Severe Lamotrigine Neurotoxicity Treated with Intralipid Emulsion Therapy

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Severe Lamotrigine Treated with Intralipid Emulsion Therapy

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Background: Intralipid emulsion (ILE) can be beneficial for cardiotoxicity related to highly lipophilic drugs. [1-2] Lamotrigine (LTG) is lipophilic; according to Merck Manual, the solubility of LTG at 25°C is 15 mg/ml in water. Though LTG's pharmacokinetics are well described, there are limited clinical data on severe LTG neurotoxicity treated with ILE.[2, 5]

Case Report: A 23-year-old male ingested up to 13 grams of LTG and 18 grams of fluridone with his friend. Forty minutes after ingestion, the patient was found slouching and drooling at the mouth. He was received at Pinnacle Health Hospital with a wide array of symptoms including drowsiness, tachycardia, hypertension, hyperreflexia, clonus, prolonged QRS and elevated CK.

Many reports of LTG toxicity are associated with serotonin syndrome. The kinetics of LTG is interesting; the concentration of LTG increased slightly after the administration of ILE. Since the peak activity for LTG is within 3 hours, at 60 hours post ingestion, this patient was probably well past peak. [5] The clinical course supports this time frame, with the serum LTG levels dropping approximately 12 hours post ILE when he again became restless and agitated, receiving 4 doses of ILE over a 6-hour period. In retrospect, the benzodiazepine likely exposed the problem; this patient was balancing bacterial growth, inflammatory response, and oxygenation related to aspiration pneumonitis.

References:


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1. The patient arrived at our institution 11 hours after ingestion. He continued to experience tachycardia, hyperreflexia, with agitation. There were episodes of moaning and screaming, opisthotonic posturing, theta waves on the EEG, and increased respiratory rate to 40 breaths per minute. On hospital day 0, the patient was agitated and restless. He experienced impulsive myoclonic jerks and, during a brief restraint period, fell over the bed rails onto the floor. Although he was not injured, the restraints were removed due to his protection. Low dose midazolam was started as an adjunctive agent for convulsive-mediated sedation. After the second dose, the patient became mildly hypotensive; the clonidine was discontinued. The patient was then resolved with his fluids. His creatine kinase climbed to 1777 U/L. An EEG demonstrated evidence of continued sodium channel blockade (see figure 2).

2. Only on hospital day 2, the patient continued to experience a slight increase in LTG concentration may be due to the effects of ILE, pulling LTG from the tissues into the lipid matrix. ILE's half-life is highly variable and 14-103 hours.[5] LTG has auto-induce its metabolism up to 25%, which is considered to be insignificant. Our patient had an apparent initial half-life of 4 hours. The half-life seemed to change after the administration of ILE, however more data points are needed to confirm if this change was related to ILE.

3. The kinetics of LTG is interesting; the concentration of LTG increased slightly after the administration of ILE. Since the peak activity for LTG is within 3 hours, at 60 hours post ingestion, this patient was probably well past peak. [5] The clinical course supports this time frame, with the serum LTG levels dropping approximately 12 hours post ILE when he again became restless and agitated, receiving 4 doses of ILE over a 6-hour period. In retrospect, the benzodiazepine likely exposed the problem; this patient was balancing bacterial growth, inflammatory response, and oxygenation related to aspiration pneumonitis.

4. This patient's hospital course supports the mechanism of LTG as an inhibitor of voltage-gated sodium channels, release of the sodium emulsion relaxes glutamate and aspartate. [4] LTG has been shown to decrease neurotransmitter release, and inhibit the serotonin transporter. The result was improved serotonin toxicity, with now unbalanced benzodiazepine agonism and dopamine blockade, resulting in overinhibition. In addition to a definitely balanced reduced neurotransmitters, there was no history of tobacco, street drug, or alcohol use. This patient had a history of tobacco, street drug, or alcohol use. This patient had a history of tobacco, street drug, or alcohol use.