for optimizing clinical outcomes while avoiding unnecessary medication exposure.

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