

UC Davis investigational medication used to resolve life-threatening seizures in children

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In its first clinical application in pediatric patients, an investigational medication developed and manufactured at UC Davis has been found to effectively treat children with life-threatening and difficult-to-control epileptic seizures without side effects, according to a research report by scientists at UC Davis and Northwestern University.

The investigational formulation of allopregnanolone was manufactured by UC Davis Health System's Good Manufacturing Practice Laboratory. Two children were treated with the allopregnanolone formulation, one at UC Davis Children's Hospital, the other at the Ann & Robert Lurie Children's Hospital in Chicago. Both children were weaned from general anesthetics and other seizure treatments and their seizures resolved. In both instances the children are recovering.

The research is published online in *Annals of Neurology*, an official journal of the American Neurological Association and the Child Neurology Society.

Super-refractory [status](#) epilepticus is a condition diagnosed in patients with refractory status epilepticus being treated with infusions of general anesthetics when seizures continue for longer than 24 hours, despite anesthesia, or when seizures recur on reduction or withdrawal of the anesthesia. Super-refractory status epilepticus has high morbidity and mortality. There are no Food and Drug Administration (FDA)-approved treatments for the condition.

Allopregnanolone is a positive allosteric modulator of GABAA receptors in the brain. Research in animals has shown that allopregnanolone protects against seizures and can stop status epilepticus. Although the allopregnanolone used to manufacture the investigational treatment was produced by chemical synthesis according to procedures regulated by the FDA, it is synthesized normally in small quantities in the body from progesterone.

"Our laboratory studies have shown that allopregnanolone is effective in stopping status epilepticus that is refractory to treatment," said Michael Rogawski, professor in the UC Davis Department of Neurology and a co-author of the report.

In both of the clinical cases, the patients continued to have seizures despite weeks of intensive treatment with medications, including infusion of anesthetics. Emergency treatment with the investigational medication was approved by the FDA; the two patients received the medication over a five-day period, during which time both were weaned from anesthetics and other seizure medications. Status epilepticus did not recur after treatment. There were no adverse drug effects, the researchers said.

Mortality rates in super-refractory status epilepticus can be as high as 50 percent, and those who survive experience high rates of subsequent neurological impairment. The authors note that progesterone and ganaxolone, a chemical analog of allopregnanolone, have been studied in clinical trials for epilepsy and have shown benefit. Researchers at UC Davis, led by Rogawski, currently are investigating the use of allopregnanolone as a treatment for traumatic brain injury.

"Neurosteroids, including allopregnanolone, are a promising treatment for epilepsy and refractory status epilepticus that may overcome resistance to benzodiazepines and barbiturates and facilitate the

withdrawal of these agents by preventing rebound [seizures](#), a key problem in [treatment](#) of super-refractory status epilepticus," Rogawski said.

Provided by UC Davis

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