JPPT | Case Report

Eslicarbazepine Overdosing in a Teenager: Case Description and Management

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Eslicarbazepine acetate has been recently licensed as an anti-epileptic medication to be used in adolescents. Data regarding dosing and overdosing are still limited in the literature. We describe a rare case of intentional eslicarbazepine overdosing in a previously healthy teenager who presented with neurological toxicity. Management of hyperhydration with diuretics, haloperidol, and midazolam proved to be helpful both in inducing rapid clearance through the kidneys and in managing symptoms of agitation, respectively.

ABBREVIATIONS IV, intravenous

KEYWORDS overdosing; eslicarbazepine acetate; neurological toxicity; adolescence; poisoning

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Information Box

What specific questions does this report address?

This case report addresses the question of eslicarbazepine acetate overdosing.

What does this report add to our current knowledge?

This case report adds knowledge to the clinical presentation and management of eslicarbazepine overdosing in adolescents.

Introduction

Eslicarbazepine acetate is a new anti-epileptic medication that has been recently licensed for the treatment of focal seizures.[1] The drug has been approved by the United States Food and Drug Administration for use in individuals 4 years and older since 2017.[2] An oral dose of 800 mg/day has been proven to be safe, effective, and well-tolerated in adults.[3] It can also be used as adjunctive therapy in adults, adolescents, and children aged older than 6 years with partial-onset seizures with or without secondary generalization.[4] Data on overdosing are limited and mainly concern seizures, status epilepticus, and cardiac toxicity (arrhythmia).[4] We report a 14-year-old female with intentional eslicarbazepine overdose and describe the clinical presentation and management.

Case Report

A 14-year-old adolescent female with a mental health history was brought to a primary health center by her foster parents, who found her unresponsive in her room. Her weight was 70 kg, and she had been prescribed eslicarbazepine for depression (off-label use) 3 months earlier. Thirteen tablets were missing from the box, so it was assumed that she had ingested 10.400 mg of eslicarbazepine 2 to 3 hours earlier. Of note, the patient had recorded the suicide attempt and had uploaded a video in a widely used video-sharing application. Hence, the exact time of ingestion became known to us a few hours later.

The National Poison Center advised gastric lavage, activated charcoal (1g/kg) administration via nasogastric tube, and transfer to a tertiary center. Upon arrival to our emergency department (6 hours postingestion), her Glasgow Coma Scale score was 7 of 15, her pupils were dilated, sluggishly responsive to light, and she was only responding to painful stimuli. She had a patent airway (SpO_2 = 97%), stable heart rate (98–120 bpm), and slightly elevated blood pressure (145/70 mm Hg). She was administered 1 mg of flumazenil, 1.2 mg of naloxone, and 100 μg of clonidine, with no effect. Cardiac monitoring revealed a sinus rhythm with a normal QTc interval (400 msec). She was admitted to the general pediatric ward of the hospital. Two hours later (8 hours postingestion), she remained in deep lethargy with stable vital signs but started having episodes of agitation with abnormal nonepileptic movements of the upper and lower extremities. She remained in a state of reduced consciousness, fluctuating between stupor and extreme agitation and irritability, with incomprehensible speech and muscle spasms or movements resembling focal seizures and myoclonus for more than 12 hours. To control the episodes of irritability, she was restrained on her bed and was given intravenous (IV) haloperidol (2.5 mg, twice), IV propofol (6 mg, once), and buccal

midazolam (10 mg, once). She was also given IV fluids and furosemide (20 mg) to maximize urine output, aided by an infusion of mannitol (50 m/l/20 min). Because of the persistent neurological symptoms, a computed tomography scan of the brain was performed, which showed no evidence of focal lesions, hemorrhage, or edema. The patient remained hemodynamically stable and gradually regained consciousness approximately 21 hours postingestion, remaining fully orientated and in good medical condition. Blood and urine toxicologic analysis detected an elevated concentration of the active metabolite eslicarbazepine, confirming overdosing (blood: 51 mcg/mL, urine: 141 mcg/mL) when the therapeutic range in urine is 5 to 35 mcg/mL. Moreover, cannabinoids were also isolated in the urine sample, indicating probable ingestion of additional drugs. She was referred for a mental health evaluation.

Discussion

Eslicarbazepine acetate is given orally and is metabolized via hydrolytic first-pass metabolism to its active metabolite eslicarbazepine, which directly blocks voltage-gated sodium channels with no involvement of cytochrome P450.[2,4,5] Its pharmacokinetic and pharmacodynamic properties have been studied in adults, and it was shown to have a half-life of 9 to 20 hours, reaching peak serum concentrations at approximately 4 hours postingestion. Subsequently, it is excreted through the kidneys.[6]

Data regarding the toxicity of eslicarbazepine acetate in children and adolescents are extremely limited. Consequently, the National Poison Center had very little information on symptoms and treatment of overdosing, and information on the upper limit of tolerated dose was unavailable. In our patient, neurological toxicity was clinically obvious and persistent. There is only 1 other reported case of intentional overdosing with this novel anti-epileptic drug. An 18-year-old female ingested 5600 mg of eslicarbazepine and suffered from clonus, seizures, and cardiac arrest. She was managed supportively and with hemodialysis.[7] Cardiac toxicity with QTc prolongation and malignant arrhythmia were also reported, a finding that was not confirmed in our patient by serial electrocardiograms.

Based on the experience gained from the described patient, we recommend the following for the management of eslicarbazepine overdose: clinicians should be aware that there is no antidote. Therefore, management is largely supportive. Apart from the cardiological side effects, overdose could cause neurological symptoms and especially a reduced level of consciousness, seizures, or agitation. The patient should be closely monitored until a full resolution of the altered level of consciousness because of possible self-harm and injury. Gastric lavage should be performed if the patient has a good level of consciousness and as soon as possible from the time of ingestion. Hemodialysis and activated charcoal are also suggested. In our case, hydration, diuretics, haloperidol, and midazolam proved helpful, but management should always be individualized and include cardiac monitoring.

In conclusion, the present case adds significant evidence to the limited data regarding eslicarbazepine acetate overdose, highlighting the persistent neurological toxicity. The use of common antidotes proved unhelpful, but haloperidol effectively controlled agitation. Rapid clearance through the renal route is recommended.

Article Information

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Ethical Approval and Informed Consent. The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national guidelines on human experimentation and have been approved by the appropriate committees at our institution. However, given the nature of this study, informed consent was not required by our institution. The parents provided informed consent regarding this publication.

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