Georgia Poison Center

Guideline for the management of Valproic Acid Ingestions

This document is written to describe our guidelines for the management of typical asymptomatic cases of human unintentional valproate ingestions, although we recognize that extenuating circumstances may make a different approach preferable in certain cases. Medical toxicology backup should be contacted if a different approach is contemplated in a specific case.

I. Obtain an initial ingestion history, including substance and amount ingested, time of ingestion, current symptoms, other medications, medical problems, and previous therapy.

	Formulations	**Strengths (mg)**
Depakote (Divalproex sodium)	EC tablets Sprinkle capsules ER tablets	125, 250, 500 125 250 and 500
Depakene (Valproic acid)	Capsules Syrup	250 250/5mL

a. Amounts <25 mg/kg – no referral to HCF and no at-home follow-up
b. Amounts >25 mg/kg, but <50 mg/kg – full at-home follow-up
c. Amounts >50 mg/kg – HCF referral

II. Recommendations include:
    a. Decontamination
        i. Consider activated charcoal within 1-2h after ingestion >50 mg/kg.
        ii. Whole bowel irrigation may be considered within 6h following ingestions >50 mg/kg of an <u>EXTENDED RELEASE or ENTERIC COATED preparation</u>.
    b. Consult toxicology backup where patient is significantly ill and/or where use of antidotes is being contemplated
    c. Labs and monitoring
        i. Obtain a valproic acid level at least 1h following an acute ingestion and STAT following an acute-on-chronic ingestion
            1. Therapeutic range usually described as 50-100 mcg/mL
                a. Higher levels generally cause more severe adverse effects
                b. Levels >450 mcg/mL are associated with moderate to severe effects
                c. Levels >850 mcg/mL are associated with potentially life threatening effects, including coma, respiratory depression,

aspiration, metabolic acidosis

2. Obtain levels Q4h until peak and down-trending x2

ii. Obtain CMP (including LFTs), CBC

1. Recommend obtaining an ammonia level ONLY if patient has altered mental status (signs of encephalopathy) or evidence of significantly abnormal hepatic function

a. Collection of ammonia levels: draw the blood into the appropriate tube, preferably from a free-flowing vein, and immediately submerge in an ice bath and hand-carry directly to the lab

d. Treatment

i. L-carnitine is an amino acid vital to mitochondrial utilization of fatty acids. (It is necessary for the transport of valproic acid into the mitochondria where it undergoes beta-oxidation. Decreased levels of carnitine also disrupt the urea cycle leading to hyperammonemia.)

1. Recommendations for use:
   a. L-carnitine *generally should be utilized* if the patient has a <u>valproate level > 200-250 mcg/mL</u> **AND** <u>signs of encephalopathy</u>
   b. L-carnitine may be *considered* in patients with <u>evidence of hepatotoxicity</u>
   c. L-carnitine may be *considered* in patients with <u>levels >450 mcg/mL</u>
   d. Additional pediatric considerations: Also consider the use of L-carnitine in patients < 2 years or in those with poor nutrition
2. Dosing
   a. IV (preferred in severe cases): L-carnitine 100 mg/kg (max. 6g) (initial dose) infused over 30 minutes, followed by 15 mg/kg Q4-6h infused over 10-30 minutes
   b. PO: L-carnitine 20-33 mg/kg/dose (maximum single dose 1g) q8h
3. Endpoints
   a. Resolution of hepatic dysfunction, hyperammonemia and encephalopathy, and
   b. Level <450 mcg/mL

ii. Multi-dose activated charcoal (MDAC)

1. The evidence for MDAC utility is weak. MDAC may be considered to improve elimination of valproic acid in patients whose levels are not decreasing appropriately or in an acute, large ingestion. Consult medical backup for further assistance when considering MDAC.

iii. Hemodialysis (HD)

1. Valproic acid is removed by HD
2. Hemodialysis for valproic acid should be considered in severely

symptomatic patients (coma or hemodynamic compromise) or in patients with valproic acid level >850 mcg/mL

Valproate.docx, LS/RJG
7-20-16