Widely used drug no more effective than FDA approved medication in treating epileptic seizures

May 14 2014

A National Institutes of Health-sponsored study published in the *Journal of the American Medical Association* (*JAMA*) showed that lorazepam - a widely used but not yet Food and Drug Administration (FDA) approved drug for children - is no more effective than an approved benzodiazepine, diazepam, for treating pediatric status epilepticus.

Status epilepticus is a state in which the brain is in a persistent state of seizure. By the age of 15, 4 to 8 percent of children experience a seizure episode, which can be life threatening if they aren't stopped immediately. Status epilepticus is a continuous, unremitting seizure lasting longer than five minutes or recurrent seizures without regaining consciousness between seizures for more than five minutes.

Before this current study, published April 23, there was no evidence indicating which of the two treatments might prove more effective. Although it is not yet approved by the FDA, James M. Chamberlain, MD, Division Chief of Emergency Medicine at Children's National Health System, the study's principal investigator, estimates that lorazepam is used as first-line therapy in most emergency departments.

"The study results provide reassurance to emergency medicine personnel who must act within minutes," said Chamberlain. The study was conducted at 11 hospitals in the United States using the infrastructure of the Pediatric Emergency Care Applied Research Network (PECARN),

under a contract from the National Institutes of Health's (NIH) Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD).

Both lorazepam and diazepam are used to treat status epilepticus. Diazepam, also known as Valium, is the only one of the two drugs to have been approved by the FDA for use in adults and children.

Lorazepam, marketed under the trade name Ativan, has been approved by the FDA only for use in adults. Once the FDA has approved a drug for use in adults, physicians may then prescribe it for other uses and in pediatric patients if, in their best judgment, they believe their patients will benefit.

"Sometimes physicians are forced to rely on their best judgment alone," said George Giacoia, MD, of the NICHD's Obstetric and Pediatric Pharmacology and Therapeutics Branch. "However, it's always better to make treatment decisions on the evidence that comes only from conducting large comparison studies. We now know that lorezapam offers no advantage over diazepam in treating pediatric seizure disorder, and that diazepam is more suited to use by emergency teams."

In 2007, the National Institutes of Health's Pediatric Seizure study sought to determine which of two drugs—diazepam or lorazepam—was more effective in treating the life-threatening condition, status epilepticus. This condition can occur without warning. For reasons not fully understood, a child may be gripped by continuous seizures, which, if not stopped within minutes, may lead to brain damage or even death.

Because of the random nature of seizures and their significantly life altering affects, lorezapam is commonly prescribed to treat status epilepticus in children, even though it hasn't been specifically approved for that use. The results of the Pediatric Seizure study do not support the

use of lorezapam instead of diazepam for treating status epilepticus, Dr. Chamberlain said. Also, because lorezapam needs to be refrigerated and diazepam does not, diazepam is more suited for use by ambulance crews.

A few previous studies indicated that lorazepam might be more effective at ending a seizure and might be less likely than diazepam to depress breathing—a side effect of benzodiazapines, the category of medications that includes both drugs.

In their study, Chamberlain and colleague wrote, "There is no conclusive evidence to support lorazepam as a superior treatment and there is little consensus as to which is the preferred agent."

The current study was the largest, most comprehensive comparison study of the two treatments for pediatric seizure disorder. Dr. Chamberlain and his colleagues enrolled 310 children at the 11 institutions, between 2008 and 2012. The researchers found that both medications successfully halted seizures in 70 percent of cases, and each had rates of severe respiratory depression of less than 20 percent.

It's important that "we get the most important scientific information about such medications so there are government approvals for pediatric use," Chamberlain said. "Pediatric patients are not just small adults."

Provided by Children's National Medical Center