Lamotrigine Intoxication Provoking Status Epilepticus in an Adult With Localization-Related Epilepsy

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Background: Various anticonvulsant medications have been associated with paradoxical aggravation of epileptic seizures in therapeutic doses and toxic concentrations. Lamotrigine has been reported to exacerbate seizures and myoclonic seizures in generalized epilepsy in a child with localization-related epilepsy.

Objective: To describe lamotrigine intoxication paradoxically producing status epilepticus in an adult with localization-related epilepsy.

Design: Observational case report.

Setting: Neurology service, inpatient hospitalization, and outpatient follow-up in a neurology clinic.

Patient: A patient with known localization-related epilepsy who ingested an overdose of lamotrigine tablets in a suicide attempt.

Intervention: None.

Main Outcome Measure: Observation of the course of the patient’s reaction to lamotrigine intoxication, monitoring of lamotrigine levels, and monitoring of ictal and postictal status.

Results: The patient developed a prolonged convulsive status epilepticus, which was eventually controlled with benzodiazepines. The patient also developed transient obtundation and severe ataxia, all of which resolved completely within 96 hours.

Conclusions: To our knowledge, in addition to being the first case report to describe convulsive status epilepticus after lamotrigine intoxication, this is the first report of the proconvulsant effect of lamotrigine in a case of localization-related epilepsy in an adult. The effects of accidental or suicidal ingestion of lamotrigine tablets seem to be reversible.

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It has been recognized for more than 40 years that anticonvulsant medications may paradoxically exacerbate seizure activity. Carbamazepine (including oxcarbamazepine), phenytoin, gabapentin, and tiagabine have been reported to aggravate seizures in idiopathic generalized epilepsies, especially myoclonic jerks and absence seizures. The mechanisms leading to a paradoxical seizure are not fully understood, but they are thought to be due to an inverse pharmacodynamic effect, the development of tolerance or an acute idiosyncratic adverse effect, or poor compliance.

Lamotrigine has been associated with exacerbation or de novo myoclonus in idiopathic generalized epilepsies. Although a case report described a paradoxical reaction to lamotrigine therapy in benign focal epilepsy of childhood with centrotemporal spikes, little is known of the association between lamotrigine intoxication and exacerbation of seizure activity in symptomatic localization-related epilepsies. We describe a case of lamotrigine intoxication provoking status epilepticus in an adult with symptomatic localization-related epilepsy.

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Various anticonvulsant medications have been observed to be paradoxically proconvulsant for epileptic patients whose intake is at toxic levels. The proconvulsant effect of high doses of anticonvulsant medications was previously reported with carbamazepine \(^1\) (including oxcarbamazepine \(^2\)) and phenytoin. \(^4\) A comprehensive review of the paradoxical aggravation of anticonvulsant medications was previously published by Genton. \(^9\) Aggravation of seizures with a certain medication does not necessitate discontinuation of the medication if it is used cautiously. A temporal relationship between the high levels and the exacerbation of seizures is crucial to identify a potential aggravation by antiepileptic medications. \(^5\) In our patient there was a clear temporal relationship between a lamotrigine overdose and status epilepticus.

Recent articles have demonstrated the proconvulsant effects of lamotrigine therapy, mostly in childhood conditions such as benign focal epilepsy of childhood with centrotemporal spikes, \(^6\) severe myoclonic epilepsy of infancy, \(^7\) Lennox-Gastaut syndrome, \(^8\) and juvenile myoclonic epilepsy. \(^9\) Although described less often in adults, the proconvulsant effects of lamotrigine therapy have been demonstrated in idiopathic generalized epilepsy alone\(^1\) and in idiopathic generalized epilepsy with myoclonic jerks. \(^10\) Moreover, nonconvulsive status epilepticus has been associated in 3 patients with idiopathic generalized epilepsy. \(^11\)

To our knowledge, localization-related epilepsy exacerbated by toxic doses of lamotrigine has not been reported previously. Moreover, this is the first report of a case describing lamotrigine provoking status epilepticus in an adult with localization-related epilepsy. The patient, without history of secondarily generalized seizures, developed tonic-clonic status epilepticus with lamotrigine intoxication. Her seizures seemed to exacerbate after the acute intoxication, but no definite relationship between increased seizure frequency and the lamotrigine intoxication can be established, as her antiepileptic medication regimen was changed. The increase in seizure frequency may merely reflect medication changes.

Lamotrigine therapy is efficacious for most seizure types, and it is widely used in the treatment of partial and generalized epilepsies. \(^12\) It is considered a relatively safe medication, with rare central nervous system adverse effects such as anxiety, ataxia, confusion, depression, headache, insomnia, irritability, and concentration problems. The most significant adverse events are skin hypersensitivity reactions, which frequently lead to discontinuation of lamotrigine therapy, due to possible progression to Stevens-Johnson syndrome. \(^13\)

Our patient became ataxic and somnolent with lamotrigine intoxication. All of those symptoms completely resolved. No skin eruptions occurred. Other articles have described ataxia and encephalopathy with accidental or suicidal lamotrigine ingestion at toxic concentrations. \(^14\) To our knowledge, no cases of fatal lamotrigine intoxication have been reported although, in a retrospective review of autopsies, death was associated with an intake of lamotrigine. \(^15\) However, those patients may have represented sudden unexplained death in epilepsy. Skin eruptions or Stevens-Johnson syndrome do not seem to be associated with lamotrigine intoxication per se. \(^16\) In summary, the aggravation of seizures with toxic concentrations of lamotrigine can occur not only in myoclonic seizures but also in localization-related epilepsy. Lamotrigine seems safe even after ingestion of high or toxic concentrations with reversible ataxia and encephalopathy.
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REFERENCES


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