**Title:** Out with the old and in with the new: Should levetiracetam replace phenytoin as the agent of choice for seizure prophylaxis following traumatic brain injury?

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**Learning Objectives:**

1. Describe the pathophysiology and implications of seizures following a traumatic brain injury.
2. Discuss the current standard of practice and guideline recommendations for seizure prophylaxis in patients with traumatic brain injury.
3. Identify the pros and cons of phenytoin vs levetiracetam for post-traumatic seizure prophylaxis.

**Abstract:**

Traumatic brain injury (TBI) is a common cause of hospitalization with over 223,000 TBI-related hospitalizations reported in the U.S. in 2019. Management of TBI is mainly centered around prevention of secondary injury, which is injury resulting from complications of the trauma. One important complication associated with TBI is posttraumatic seizures (PTS). Prophylactic use of anti-seizure medication (ASM) for the first 7 days following TBI can help prevent early PTS. Phenytoin has been the historical agent of choice and standard of practice for seizure prophylaxis following TBI and is the recommended agent by the Brain Trauma Foundation guidelines because it is backed by the most evidence. However, phenytoin has many disadvantages such as an unfavorable side effect profile, a multitude of significant drug interactions, a narrow therapeutic window, and variable non-linear kinetics necessitating therapeutic drug monitoring. Levetiracetam is a newer ASM which is gaining popularity as an alternative to phenytoin for seizure prophylaxis following TBI. Levetiracetam is better tolerated with less adverse effects and less risk of toxicity compared to phenytoin. It also displays predictable linear kinetics so monitoring of drug levels is not necessary. However, there is a lack of high-quality studies to support its use for prevention of PTS following TBI. This dilemma has created a controversy over whether or not levetiracetam should replace phenytoin as the agent of choice for seizure prophylaxis following TBI.

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**Audience Response Questions:**

1. TS is a 55-year-old male who fell off a ladder and hit his head. He lost consciousness for 1 hour and has a GCS of 9. What is his severity of TBI?
   1. Mild
   2. Moderate
   3. Severe
   4. Unable to determine
2. LM is a 92-year-old female who suffered a severe TBI following a car accident for which she underwent a decompressive craniectomy 10 days ago. LM currently has a GCS of 8. What posttraumatic seizure prophylaxis should she receive?
   1. Fosphenytoin 20 mg/k/d IV once, then 5 mg/kg/day
   2. Phenytoin 5 mg/kg/day po divided into 3 doses
   3. Levetiracetam 500 mg IV q12h
   4. none
3. Which of the following describe disadvantages of phenytoin/fosphenytoin?
   1. Does not come in an oral liquid form and is a strong inducer of CYP3A4
   2. Displays nonlinear elimination kinetics and is less effective than keppra
   3. Has a narrow therapeutic index and is has a shorter half-life than Keppra
   4. Extravasation causes tissue necrosis and is a strong inducer of CYP2B6