Valproic Acid

Valproic acid (VPA), sold under the brand names Depakene® or Depakote®, is used to treat seizures, mania, and for migraine prophylaxis. In overdose, you can see symptoms such as CNS depression, hepatotoxicity, GI symptoms, QTc prolongation, leukopenia, seizures, and cerebral edema. Hyperammonemia is caused by a VPA-induced carnitine deficiency which ultimately causes a urea cycle disruption and an increase in ammonia.

Laboratory Studies
Follow VPA levels every 4-6 hours until peaked and trending downward. If patient has mental status changes, check an ammonia level (may want to use oxalate/gray-top tube to prevent false elevation of ammonia). Check an ammonia level every 12 hours if treating with levocarnitine. Other useful labs: electrolytes, glucose, BUN, creatinine, calcium, LFT’s, prothrombin time, measured serum osmolality, CBC and ABG. VPA may cause false-positive urine ketones.

Pharmacokinetics and Toxicokinetics
Elimination half-life of VPA is 9-16 hours in therapeutic doses and in an overdose can be prolonged up to 30 hours. Peak levels have been reported up to 18 hours post ingestion and even later with extended release products.

Treatment
- **Levocarnitine**: FDA approved drug used to treat carnitine deficiency associated with VPA toxicity.
  - Indications for use: Hepatotoxicity, Hyperammonemia, Encephalopathy, High risk patients (i.e. children who ingest large amounts of VPA), VPA level greater than or equal to 450 mg/L
- **Hemodialysis**: VPA is highly protein bound with a small volume of distribution. However, in overdose protein binding becomes saturated and one can consider dialysis for these patients.
- **Multi-dose oral activated charcoal**: theoretically can be considered because VPA is metabolized by the liver and undergoes enterohepatic recirculation. The patient’s level of consciousness and aspiration risk must be determined prior to initiating oral activated charcoal.

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