

Dyskinesia due to mexiletine overdose: a rare presentation

Zeynelabidin Öztürk¹*, Orkun Aydın²*, İlknur Bodur²*,
Raziye Merve Yaradılmış²*, Hale Atalay Çelik³*, Nilden TuYGun²*

¹Department of Pediatric Intensive Care, University of Health Sciences, Dr. Sami Ulus Obstetrics and Gynecology, Pediatric Health and Disease Training and Research Hospital, Ankara; ²Department of Pediatric Emergency Medicine, University of Health Sciences, Dr. Sami Ulus Obstetrics and Gynecology, Pediatric Health and Disease Training and Research Hospital, Ankara; ³Department of Pediatric Neurology, University of Health Sciences, Dr. Sami Ulus Obstetrics and Gynecology, Pediatric Health and Disease Training and Research Hospital, Ankara, Türkiye.

ABSTRACT

Background. Mexiletine, a class IB antiarrhythmic, is a structural analog of lidocaine. Our knowledge of mexiletine overdose is based on lidocaine overdose reports. Only a few cases of mexiletine overdose have been reported, including fatal overdoses. Mexiletine toxicity primarily affects the central nervous, cardiovascular, and gastrointestinal systems.

Case. A 16-year-old female was brought to our hospital by ambulance after taking an unknown dose of mexiletine in a suicide attempt. Ventricular fibrillation developed while in the ambulance; cardiopulmonary resuscitation was started and spontaneous circulation returned within 1 min. The patient had been taking oral mexiletine for 1 month to treat primary erythromelalgia. Her vital signs were normal, but she was unconscious. Following gastric lavage she was transferred to the pediatric intensive care unit. Midazolam and levetiracetam were required due to uncontrolled seizures. During the first hour of hospitalization, severe dyskinesia characterized by abnormal involuntary large hyperkinetic movements in all 4 extremities was observed and successfully treated with 2 doses of intravenous biperiden. The patient was discharged on day 6 of hospitalization.

Conclusions. Mexiletine overdose can be life-threatening. In addition to rapid and effective resuscitation, rapid identification and management of cardiovascular and central nervous system manifestations are key to preventing morbidity and mortality. The presented case had severe dyskinesia that was successfully treated with repeated doses of biperiden. Biperiden did not cause arrhythmia. Based on the presented case, we think biperiden should be considered for the treatment of movement disorders in cases of mexiletine overdose.

Key words: biperiden, dyskinesia, intoxication, mexiletine, poisoning.

Mexiletine, a class IB antiarrhythmic, is a structural analog of lidocaine, but with higher oral bioavailability, and is, therefore, administered orally.¹ Mexiletine can be used to treat neuropathic pain and is also reported to be beneficial for erythromelalgia.^{2,3} Our knowledge of mexiletine overdose is based on reported cases of lidocaine overdose.^{1,4-7} Both drugs have similar effects, but the literature includes only a few cases of

mexiletine overdose.^{1,4-7} Mexiletine toxicity primarily affects the central nervous system, cardiovascular system, and gastrointestinal system.¹ The possible clinical findings of mexiletine overdose include dizziness, visual impairment, paresthesia, dysarthria, ataxia, memory loss, euphoria, agitation, confusion, lethargy, coma, disorientation, psychosis, tremors, muscle twitches, seizures, respiratory arrest, arrhythmia and hypotension, and nausea and vomiting.¹ Fatal cases of mexiletine overdose have also been reported.^{5,7} Herein we present a case of dyskinesia due to mexiletine overdose that was successfully treated with biperiden.

✉ Zeynelabidin Öztürk
zeynelabidin_ozturk@hotmail.com

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Case Report

A 16-year-old female was brought to our hospital by ambulance after taking an unknown dose of mexiletine in a suicide attempt. Ventricular fibrillation developed while in the ambulance; cardiopulmonary resuscitation was started while preparing for defibrillation and spontaneous circulation returned within 1 min, without the need for defibrillation. The patient had been taking oral mexiletine for 1 month to treat primary erythromelalgia. Her parents reported that the patient took 16 mexiletine pills; however, 50 pills were missing from the pill packets. The parents reported that they did not think the patient to took any other drugs.

Upon hospital admission the patient's vital signs were normal, but she was unconscious with a Glasgow coma score of 9. Blood cell count, and liver and kidney function tests were normal. Blood gas analysis showed mixed acidosis with pH 7.16 and partial carbon dioxide pressure of 56 mmHg, lactate level of 73 mg dL⁻¹, and bicarbonate level of 16 mmol L⁻¹. Gastric lavage was performed, but no drugs were noted. A bolus of sodium bicarbonate (1 mEq kg⁻¹) was administered. In addition, 2 boluses of midazolam were required due to generalized tonic-clonic seizures that occurred 10 min after admission. The patient was transferred to the pediatric intensive care unit, and levetiracetam was loaded. As the patient's seizures recurred frequently, midazolam infusion was started. Severe dyskinesia characterized by abnormal involuntary large hyperkinetic movements in all 4 extremities was observed during the first hour of hospitalization; therefore, 2 mg of intravenous biperiden was administered and the dyskinesia improved rapidly. A second dose of biperiden was required, as dyskinesia recurred 2 hours later; after the second dose dyskinesia did not recur. On day 2 of hospitalization the patient was fully conscious and midazolam infusion was withdrawn following 24 hours of no seizures. Electrocardiography, electroencephalography, and brain magnetic resonance imaging were normal. Following a psychiatric evaluation the patient was

discharged on day 6 of hospitalization. The patient's parents provided written informed consent to have their daughter's case published.

Discussion

Patients with mexiletine overdose, and severe central nervous system or cardiovascular manifestations should be followed-up in the intensive care unit, as in the presented case. Moreover, removal of the drug via gastric lavage and activated charcoal should be considered.¹ Mexiletine is rapidly metabolized, highly protein-bound, and extensively distributed to tissues; therefore, it is not expected to be removed from the body via hemodialysis or other extracorporeal methods.¹ Although it was reported that dialysis might be beneficial, it was not considered in the presented case.⁸ Gastric lavage was performed in the presented case, but we were unsure whether the drug could be removed.

Arrhythmias, including sinus bradycardia, sinus arrest, atrioventricular nodal or ventricular rhythms, heart blocks and asystole can occur in cases of mexiletine overdose.¹ Bradyarrhythmia that causes hypotension can be managed with isoproterenol infusion; however, heart blocks are common, and pacemaker implantation may be required.^{4,5} In such cases extracorporeal life support should be a consideration.^{4,5} Sodium bicarbonate is beneficial in cases of massive overdose with prolongation of the QRS interval based on the electrocardiography.¹ As the presented case had ventricular fibrillation, sodium bicarbonate treatment was administered.

Prolonged seizures do not usually occur in cases of lidocaine overdose; however, seizures after mexiletine overdose have been frequently reported.^{1,4,9} Because mexiletine has a long redistribution time and prolonged presence in the gastrointestinal tract, its toxicity is expected to persist longer than that of lidocaine.⁴ In the presented case benzodiazepine infusion and levetiracetam were required for seizures.

Dyskinesia is a rare side effect of mexiletine.¹⁰ A study on the side-effects of mexiletine in 40 patients reported that only 1 had dyskinesia and the drug was discontinued.¹⁰ To the best of our knowledge the present case report is the first to describe dyskinesia following mexiletine overdose.

Biperiden is an anticholinergic drug that can successfully treat dyskinesia.¹¹ It did not cause arrhythmia or other side-effects while providing very rapid improvement in the clinical condition of the presented case.

Mexiletine overdose can be life-threatening. Rapid identification and management of cardiovascular and central nervous system manifestations are key to preventing morbidity and mortality. In the presented case severe dyskinesia was successfully treated with biperiden; therefore, we think biperiden should be considered for treating movement disorders in cases of mexiletine overdose.

Ethical approval

Written informed consent for patient information to be published was provided by the patient's parents.

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: ZO, NT; data collection: ZO, OA; draft manuscript preparation: ZO, İB, RMY, HAÇ. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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