ToxTidbits

Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

October 2021 Poison Center Hotline: 1-800-222-1222

The Maryland Poison Center's Monthly Update: News, Advances, Information

Levocarnitine in valproic acid poisoning

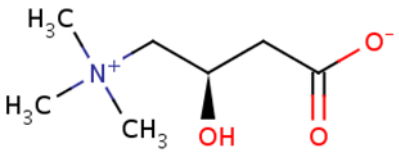
L-carnitine (levocarnitine) is used off-label as an antidote for hyperammonemia and hepatotoxicity from valproic acid (VPA) toxicity. Acute overdose and chronic use of VPA are associated with decreased carnitine concentration, resulting in mitochondrial dysfunction. A lower carnitine level may shift toward a greater degree of omega-oxidation metabolism. One of the omega-oxidation toxic metabolites, 4-en-VPA, inhibits carbamyl phosphate synthetase 1. This enzyme is responsible for incorporating ammonia into the urea cycle and its inhibition leads to hyperammonemia. Carnitine works as a carrier to transport VPA into the mitochondria for metabolism. There is evidence for using L-carnitine to treat VPA toxicity associated with chronic therapy as well as overdoses.

One retrospective cohort study investigated L-carnitine in patients with VPA-associated liver failure *(Neurology. 2001;22;56(10):14-5-9).* Transplant-free survival was higher in the L-carnitine treated group (47%) compared to the untreated group (10%), and intravenous (IV) L-carnitine was associated with better outcomes. A case series reported 13 children with symptomatic VPA-induced hyperammonemia *(Am J Ther. 2019;26(3)e344-9)*. Eleven patients were on therapeutic dosing and two overdosed. The mean baseline ammonia concentration was 231.7 µg/dL (136 µmol/L). Twelve patients received L-carnitine 33 mg/kg IV q8h, and one received 67 mg/kg IV q8h, until clinical improvement. All patients recovered.

A systematic review analyzed eight patients from seven different case reports of VPA overdose *(Ann Pharmacother. 2010;44(7-8):1287-93).* Different L-carnitine doses and routes were administered. All patients recovered. Based on those cases, the authors recommended L-carnitine 100 mg/kg IV x 1, followed by 50 mg/kg IV q8h (max 3 g/dose) until clinical improvement or if an adverse event occurs with L-carnitine. A randomized controlled trial included 62 adult patients admitted to the ICU-Toxicology Unit with a VPA concentration of > 100 µg/mL *(Farmacia. 2017(65):396-400)*. Mean baseline VPA was 264 µg/mL and mean baseline ammonia concentration was 450 µg/dL (264 µmol/dL). Patients were randomized to receive standard therapy with or without L-carnitine 1800 mg/day for 3 days (route unspecified). L-carnitine administration resulted in a faster reduction in ammonia and valproic acid concentrations with statistical differences noted approximately 36 hours after admission.

There is no consensus when L-carnitine therapy should be initiated, but it is appropriate to use in massive VPA overdoses and symptomatic patients with hyperammonemia with therapeutic or elevated VPA level. There are varying L-carnitine dosing regimens. Some recommended doses are 100 mg/kg IV x 1 (maximum 6 g) followed by 33-50 mg/kg (max 3 g) IV q8h. It can be given as a bolus injection over 2-3 min or as an infusion.

The poison center can assist in making individualized L-carnitine dosing and monitoring recommendations. Contact the poison center at 1-800-222-1222 for expert guidance when caring for patients with VPA toxicity.



Levocarnitine

Did you know?

Levocarnitine can be given by both oral and intravenous route. We generally recommend intravenous route when treating acutely poisoned patients. Oral administration is most appropriate for patients who are not acutely ill and need chronic supplementation. Dosing recommendations range from 50 to 100 mg/kg/day in divided doses. The systemic bioavailability is only about 15%, so the amount reaching the cells is likely considerably lower than when dosing intravenously.

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