Introduction

Lamotrigine is commonly prescribed for the treatment and prophylaxis of seizures, fibromyalgia, bipolar disorder, and bipolar depression (Betchel & et al 2022; Mufson 2018; Karaoulanis & et al 2016) and around 1.8 million patients are currently on the medication (Lamotrigine 2022). Unfortunately, individuals prescribed Lamotrigine for bipolar disorder often experience an elevated incidence of suicidal ideation, with approximately 25-60% attempting suicide, and 4-19% completing it (Novick & et al 2010). Lamotrigine has been noted to potentially increase suicidality when compared to other antiepileptics/mood stabilizers (Patorno & et al 2010).

Understanding the implications of lamotrigine is crucial in clinical practice due to the intersect of a vulnerable population with a medication that may exacerbate their suicide risk. Lamotrigine’s mechanism of action is related to the blockade of voltage-gated sodium channels, and so toxicity manifests primarily as neural suppression (Betchel & et al 2022; Mufson 2018). Mild overdoses result in somnolence, nausea, vomiting, vertebrobasilar symptoms, and tachycardia (Alyahya & et al 2018; Karaoulanis & et al 2016). Severe symptoms include seizures, the most common life-threatening symptom, severe CNS depression/coma, QRS prolongation, cardiac dysfunction, and hypotension (Alyahya & et al 2018; Karaoulanis & et al 2016). Children develop symptoms at lower blood concentrations and smaller ingestions and tend to have more seizures when compared to adults (Alyahya & et al 2018; Karaoulanis & et al 2016). Despite the lamotrigine’s frequent use and potential for overdose, only two deaths were found upon literature review, resulting from ingestions of 4 grams and 7.5 grams respectively (Alyahya & et al 2018; Karaoulanis & et al 2016).

CASE REPORT - OPEN ACCESS

LAMOTRIGINE OVERDOSE CAUSING SEIZURE AND APNEA WITH RAPID CLINICAL IMPROVEMENT: A CASE REPORT

Kaitlyn Lizardo, MD, Mackenzie Brown, MD, S Aaron Ralston, DO
Kaitlyn Lizardo, MD, 1500 S Main Street, Fort Worth, TX 76104, Email: klfzdaro@jspshealth.org
Mackenzie Brown, MD, 1500 S Main Street, Fort Worth, TX 76104, Email: Mbrown12@jspshealth.org
S Aaron Ralston, DO, 1500 S Main Street, Fort Worth, TX 76104, Email: aralston@ies.healthcare.org

Article history:
Received 04 June 2024
Revised 17 June 2024
Accepted 22 June 2024
Published 30 June 2024

Keywords:
Apnea,
Lamotrigine,
overdose,
seizure,
Toxicity.

overdose on less than a month’s supply of low dose Lamotrigine can result in significant morbidity. In this case report, we detail the instance of a 25-year-old male who overdosed by consuming a 20-day supply of his prescribed lamotrigine, amounting to approximately 4 grams in total. The patient arrived approximately 90 minutes post-ingestion, displaying symptoms of nystagmus, somnolence, and mild fatigue. Within the subsequent two hours, seizures and apnea emerged, necessitating intubation. Effective treatment was administered, and the patient had symptom resolution within 12 hours. The patient’s symptoms correlated with the expected time to peak serum concentration; however, his rapid resolution is at odds with previously measured elimination half-lives of lamotrigine. This case contributes to the existing literature on a relatively uncommon but possibly rising overdose occurrence. It also emphasizes the clinical importance of delineating the trajectory of symptom manifestation and resolution and advocating for additional scrutiny of the anticipated clinical progression.

© 2024; Kaitlyn Lizardo, et al., This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License, which permits unrestricted use, distribution and reproduction in any medium, provided the original author and source are credited.

Highlights
1. Patient overdosed on approximately 4 grams of lamotrigine resulting in seizures and apnea approximately 4 hours after ingestion.
2. Patient experienced rapid improvement of symptoms, inconsistent with known elimination half-life of lamotrigine.
3. The rapid improvement of the patient may suggest that a large lamotrigine overdose can induce self-metabolism.

Introduction

Lamotrigine is commonly prescribed for the treatment and prophylaxis of seizures, fibromyalgia, bipolar disorder, and bipolar depression (Betchel & et al 2022; Mufson 2018; Karaoulanis & et al 2016) and around 1.8 million patients are currently on the medication (Lamotrigine 2022). Unfortunately, individuals prescribed Lamotrigine for bipolar disorder often experience an elevated incidence of suicidal ideation, with approximately 25-60% attempting suicide, and 4-19% completing it (Novick & et al 2010). Lamotrigine has been noted to potentially increase suicidality when compared to other antiepileptics/mood stabilizers (Patorno & et al 2010).

Understanding the implications of lamotrigine is crucial in clinical practice due to the intersect of a vulnerable population with a medication that may exacerbate their suicide risk. Lamotrigine’s mechanism of action is related to the blockade of voltage-gated sodium channels, and so toxicity manifests primarily as neural suppression (Betchel & et al 2022; Mufson 2018). Mild overdoses result in somnolence, nausea, vomiting, vertebrobasilar symptoms, and tachycardia (Alyahya & et al 2018; Karaoulanis & et al 2016). Severe symptoms include seizures, the most common life-threatening symptom, severe CNS depression/coma, QRS prolongation, cardiac dysfunction, and hypotension (Alyahya & et al 2018; Karaoulanis & et al 2016). Children develop symptoms at lower blood concentrations and smaller ingestions and tend to have more seizures when compared to adults (Alyahya & et al 2018; Karaoulanis & et al 2016). Despite the lamotrigine’s frequent use and potential for overdose, only two deaths were found upon literature review, resulting from ingestions of 4 grams and 7.5 grams respectively (Alyahya & et al 2018; Karaoulanis & et al 2016).
Treatment of Lamotrigine is primarily supportive in nature. Seizures should be controlled with benzodiazepines, barbiturates, and propofol. Airway support is critical, as symptoms can range from mild respiratory depression requiring only supplemental oxygen to, as was seen in our case, total respiratory failure requiring endotracheal intubation. QRS prolongation can be treated with sodium bicarbonate or hypertonic saline, and hypotension should be treated with fluids and pressor support (Alyahya et al. 2018; Betchel et al. 2022; Karaulanlis et al. 2016; Mufson 2018). Case reports indicate that dialysis and intralipids should be considered for severe intoxications (Agraval et al. 2019; Alyahya et al. 2018; Gastanares-Zapatero et al. 2012).

**Case Presentation**

A 25-year-old male with past medical history of bipolar disorder unspecified type I or II, presented to the ER at midnight after attempted suicide by ingesting approximately 20 tablets of his 200mg lamotrigine 90 minutes prior to arrival. Upon arrival, the patient was alert and oriented, reporting depression and suicidal ideation, but denying any symptoms from his overdose.

Physical exam at that time revealed a heart rate of 162, blood pressure of 162/96, and normal respiratory rate and oxygen saturation on room air. He exhibited signs of anhedonia, depression with a flat affect, and mildly anxious. Neurologic exam demonstrated bilateral lower and upper extremity clonus, bidirectional nystagmus, mild ataxia with finger to nose testing. Lab evaluation was unremarkable, and EKG showed mild sinus tachycardia with a QRS of 103, QTc of 421. He received a liter of IV fluids for his tachycardia, placed on end-tidal CO2 capnography, and assigned a sitter for monitoring.

Over the next few hours, the patient’s symptoms progressively worsened, most notably exhibiting deteriorating vertebrobasilar symptoms. At approximately 0300, the patient abruptly decompensated, culminating in a generalized tonic-clonic seizure and subsequent apnea. His seizure terminated after a total of 4 mg of IV lorazepam intravenous; however, his apnea persisted which he survived with the patient decompensating approximately 4 hours post ingestion (Rambeck & Wolf 1993), which relatively correlated with the patient decompensating approximately 4 hours post ingestion. Interestingly, the patient’s swift improvement in symptoms contradicts the known elimination half-life of lamotrigine, which ranges from 22.8 to 37.4 hours (Rambeck & Wolf 1993). It has been previously suggested that lamotrigine may induce its own metabolism due to a potential increase in suicidality (Novick & et al 2010; Patorno & et al. 2010). Lamotrigine toxicity is attributed to the sodium channel blockade. Toxicity typically manifests with somnolence, ataxia, and nystagmus. Developing seizures and apnea are rare (Mufson 2018; Karaulanlis et al. 2016), and deaths from ingestion are exceedingly uncommon (Alyahya et al. 2018; Karaulanlis & et al 2016). This case highlights severe lamotrigine toxicity, with the patient experiencing respiratory failure post-seizure, which could have been fatal without prompt emergency department intervention.

Recognizing symptoms of lamotrigine overdose and knowledge of treatment is crucial for emergency providers, as well as understanding both the expected and rare manifestations of toxicity (Lamotrigine 2022; Novick & et al. 2010), as Lamotrigine continues to be prescribed in high risk populations. This case adds to the growing body of literature describing a relatively rare overdose of increasing significance. Although our patient had an optimal outcome with acute emergency room intervention, the rapid improvement in symptoms contradicts the reported elimination half-life of lamotrigine, suggesting potential induction of its metabolism in overdose.

While this case is limited by the fact that a serum lamotrigine level was not obtained, there was a correlation between known peak absorption and toxicity in our patient. Lamotrigine is known to have a peak serum concentration generally reported to be about 3 hours post ingestion (Rambeck & Wolf 1993), which relatively correlated with the patient decompensating approximately 4 hours post ingestion. Interestingly, the patient’s swift improvement in symptoms contradicts the known elimination half-life of lamotrigine, which ranges from 22.8 to 37.4 hours (Rambeck & Wolf 1993). It has been previously suggested that lamotrigine may induce its own metabolism in overdose, and this may be indicative of that (Goa et al. 1993).

Despite previous overdoses of similar magnitude resulting in fatalities (Alyahya & et al. 2018; Karaulanlis et al. 2016), there remains a lack of established timelines for the expected clinical course following single ingestions of lamotrigine (Rambeck & Wolf 1993). Hence, this case underscores the need for further study aimed to ascertain the expected course after significant overdose and determine appropriate observation periods for patients.

**Table 1:** Timeline of Events for a patient with Lamotrigine overdose.

<table>
<thead>
<tr>
<th>Time</th>
<th>Event Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>22:30</td>
<td>Patient ingested 4 grams of Lamotrigine</td>
</tr>
<tr>
<td>00:00</td>
<td>Patient demonstrating bilateral bidirectional nystagmus, upper and lower extremity clonus, ataxia, GCS 15 without any difficulty with tasks, moving all extremities well. Placed on end tidal-capnography, labs drawn, given fluids</td>
</tr>
<tr>
<td>01:10</td>
<td>Poison control contacted. Patient started slurring words and experiencing increasing somnolence.</td>
</tr>
<tr>
<td>02:00</td>
<td>Patient reassessment showed worsening somnolence, GCS of 13 (M5 E3 V4), continuing clonus well past 3 beats. Severe slowing of mentation with worsening slurring of words, bidirectional nystagmus now without ocular movement.</td>
</tr>
<tr>
<td>03:00</td>
<td>Notified of generalized tonic-clonic seizure. Patient required a total 4mg Ativan for seizure cessation.</td>
</tr>
<tr>
<td>03:06</td>
<td>Post ictal. Patient complete GCS of 3, with complete apnea when not getting painfully stimulated. Required bagging for hypoxia and hypocapnia.</td>
</tr>
<tr>
<td>03:12</td>
<td>Patient intubated, maintained sedation with propofol and versed. ICU consulted.</td>
</tr>
<tr>
<td>04:05</td>
<td>Patient transferred to ICU, maintained on propofol and versed, GCS 3T.</td>
</tr>
<tr>
<td>07:30</td>
<td>Sedation stopped.</td>
</tr>
<tr>
<td>10:00</td>
<td>Patient now returned to a GCS of 15, mildly somnolent but awake, reactive, responding well.</td>
</tr>
<tr>
<td>11:00</td>
<td>Patient extubated, passed swallowing and PO challenge, reportedly well appearing per notes.</td>
</tr>
<tr>
<td>14:00</td>
<td>Returned to complete neurological baseline per hospitalist notes. No signs of clonus, nystagmus, or any other toxicodynamic symptoms.</td>
</tr>
</tbody>
</table>
Conclusion

In conclusion, lamotrigine is typically considered a safe and well tolerated antiepileptic and mood stabilizer. Instances of severe toxicity or fatalities due to lamotrigine overdose are rare. However, our patient exhibited severe toxicity, but showed unexpected rapid improvement after medical resuscitation. This suggests that lamotrigine may prompt its own metabolism during overdose, contributing to the patient’s rapid improvement.

Conflict of Interests: There are no conflict of interests.

Financial Support and Sponsorship: Nil

Ethical Considerations: Nil

REFERENCES


10. Patorno, Elisabetta; Bohn, Rhonda L; Wahl, Peter M; Avorn, Jerry; Patrick, Amanda R; Lin, Jun; Sebastian Schneeweiss. Anticonvulsant Medications and the Risk of Suicide, Attempted Suicide, or Violent Death. JAMA. 2010;303(14):1401. doi:10.1001/jama.2010.410