

## INTRAVENOUS VALPROATE FOR PEDIATRIC STATUS EPILEPTICUS

**Safety and Efficacy of Intravenous Valproate in Pediatric Status Epilepticus and Acute Repetitive Seizures**

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**METHODS:** Retrospective review was performed on 40 pediatric patients with intravenous valproate (VPA) loading. Patients were classified into two groups: status epilepticus (SE) ( $n = 18$ ) and acute repetitive seizures ( $n = 22$ ). Thirty-one patients were VPA naïve and received a full loading dose of 25 mg/kg; nine had subtherapeutic plasma VPA levels and received a partial loading dose. Average infusion rate was 2.8 mg/kg/min. Heart rate and blood pressure were measured before, during, and after infusion.

**RESULTS:** Intravenous VPA loading stopped seizures in 18 patients with SE within 20 minutes. All 18 patients regained baseline mental status within 1 hour of seizure cessation. Among 22 patients with acute repetitive seizures, only one had further seizures after VPA infusion. One patient in the SE group complained of transient tremors. No significant changes in blood pressure or heart rate were found in either group. Postinfusion plasma VPA levels ranged from 51 to 138 g/mL (mean  $\pm$  SD = 88  $\pm$  21.5 g/mL).

**CONCLUSIONS:** Intravenous VPA loading is safe and effective for treating acute seizure emergencies in children.

tubation and mechanical ventilation, especially in infants and children. Intravenous VPA has the potential to avoid these side effects.

Initial prescribing information recommended intravenous VPA dosing at 10 to 15 mg/kg, administered over a 1-hour period. These parameters are inadequate for the emergency treatment of SE and acute repetitive seizures, and several reports have found that administration of higher doses at faster infusion rates have been well tolerated by adults (1–3). New product-labeling data suggest that intravenous VPA, infused over 5 to 10 minutes at rates up to 3 mg/kg/min and doses up to 15 mg/kg, is generally well tolerated by adult patients. However, few studies have specifically assessed the safety and efficacy of rapid infusions of intravenous VPA in children (4).

The study by Yu, Mills, Thompson, and Cunanan was retrospective, and thus, there was no control group. Nevertheless, it suggests that a loading dose of intravenous VPA, when infused rapidly into pediatric patients, was remarkably effective at terminating ongoing seizures *and* was well tolerated. The majority of patients had generalized tonic-clonic seizures, but small numbers of patients had other seizure types that also responded to intravenous VPA. Patients ranged in age from 1 month to 19 years. Nine patients had seizures in the setting of subtherapeutic VPA levels, three patients had refractory SE after loading doses of PHT, phenobarbital (PB), or both, and 28 of the patients continued to seize after receiving lorazepam (LZP). Only one patient's seizures failed to respond to intravenous VPA. All of the 39 responders remained seizure free for 12 hours after infusion.

A 2001 panel of epilepsy experts considered intravenous VPA to be a first-line agent for absence SE and a second-line agent for generalized or partial SE, either as an initial treatment or as a follow-up treatment after one or two other therapies had failed (5). The article by Yu and colleagues supplies further evidence to support the use of intravenous VPA as a treatment for SE and acute repetitive seizures in children. It may be particularly appropriate in the following settings: (a) known or suspected subtherapeutic VPA level; (b) seizure type that does not typically respond to PHT or barbiturates (infantile spasms, myoclonic, atonic); and (c) when the risk of adverse respiratory or hemodynamic reactions to standard agents must be avoided.

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## COMMENTARY

Intravenous valproic acid (VPA) was approved by the Food and Drug Administration in late 1996, as an intravenous alternative when oral administration of VPA is not feasible. Since then, there has been widespread interest in using VPA as an acute therapy for repetitive seizures and status epilepticus (SE). Other intravenous alternatives, including phenytoin (PHT), fosphenytoin, barbiturates, and benzodiazepines (BZDs), sometimes fail to stop seizures and may cause hemodynamic instability when rapidly administered. The sedation caused by barbiturates and BZDs frequently necessitates in-

## References

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