

Study finds three anti-seizure drugs equally effective for severe form of epilepsy

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Generalized 3 Hz spike and wave discharges in a child with childhood absence epilepsy. Credit: Wikipedia.

There are three treatment options commonly used by doctors in the emergency room to treat patients with refractory status epilepticus, severe seizures that continue even after benzodiazepine medications, which are effective in controlling seizures in more than two-thirds of patients. New findings published in the *New England Journal of Medicine* reveal that the three drugs, levetiracetam, fosphenytoin, and valproate, are equally safe and effective in treating patients with this condition. The study was supported by the National Institute of Neurological Disorders and Stroke (NINDS), part of the National Institutes of Health.

"Doctors can be confident that the particular treatment they choose for their patients with status

epilepticus is safe and effective and may help them avoid the need to intubate the patient as well as stays in the intensive care unit," said Robin Conwit, M.D., NINDS program director and an author of the study. "This was a truly collaborative, multidisciplinary study that involved pediatricians, emergency medicine doctors, neurologists, pharmacologists, and biostatisticians all contributing their expertise."

In the Established Status Epilepticus Treatment Trial (ESETT), led by Robert Silbergleit, M.D., professor at the University of Michigan, Ann Arbor; Jordan Elm, Ph.D., professor at Medical University of South Carolina; James Chamberlain, M.D., professor at George Washington University; and Jaideep Kapur, M.B., B.S., Ph.D., professor at the University of Virginia, more than 380 children and adults were randomized to receive levetiracetam, fosphenytoin, or valproate when they came to the [emergency room](#) experiencing a [seizure](#). The researchers were trying to determine which of the anticonvulsant drugs was most effective in stopping seizures and improving a patient's level of responsiveness within 60 minutes of administering treatment.

The results showed that the three drugs stopped seizures and improved responsiveness in approximately half of the study participants. Specifically, these benefits were seen in 47% of subjects in the levetiracetam group, in 45% of participants in the fosphenytoin group and in 46% of subjects in the valproate group. These differences were not statistically significant.

There were no differences in [serious side effects](#) among the drugs.

"Our study suggests that clinical outcomes are driven by factors other than drugs. Differences in how doctors decide to treat status epilepticus, such as when they give more drugs or when to anesthetize patients and put them on a mechanical

ventilator, may be more important than the specific treatments used to control seizures in patients," said Dr. Silbergleit.

The study was stopped early when a planned interim analysis found that the drugs were equally safe and effective.

ESETT researchers utilized a [clinical trial design](#) known as response adaptive randomization to improve the study's efficiency and maximize the chances of identifying the best treatment. The study used an algorithm to determine which drugs patients would receive based on accumulating trial data.

"Using an innovative design for this clinical trial, we were able to answer this important question in a timely and cost-effective manner," said Dr. Kapur. "In addition, this design lowered risk by reducing the chances that participants could have received what might have been determined to be the least effective treatment."

Status epilepticus is characterized by individual seizures or multiple seizures close together lasting more than five minutes, with a loss of consciousness. If not treated, it can lead to severe brain damage or death. Benzodiazepines are the first line of treatment for status epilepticus and are effective in two-thirds of patients. Refractory status epilepticus occurs in those patients in whom benzodiazepines do not stop their seizures.

Additional research is needed to prevent refractory status epilepticus and to find treatment options for the patients whose seizures do not respond to the three drugs investigated in this study.

More information: Kapur et al. "Randomized Trial of Three Anticonvulsant Medications for Status Epilepticus," *New England Journal of Medicine*, November 28, 2019.
[dx.doi.org/10.1056/NEJMoa1905795](https://doi.org/10.1056/NEJMoa1905795)

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