**Introduction**

Lamotrigine was first marketed in the early 1990s. It is a newer generation, broad spectrum anti-epileptic drug (AED) and is also used for mood disorders. It is one of the most commonly used AEDs in paediatrics. Lamotrigine is a phenyltriazine compound that stabilizes the presynaptic neuronal membranes by blocking voltage-dependent sodium channels and thereby preventing the release of excitatory amino acids particularly glutamate and aspartate. (1)

Unintentional paediatric ingestion in the majority of cases have minimal or nil symptoms. (2) Reported symptoms in overdose include ataxia, dizziness and tachycardia. There have also been reports of more serious clinical effects in overdose including coma, seizures and respiratory depression.

We are reporting two paediatric cases of accidental lamotrigine ingestion where both children had prolonged agitation, altered sensorium and abnormal movements.

**Case One**

An 18-month-old 9 kg female was brought to a regional Emergency Department by her mother. The child had been well that morning, and then became acutely distressed and agitated. She had earlier been found playing with her mother’s wallet, that contained a blister pack of lamotrigine 100mg tablets. This child had no known health issues, was up to date with her immunisations and not on any regular medications.

On arrival to the Emergency Department, she was alert, her eyes were open but not focusing or following objects. She was not responding as would be expected for her age and was screaming. She required 5 adults to restrain her for intravenous access. Her behaviour was described as agitated, with ‘thrusting’ movements, symmetrical, not rhythmic and not purposeful. There were several discrete episodes each lasting 15-20 minutes with opisthotonus and extension posturing near normal tone in between. Her heart rate varied from 118-155, blood pressure 96/54 and temperature 37C. Cardiorespiratory examination was unremarkable apart from episodic tachypnoea; she had normal central capillary return but was described as peripherally mottled. She had horizontal nystagmus; her movements were choreoathetoid rather than seizure-like. Pupils were 3mm and reactive. It was noted she was bruising to her cheek, forehead and thigh. Provisional diagnoses included seizure disorder, encephalitis, lamotrigine ingestion, extrapyramidal syndrome and non-accidental injury.

Initial treatment included IV midazolam in 1mg boluses that had the effect of ‘settling’ the episodes although from case notes the episodes continued. She was given a loading dose of phenytoin (200mg IV) and cefotaxime (500mg IV). Benztropine 0.4mg IV was given with no apparent change in behaviour.

The child was retrieved to a paediatric hospital for ongoing investigations and management. A non-contrast brain CT showed no abnormality. The episodes of abnormal posturing and movements continued. Her GCS varied from 9-11. She was managed in the paediatric ICU overnight and received further IV midazolam and morphine sedation for agitation.

All basic investigations were normal. She developed an elevated creatinine kinase which peaked that night at 6320IU/L. Her ammonia level was initially elevated at 127mmol/L (6 hours post arrival, reference range 15-50mmol/L), but was 48mmol/L on subsequent testing.

She was treated with IV vancomycin, acyclovir and cefotaxime to cover encephalitis. She had a cumulative total of 6.9mg midazolam, 0.4mg benztropine, 200mg phenytoin, and 1.5mg morphine over 16 hours.

The child had improved by the next day, but remained hypertonic, lower limbs to a greater extent than upper. She was alert and responsive to her mother, with intermittent mild agitation and slightly bizarre posture when picked up.

It was confirmed that the child had no access to other medications; there were no pesticides in the house. The lamotrigine level was available 52 hours after the initial presentation. The level was 118.2mmol/L upon her arrival at hospital (reference range 3.9-15.4mmol/L). A repeat level 7 hrs later was 114mmol/L. Graph 1 shows her lamotrigine levels from arrival till discharge. The child improved and was ready for discharge after 3 days with no apparent deficit.

**Case Two**

An otherwise healthy 20 month old, 11kg boy, presented 16 hours after possible ingestion of his mother’s tablets. The previous evening he had been playing in his mother’s bedroom, he woke up with a blister pack of lamotrigine 100mg tablets, and took a 150mg tablet and paroxetine 20mg. A sibling reported to his mother that he had been seen eating tablets. He was well so she placed him in bed, but states when she kissed his lips, they did taste of lamotrigine tablets. The following morning while getting him dressed, his mother noted him to be flushed and agitated. She took him for review by his local doctor and he was subsequently referred to a tertiary paediatric hospital.

On arrival in the emergency department, 16 hours post possible ingestion, he was noted to be agitated, had an altered sensorium and was jittery. On examination he had dilated pupils, heart rate =110 beats/min, BP =100 systolic, O2asts =99% on room air. Neurologically he was drowsy with a delirium. He had abnormal movements of his body that were non purposeful, thrusting like movements with extensor posturing. He had normal tone, with brisk reflexes, but no clonus. ECG showed a normal sinus rhythm with a normal QRS duration. He was treated with a small dose of 0.5mg of IV midazolam.

Over the next 24 hours he was noted to have a few abnormal movements of all 4 limbs lasting a minute. They were not associated with any daydreams or a post- lctal period. His symptoms improved to the following morning and resolved after 48 hours. He was discharged with no neurological deficit.

After discharge his lamotrigine levels became available, a level collected 16 hours post ingestion was 20.4mmol/L (reference range for therapeutic doses 3.9-15.4mmol/L). A repeat lamotrigine level 40 hours post ingestion was 9.6mmol/L.

**Discussion**

The first case report of lamotrigine overdose was in 1997, as a 26 year old man ingested 1350mg and was described as hypertonic, with nystagmus; he had an ECG with QRS prolongation. They had a flush and flushed skin. There are only a few pediatric case reports of lamotrigine overdose in the literature. These include a 19-month child who had 2 tonic-clonic seizures after an unknown dose of lamotrigine. The lamotrigine level at one-hour post ingestion was 79mmol/L. The child was observed in ICU with no further complications. Similarly, there was a case report of a 2yo child who ingested 800mg of lamotrigine and had a tonic-clonic seizure. The lamotrigine level was 15mmol/L, 2hrs post ingestion. After two days, this child’s symptoms had resolved. (5)

And a 5yo child had a medication error with the lamotrigine dose increased from 15mg/kg/day to 25mg/kg/day only for one day and developed ataxia, confusion, seizures with all symptoms resolving by 30 hours. (6)

Lofton and Klein-Schwartz reviewed cases of single substance lamotrigine ingestions, reported to the American Association of Poison Control Centers Toxic Exposure Surveillance System between 2000 and 2001. They found 493 cases of lamotrigine ingestion, of which 173(35.1%) were in children under 4 years old. The majority of patients(52.1%) had no significant toxic effects. Effects were minor in 30.4%, moderate in 14.8%, major in 2.6%. There were no reported deaths related to lamotrigine ingestion alone. Minor and moderate symptoms included: drowsiness/ lethargy(20.9%), vomiting(11%), nausia(5.1%), ataxia(4.9%), dizziness(4.5%) and tachycardia(4.3%). Major symptoms included: coma in 1.2%(n=6), seizures in 1.6%(n=8) and respiratory depression in 0.6%(n=3). There were no major symptoms reported in children.

We have reported 2 cases of accidental pediatric ingestion of lamotrigine, both with elevated lamotrigine levels. The first case had markedly elevated levels much higher than those reported in other paediatric exposures. The patient in case one had symptoms of severe agitation, horizontal nystagmus with hyperreflexia, intermittent episodes of hypertonicity and choreoathetoid movement. The second case also had delirium and abnormal movements. It is important to note that case two may have also ingested bupropion and a SBRi. Bupropion in severe overdoses is known to cause tachycardia, agitation, seizure and delirium and possible ingestion of this drug, may have contributed to this child’s clinical presentation.

These cases highlight that accidental lamotrigine ingestion in children may cause abnormal movements and a prolonged delirium of greater than 24 hours. However despite very high lamotrigine levels in case one, both children made a full recovery with good supportive care.

**References**


**Graph 1:** The child’s serum lamotrigine levels taken over the admission

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