Successful Use of Intralipid Therapy to Reverse Acute ECG Changes in a Poly-Anticonvulsant drug Overdose: A Case Report

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ABSTRACT

Introduction: Epilepsy, a prevalent neurological disorder, necessitates the use of anticonvulsant medications. Since the introduction of phenobarbital in 1912, numerous antiepileptic drugs (AEDs) have emerged, each targeting seizures via distinct mechanisms. Newer AEDs like Lamotrigine, Topiramate, Levetiracetam, and Lacosamide offer improved safety profiles but can present severe side effects, especially in overdose scenarios. This case report details the management of a poly-anticonvulsant overdose in a 57-year-old male, highlighting the successful use of intralipid emulsion therapy to reverse acute ECG changes.

Case: A 57-year-old male with a history of bipolar disorder, depression, seizure disorder, hypothyroidism, and hyperlipidemia was brought to the emergency department after an intentional overdose involving approximately 3000 mg of Lacosamide, 800 mg of Lamotrigine, 2400 mg of Quetiapine, and an unknown amount of Carbamazepine. Initial treatment with sodium bicarbonate and magnesium sulfate failed to resolve the patient's widened QRS (146 ms) and prolonged QTc (520 ms), which deteriorated to 158 ms and 580 ms, respectively. Following expert consultation, intralipid therapy was administered, resulting in rapid normalization of ECG findings and subsequent full recovery.

Conclusion: This case underscores the efficacy of intralipid therapy in reversing ECG changes in poly-anticonvulsant overdose, particularly when conventional treatments are inadequate. The rapid improvement following intralipid administration supports its consideration in similar overdose scenarios, warranting further research to optimize its use in clinical practice.

Keywords: Epilepsy, wide QRS, intra-lipid therapy, Antiepileptic.

INTRODUCTION

Epilepsy, characterized by recurrent seizures, is the most common serious neurological disorder, affecting many people globally. Treating epilepsy often requires anticonvulsant medications. The treatment of seizure disorders with antiepileptic medications dates to 1912, beginning with the introduction of phenobarbital. Over the past century, numerous antiepileptic drugs (AEDs) have been developed, each with distinct mechanisms of action targeting seizures. The 1990s saw the advent of newer AEDs, including Lamotrigine, Topiramate, Levetiracetam, and Lacosamide, which offer improved safety profiles. Beyond their primary use in managing epilepsy, these medications are also employed in the treatment of various other conditions such as mood disorders, refractory pain syndromes, headaches, and social phobias.

The latest anticonvulsant drugs, while generally more tolerable than their older counterparts, still present a range of side effects from minor inconveniences to severe and potentially life-threatening reactions. An overdose involving these newer anticonvulsants presents significant challenges for emergency and critical care physicians, given the diverse pharmacological classes they encompass. This report presents a case of intentional poly-anticonvulsant overdose in a 57-year-old male with new ECG changes (wide QRS and Prolonged QTc) that was successfully reversed with intralipid emulsion therapy.

CASE

A 57-year-old male with a significant medical history of bipolar disorder, depression with a previous suicide attempt resulting in a gunshot wound to the head, seizure disorder, hypothyroidism, and hyperlipidemia brought to the emergency department by ambulance after being found agitated, combative, and confused at home. His parents reported that he had been thrashing on the floor near his empty pill bottles, approximately one hour after ingestion, and expressing wishes to end his life. Upon EMS arrival at the patient's house, he was agitated and combative. During transport, he received a total of 5 mg of Midazolam and vomited multiple times.

Medication reconciliation and limited history provided by his parents suggested the ingestion of approximately 3000 mg (15x200 mg) of Lacosamide, 800 mg (4x200 mg) of Lamotrigine, 2400 mg (6x400 mg) of Quetiapine, and an unknown amount of Carbamazepine tablets. The patient had recently experienced a seizure episode, leading to an increase in his Carbamazepine dosage from 300 mg daily to 500 mg daily.

Upon arrival at the Emergency Department (ED), the patient remained agitated and combative but was protecting his airway. His respiratory rate was 23 breaths per minute, and his heart rate was 101-105 beats per minute. He was afebrile (36.5°C) with mildly elevated blood pressure (148/67 mmHg) and a pulse oximeter reading of 92% on room air, which improved to 98% with 2 liters/minute oxygen via nasal cannula. Patient's pupils were equal, round, and reactive to light, and extraocular movements were normal. He had a Glasgow Coma Scale score of 11 and an otherwise normal physical examination. The initial ECG (Figure 1) revealed a widened QRS (146 ms) and a prolonged QTc (520 ms), which were new findings compared to his previous ECG. Initial treatment included eight 50 mEq ampules of sodium bicarbonate administered 15-20 minutes apart, 1 g of magnesium sulfate, and 1 liter of normal saline. Investigations revealed leukocytosis (15.25, normal

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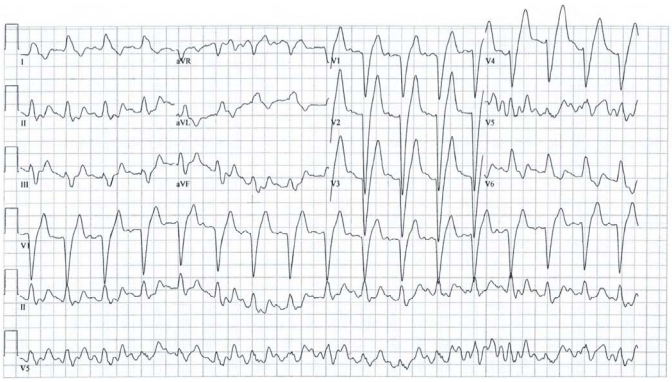
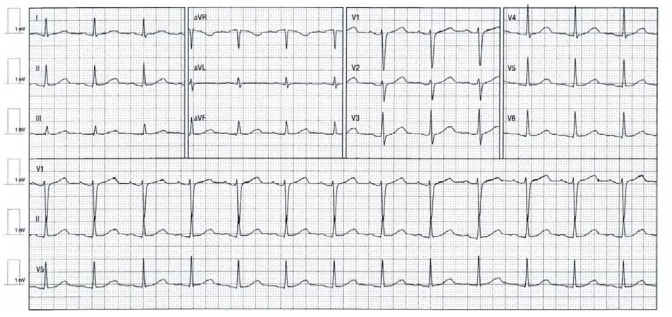
range 3.5-10.8), which the team attributed to stress, and metabolic alkalosis likely secondary to bicarbonate boluses. There was no evidence of co-ingestion with acetaminophen, salicylate, alcohol, or opiates. A chest X-ray was performed and was normal.



Despite these initial interventions, the QRS widening and QTc prolongation worsened to 158 ms and 580 ms, respectively, over the following 90 minutes, without any improvement in mental status. After consulting with experts from the national poison control center and the hospital ICU team, the initiation of intralipid therapy was chosen as the next step in management due to the poor response to bicarbonate and the variety of medications the patient had ingested. The patient received 1.5 ml/kg of 20% lipid emulsion over 1-2 minutes, followed by an infusion of 0.25 ml/kg/min for 30-60 minutes, totaling three 60 ml doses. Subsequent ECG within less than 10 minutes from 1st bolus showed complete normalization of previous ECG findings and back patient's baseline (Figure 2). The patient was admitted to ICU and got discharged within 5 days after complete mental status recovery.



DISCUSSION

The management of poly-anticonvulsant overdose presents significant challenges due to the diverse mechanisms of action of the involved drugs. Each anticonvulsant in this case (lacosamide, lamotrigine, quetiapine, and carbamazepine) has a unique pharmacodynamic profile, contributing to a complex clinical presentation and necessitating a multifaceted treatment approach. Lacosamide enhances slow inactivation of voltage-gated sodium channels, while lamotrigine inhibits glutamate release and sodium channels. Quetiapine, an atypical antipsychotic, has strong antagonism at serotonin and dopamine receptors, and carbamazepine stabilizes inactivated sodium channels, reducing synaptic transmission. These varied mechanisms can lead to cumulative and severe toxic effects, including profound CNS depression and significant cardiotoxicity, as seen in this case.

The presented patient's ECG changes, particularly QRS widening and QTc prolongation, are manifestations of these toxic effects. The initial management with sodium bicarbonate and magnesium sulfate aimed to address these cardiac abnormalities but proved insufficient. Intralipid therapy, which sequesters lipophilic drugs, offered a successful alternative by reducing the bioavailability of these medications. This highlights the need for an integrated and adaptive approach in treating complex poly-anticonvulsant overdoses.

Lacosamide, a newer anticonvulsant, is known for its relatively benign side effect profile at therapeutic doses. However, in overdose, it can lead to significant toxicity, including dizziness, ataxia, nausea, and cardiac effects such as PR interval prolongation [1,2]. There have been reports of severe cardiovascular complications, including ventricular arrhythmias and cardiac arrest, in cases of lacosamide overdose [1,2]. In the current case, the ingestion of approximately 3000 mg of lacosamide likely contributed to the severe cardiac conduction abnormalities leading to QRS widening and QTc prolongation.

Lamotrigine is another widely used anticonvulsant with a broad therapeutic index. Overdose with lamotrigine can cause severe neurologic and cardiac symptoms, including ataxia, seizures, and life-threatening arrhythmias [3]. Case reports have documented prolonged QTc and ventricular tachycardia in significant lamotrigine overdose [3]. Recent studies have detailed the complex pharmacokinetics and potential for serious adverse effects in overdose situations, including QTc prolongation and arrhythmias [4]. The dose ingested by our patient (800 mg) exceeds the typical therapeutic range and likely contributed to the observed cardiac toxicity.

Quetiapine, an atypical antipsychotic, is frequently prescribed for mood disorders and is known to cause dose-dependent toxicity. In overdose, it can lead to profound CNS depression, hypotension, and cardiac effects, including prolonged QTc and QRS widening [5,6]. Previous studies have shown that quetiapine can significantly prolong the QT interval, increasing the risk of torsades de pointes and other severe arrhythmias [5,6]. The ingestion of 2400 mg of quetiapine in our patient represents a significant overdose, contributing to the observed ECG changes.

Carbamazepine, a tricyclic-like anticonvulsant, is well-known for its narrow therapeutic index and potential for severe toxicity in overdose. Symptoms can range from dizziness and ataxia to seizures and cardiovascular collapse [7,8]. Cardiovascular effects include QRS widening and arrhythmias, often necessitating aggressive management [7,8]. The recent increase in the patient's carbamazepine dosage, along with the unknown quantity ingested, likely played a role in the observed cardiac manifestations.

The rationale for using intralipid therapy in drug overdose stems from its ability to sequester lipophilic drugs, thus reducing their bioavailability and toxicity. The "lipid sink" theory posits that intralipid emulsion creates a lipid phase in the blood, into which lipophilic drugs partition, thereby reducing their plasma concentration and toxicity [9]. This case demonstrates the rapid and effective reversal of ECG changes following intralipid therapy, consistent with the outcomes reported in other studies [9].

Previous reports have documented the successful use of intralipid therapy in various drug overdoses, including tricyclic antidepressants, calcium channel blockers, and local anesthetics [10]. However, its use in poly-anticonvulsant overdose is less well-documented. This case adds to the growing body of evidence supporting intralipid therapy's utility in managing severe cardiotoxicity from lipophilic drug overdoses.

CONCLUSION

This case report illustrates the successful use of intralipid therapy in reversing acute ECG changes associated with a poly-anticonvulsant drug overdose. Given the patient's poor response to initial treatment with sodium bicarbonate and magnesium sulfate, the rapid normalization of ECG findings following intralipid administration highlights its potential as a critical intervention in similar overdose scenarios. Further studies are warranted to elucidate the mechanisms and optimize the use of intralipid therapy in the management of poly-anticonvulsant and other lipophilic drug overdoses.

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