

# Neuroprotective effects of Vitamin D3 supplementation combination with valproate and perampanel in an experimental model using status epilepticus induction

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## Abstract:

**BACKGROUND:** Status epilepticus (SE) is a severe form of epilepsy with neurological sequelae and high mortality. Considering the neuromodulatory effects of Vitamin D3 (Vit-D3), this study investigated the potential role of Vit-D3 alone and in combination with antiseizure medications (ASMs).

**MATERIALS AND METHODS:** Male Wistar rats were assigned into seven groups: SE-control, healthy control, valproate (VPA) (370 mg/kg), perampanel (PER) (1.5 mg/kg), Vit-D3 (6000 IU/kg/day), VPA + Vit-D3, and PER + Vit-D3. After 14 days of pretreatment, SE was induced by LiCl-pilocarpine administration, followed by acute (17 days) and long-term (29 days) drug effect studies. Seizure details and learning-memory were assessed along with evaluation of brain tissue for neurodegeneration (electronmicroscopy), histopathology, neuronal viability (neuron-specific nuclear protein), reactive astrocytes (glial fibrillary acidic protein) by immunohistochemistry, total antioxidant capacity, and neuroinflammation biomarkers.

**RESULTS:** Vit-D3 combination with VPA or PER significantly reduced the percentage of rats experiencing stage-3/4 seizures and increased latency compared to the SE-control group ( $P < 0.001$ ). Drug-treated groups had better memory retention ( $P < 0.001$ ) than SE-control, with significantly better protection in the combination group. In immunohistochemistry, Vit-D3 in combination with ASMs had less neurodegeneration and reactive astrocytes in the hippocampus and cerebral cortex ( $P < 0.001$ ). Through electron microscopy, the SE-control group exhibited significant damage in hippocampus's myelin sheath and axons (grade 3) on days 17 and 29. Vit-D3 alone and in combination with ASMs attenuated these changes ( $P < 0.001$ ), with combination groups showing the least neurodegeneration (day 29).

**CONCLUSION:** Vit-D3 supplementation, especially in combination with ASMs, showed promising neuroprotective effects in the SE model in rats by improving seizure control, memory, hippocampal health, and antioxidant levels.

## Keywords:

Adjuvant effect, epileptogenesis, learning and memory, neurodegeneration, Vitamin D3