

THERAPEUTIC PLASMA EXCHANGE FOR VALPROIC ACID POISONING – AN INNOVATIVE APPROACH

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Divalproex sodium is an antiepileptic compound that dissociates into sodium valproate and valproic acid. Valproic acid poisoning can cause hyperammonemia, toxic hepatitis, hypotension, hypothermia, coma and fatal cerebral edema. Renal manifestations include hypocalcemia, hypernatremia, anion gap metabolic acidosis and hyperosmolality. We are not aware of prior reports of treating severe divalproex sodium overdose with therapeutic plasma exchange (TPE).

A 30-year-old woman presented to the emergency department after ingesting 90 enteric-coated divalproex sodium tablets. She became lethargic and required tracheal intubation. She had a history of bipolar disorder, hypertension and previous suicide attempts. Her medications also included atenolol. On examination she was obtunded and responded only to painful stimuli. The Na was 143 mmol/L, K 7.4 mmol/L, Cl 117 mmol/L and bicarbonate 18 mmol/L. BUN and Cr were normal. The ammonia level was 485 mcg/dL and valproic acid level was 761 mcg/ml. She was treated with activated charcoal, levocarnitine for hyperammonemic encephalopathy, and dexamethasone to help prevent or treat cerebral edema. She was treated urgently with TPE. After 2 exchanges the ammonia level was 38 mcg/dL and the valproic acid level was 66 mcg/ml. She was extubated within 18 hours and did well.

Valproic acid is 90% protein-bound at therapeutic drug levels. Following massive overdose saturated protein binding sites lead to an increased fraction of unbound valproic acid in the serum. Adjuvant therapy for valproate poisoning with hemodialysis, hemoperfusion, continuous venovenous hemodiafiltration and sustained low efficiency dialysis with filtration has been described. These methods are more effective when the serum level is >850 mcg/ml. We decided to use TPE in this patient since valproic acid is protein bound. Thus this case illustrates the potential effectiveness of TPE as adjuvant therapy in the management of severe valproic acid toxicity.