toxtidbits
the maryland poison center's monthly update. news. advances. information.
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Valproic Acid

Valproic acid is the active ingredient in the prescription medications Depakote, Depakote ER, Depakene, and Depacon. These medications are used for the treatment of seizure disorders, prevention of migraine headaches, and treatment of manic episodes related to bipolar disorder. The exact mechanism by which valproic acid exerts its therapeutic effect is not known. The most prominent theory is that valproic acid increases the concentration of gama-aminobutyric acid (GABA), an inhibitory neurotransmitter in the brain.

Hepatotoxicity and liver failure resulting in death have occurred in patients receiving therapeutic doses of valproic acid, usually within the first six months of starting therapy. Patients with an increased risk of liver toxicity from valproic acid include children, patients with congenital metabolic disorders, and those on multiple antiseizure drugs. Patients should be closely monitored for weakness, lethargy, vomiting, facial swelling, and anorexia while taking this medication.

Acute valproic acid overdoses may cause vomiting, confusion, and tachycardia. Coma, hypotension, respiratory depression, metabolic acidosis, hyperammonemia, renal failure, QTc prolongation and cardiopulmonary arrest can occur in severe overdoses and can be seen up to 18 hours following ingestion. Serum valproic acid levels may be obtained but these levels are usually not reliable at predicting clinical effects. A level of 50-100 mcg/ml is considered therapeutic, and levels above 850 mcg/ml are generally seen in patients with more serious effects such as coma and respiratory depression. Enteric coated valproic acid (Depakote, Depakote ER) absorption may be delayed with peak levels occurring 6-8 hours following ingestion; therefore, repeat valproic acid levels should be obtained to ensure that levels are not continuing to rise.

In patients who have ingested an overdose of valproic acid, treatment includes a dose activated charcoal to prevent absorption, a second dose of activated charcoal if a sustained release formulation is ingested or if levels continue to rise, L-carnitine for hyperammonemia or hepatotoxicity, and possibly hemodialysis or hemoperfusion in patients with severe intoxication not responding to supportive therapy.

Michael Cuda
Pharmacy Student
University of Maryland School of Pharmacy

DID YOU KNOW THAT… *L-carnitine has been shown to reduce ammonia levels and improve outcomes in patients with chronic valproic acid toxicity?*

L-carnitine has been used orally as a supplement by patients taking valproic acid chronically who develop high ammonia levels. In acute valproic acid toxicity, L-carnitine is indicated in patients with symptomatic hepatotoxicity or increasing serum ammonia levels. The usual dosing for these acutely toxic patients is a loading dose of 100mg/kg IV over 30 minutes followed by maintenance doses of 15mg/kg IV over 30 minutes every 4 hours. Call the specialists at the Maryland Poison Center for advice on using L-carnitine for valproic acid toxicity.

Maryland Poison Center
University of Maryland School of Pharmacy

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