International Journal of Emergency Medicine

CASE REPORT Open Access

Successful outcome following intralipid emulsion and plasmapheresis in a patient with profound neurologic and cardiovascular manifestations due to nortriptyline poisoning: a case report

Asma Ahmadinejad[1], Amir Saeed[2] and Marzieh Davoodi[3*]

Abstract

Objective Tricyclic antidepressants (TCAs) are used to treat depression, but if abused or misused, they can cause poisoning, which can be fatal. The main treatment for TCA poisoning is administering sodium bicarbonate.

Methods We report a 16-year-old girl diagnosed with nortriptyline poisoning with a profound neurologic and cardiovascular manifestations, successfully treated using sodium bicarbonate, intralipid emulsion, and plasmapheresis.

Conclusions Plasmapheresis can be a good treatment modality for patients with TCA poisoning who do not respond well to classic treatments.

Keywords TCA, Plasmapheresis, Intralipid

Introduction

Tricyclic antidepressants (TCA) treat many psychological disorders, such as depression, obsessive-compulsive disorder, and neuropathic pain; they are also indicated for migraine headache prophylaxis. However, if abused or misused, they can lead to poisoning, which can be fatal. In Iran, nortriptyline is a common antidepressant drug, and its overdose cases are routinely reported in the emergency departments; nonetheless, accurate data regarding its incidence or prevalence are unavailable.

Patients with TCA overdose can develop euphoria, hallucination, reduced level of consciousness, seizure, coma, and rarely, serious arrhythmias. The cornerstone of therapy is administering sodium bicarbonate intravenously; however, adjunctive therapies like lipid emulsion infusion and plasmapheresis can also be utilized [1].

Herein, we report a 16-year-old girl with a nortriptyline overdose due to attempted suicide. She was brought to the emergency department with a decreased level of consciousness and tachyarrhythmia, which was successfully treated using lipid emulsion and plasmapheresis in addition to sodium bicarbonate.

*Correspondence:
Marzieh Davoodi
Davoodi.ma@gmail.com
[1]Department of Pediatrics, Division of Pediatric Cardiology, Shiraz University of Medical Sciences, Shiraz, Iran
[2]Department of Pediatrics, Division of Pediatric Intensive Care, Shiraz University of Medical Sciences, Shiraz, Iran
[3]Neonatal Research Center, Department of Pediatrics, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran

Case presentation

A 16-year-old girl with multiple sclerosis and major depression was found unconscious by her parents. She had taken excessive nortriptyline, and the emergency medical service intubated her due to a decreased level of consciousness (Glasgow coma scale [GCS] = 6). Next, she was transferred to the emergency department. Her parents stated that nortriptyline was prescribed for her depression, and there were at least 60 tablets of nortriptyline 25 mg (1500 mg) missing from its container.

Upon arrival, her vital signs were as follows: GCS: 5; blood pressure (BP): 113/63 mmHg; heart rate (HR): 150/min. Soon after, she developed ventricular tachycardia (Fig. 1), and 100 mEq sodium bicarbonate was intravenously injected over 10 min. After the injection of sodium bicarbonate, the electrocardiogram (ECG) revealed a QRS duration of 200 ms (wide complex tachycardia), QTc of 500 ms (> 430 ms), and R/S ratio of 1/6 (> 0.7 in lead aVR); ST/T wave changes were also observed in the chest leads (Fig. 2). Hence, lidocaine was prescribed. As the arterial blood gas pH was measured at 7.6, sodium bicarbonate was not given as a second bolus dose but was rather added to the 24-hour intravenous maintenance fluid. The patient responded well, and her ECG became normal; nevertheless, she had one episode of generalized tonic-colonic convulsion that lasted less than one minute and ended spontaneously without any treatment. The patient was transferred to the pediatric intensive care unit (PICU). In the PICU, her HR was 124/min, but the QRS duration was about 150 ms, her BP decreased to 75/25 mmHg, and her GCS was 3. Even though she had not received any sedative drugs, norepinephrine was initiated as an inotrope, and intralipid 20% 1.5 ml per kilogram was injected as a bolus over a minute followed by 0.25 ml/kg/min over one hour (in addition to sodium bicarbonate in dextrose, which was 1.5 times more than the maintenance fluid). Additionally, magnesium was prescribed, and her BP increased to 0.35 micrograms per kilogram per minute (mcg/kg/min). Nevertheless, her GCS was 3; hence, an electroencephalogram was obtained, which revealed encephalopathy without any sign of convulsions. Plasmapheresis was performed after 12 h of her admission. She underwent *TWO* 1-volume plasma exchange via centrifugal plasmapheresis with 5% albumin as the replacement fluid.Her BP increased for two days, and the inotrope was titrated following the first plasmapheresis. After the second plasmapheresis session, the inotrope was discontinued, and her GCS increased; consequently, she was extubated. On the fifth day, she was discharged in good condition and without any sequelae.

Discussion

Tricyclic antidepressants (TCAs) are among the most lethal antidepressants used to commit suicide [2]. This report describes an effective treatment of nortriptyline overdose with cardiovascular compromise (hypotension, arrhythmia) and convulsion.

To treat a patient with TCA overdose, we should first evaluate the patient's airways and breathing. Next, intubation should be considered for those with decreased GCS (less than 8), hypoventilation, respiratory failure, or uncontrolled seizures [3]. Activated charcoal and gastric lavage should be considered if the drug was ingested less than an hour earlier and if the patients can protect their airways [1].

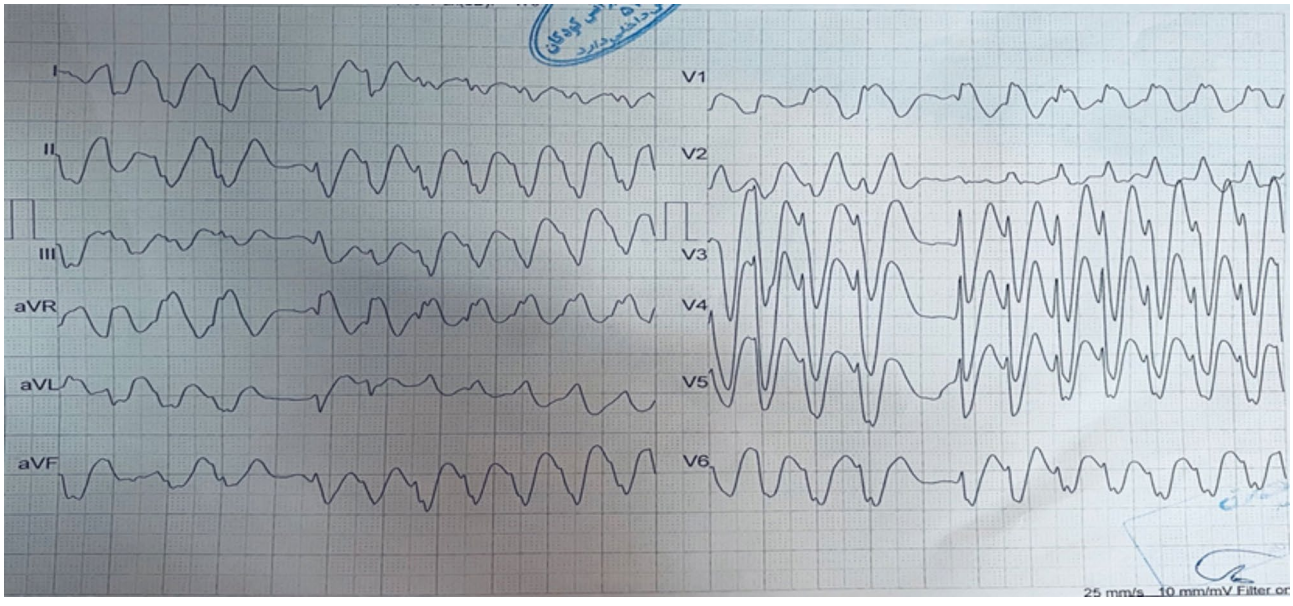

Fig. 1 The initial EKG. *ventricular tachycardia*

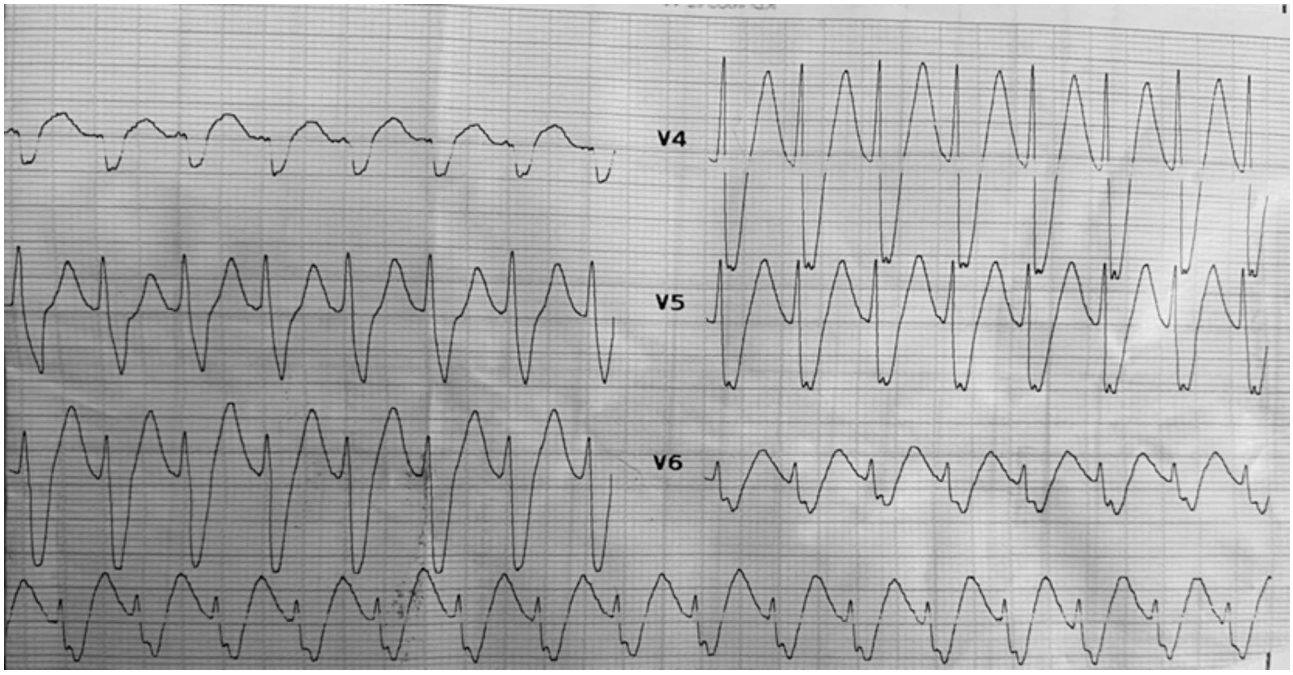

Fig. 2 The 2nd EKG after infusion of sodium bicarbonate. revealed a QRS duration of 200 ms (wide complex tachycardia), QTc of 500 ms (> 430 ms), and R/S ratio of 1/6 (> 0.7 in lead aVR); ST/T wave changes were also observed in the chest leads

Although TCA overdose rarely results in cardiac arrhythmias or seizures, those with the aforementioned manifestations have a poor prognosis [4]. Ingesting more than 5 mg/kg of TCA can result in serious cardiovascular and central nervous system (CNS) symptoms. Typical ECG changes are QRS widening (> 100 ms), QTc prolongation > 430 ms, and R/S ratio > 0.7 in lead aVR [1, 5].

An ECG seems to be the simplest apparatus to predict the severity of TCA poisoning in the emergency department. QRS widening and QT prolongation are observed in severe TCA poisoning cases and seem to better predict morbidity in TCA poisoning than serum levels [5]. Our patient exhibited extreme QRS widening (200 ms), susceptible to fatal ventricular arrhythmias, which was an indication to administrate bicarbonate. In her case, we injected 100 mEq of sodium bicarbonate, and subsequently, 150 mEq per liter was added to maintenance IV fluid to achieve a pH of 7.5. Sodium bicarbonate is the drug of choice to treat TCA overdose with induced alkalosis to prevent acidosis. Since sodium load improves cardiac conduction, alkalosis can increase protein binding and decrease the free drug [6]. Nevertheless, in some cases, patients have ventricular arrhythmias in spite of sodium bicarbonate injection. As a result, the physician should consider other adjuvant treatments.

Intralipid emulsion (ILE) was first used as an anesthetic agent; ever since, it has been used for toxicity with lipophilic, cardiotoxic drugs such as TCAs when initial supportive therapies fail (2) The exact mechanism of ILE therapy in the treatment of acute lipophilic drug toxicity remains unclear despite decades of publications. ILE may act as a 'lipid sink' by trapping lipophilic drug molecules and rendering them biologically inactive.4 Other theories include ILE helping shuttle encapsulated lipophilic toxins to the liver and/or kidney for elimination and improving cardiac function by providing the myocardium with readily available fatty acids for energy. Finally, ILE may mitigate hypotension during overdose by decreasing nitric oxide-induced vasodilation [7].

ILE is given at 1-1.5 ml/kg as a bolus dose over a minute, followed by 0.25 ml/kg/minute after that to a maximum of 12 ml/kg [2, 8, 9]. In our patient, 60 g of ILE 20% (1.5 ml/kg) was given as a bolus, followed by 600 ml over an hour.

plasmapheresis separates the patient's blood into constituents based on density, and the component of interest can be removed and replaced with another fluid [10].

Our patient had refractory hypotension; she remained hemodynamically unstable after all initial treatments. Even with inotrope support for two consecutive days with plasmapheresis, our patient's response was unexpected. Inotrope could be tapered with improved hemodynamic and consciousness level. The Extracorporeal Treatments in Poisoning (EXTRIP) Working Group does not recommend the usage of plasmapheresis treatment for TCA poisoning [3]; its use is mainly limited to case reports [11–13]. Its possible mechanism is due to high lipid solubility and binding of TCAs.

In TCA overdose, hypotension may occur, which is due to decreased cardiac contractility, since peripheral

alpha-1 adrenergic receptors have a blocking effect that result in vasodilation. In TCA poisoning, refractory hypotension is the most common cause of death [14]. In patients with hypotension who are not responsive to fluid therapy, it is highly recommended to initiate inotropes, and it seems that norepinephrine is the best choice [15]. In our patient, norepinephrine was prescribed, but it was impossible to reduce its dose until the first session of plasmapheresis, after which the inotrope dose could surprisingly be reduced. After the second session, it was discontinued, and her GCS increased. Hence, on the third day, she was extubated.

The CNS manifestations in TCA poisoning are decreased levels of consciousness and seizures. Coma occurs due to both antihistamine and anticholinergic effects [16]. The antagonist effect of TCAs in GABA-A receptors in the brain can result in seizures. Recurrent seizures can be managed with benzodiazepines or barbiturates, though phenytoin is contraindicated [14]. In the emergency department, our patient developed a decreased level of consciousness and a seizure that stopped spontaneously.

In conclusion, plasmapheresis can be a good treatment modality for patients with TCA poisoning who do not respond well to classic treatments.

Author contributions

AS and MD designed the study and composed the manuscript. AA collected the patients' data and submitted the manuscript. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Funding

The authors declare no grants for this research from public, commercial, or nonprofit organizations.

Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Shiraz University of Medical Sciences (IR.SUMS.MED.REC.1400.230). participate All methods were carried out in accordance with the ethical standards as laid down in the Declaration of Helsinki and its later amendments or comparable ethical standards. Written informed consent was obtained from the patient's parents for participation. A copy of the written consent is available for review by the editor in chief of this journal Written informed.

Consent for publication

Obtained.

Competing interests

The authors declare no competing interests.

Received: 5 November 2024 / Accepted: 4 February 2025
Published online: 27 March 2025

References

1. Body R, Bartram T, Azam F, Mackway-Jones K. Guidelines in emergency medicine network (GEMNet): guideline for the management of tricyclic antidepressant overdose. Emerg Med J. 2011;28(4):347–68. https://doi.org/10.1136/emj.2010.091553. Epub 2011/03/26.
2. Mandour RA. Antidepressants medications and the relative risk of suicide attempt. Toxicol Int. 2012;19(1):42–6. https://doi.org/10.4103/0971-6580.94517. Epub 2012/06/28.
3. Yates C, Galvao T, Sowinski KM, Mardini K, Botnaru T, Gosselin S, et al. Extracorporeal treatment for tricyclic antidepressant poisoning: recommendations from the EXTRIP workgroup. Semin Dial. 2014;27(4):381–9. https://doi.org/10.1111/sdi.12227. PubMed PMID: 24712820; PubMed Central PMCID: PMCPMC4282541. Epub 2014/04/10.
4. Paksu S, Duran L, Altuntas M, Zengin H, Salis O, Ozsevik SN, et al. Amitriptyline overdose in emergency department of university hospital: evaluation of 250 patients. Hum Exp Toxicol. 2014;33(9):980–90. https://doi.org/10.1177/0960327113520019. Epub 2014/02/08.
5. Woolf AD, Erdman AR, Nelson LS, Caravati EM, Cobaugh DJ, Booze LL, et al. Tricyclic antidepressant poisoning: an evidence-based consensus guideline for out-of-hospital management. Clin Toxicol (Phila). 2007;45(3):203–33. https://doi.org/10.1080/15563650701226192. Epub 2007/04/25.
6. Bradberry SM, Thanacoody HK, Watt BE, Thomas SH, Vale JA. Management of the cardiovascular complications of tricyclic antidepressant poisoning: role of sodium bicarbonate. Toxicol Rev. 2005;24(3):195–204. https://doi.org/10.2165/00139709-200524030-00012. Epub 2006/01/05.
7. Ollier MMA, Giles SMD, Gosselin, Sophie MD. FRCP[3,4,5]. The occasional intralipid emulsion therapy. Can J Rural Med. 2023;28(4):195–200.
8. Lipid therapy and plasmapheresis in tricyclic poisoning. Proc (Bayl Univ Med Cent). 2016;29(4):444–5. Epub 2016/12/27. PubMed PMID: 28018049; PubMed Central PMCID: PMCPMC5178867.
9. Angel-Isaza AM, Bustamante-Cristancho LA, Uribe BF. Successful outcome following intravenous lipid emulsion rescue therapy in a patient with cardiac arrest due to amitriptyline overdose. Am J Case Rep. 2020;21. https://doi.org/10.12659/ajcr.922206. Epub 2020/05/25.:e922206.
10. Laffin, Ryan C., Cunningham, Ashley M., Fitzgerald, Sean A., Wiebe, Donald A., Wells, Jeffrey A., Linzell, Janice Robin, Rose, William Nicholas, Use of iatrogenic lipid emulsion and subsequent plasmapheresis for the treatment of amitriptyline overdose, case reports in critical care, 2022, 1090795, 3 pages, 2022. https://doi.org/10.1155/2022/1090795.
11. Kolsal E, Tekin IO, Piskin E, Aydemir C, Akyüz M, Cabuk H, et al. Treatment of severe Amitriptyline intoxication with plasmapheresis. J Clin Apher. 2009;24(1):21–4. https://doi.org/10.1002/jca.20185. Epub 2009/01/14.
12. Odigwe CC, Tariq M, Kotecha T, Mustafa U, Senussi N, Ikwu I, et al. Tricyclic antidepressant overdose treated with adjunctive lipid rescue and plasmapheresis. Proc (Bayl Univ Med Cent). 2016;29(3):284–7. PubMed PMID: 27365872; PubMed Central PMCID: PMCPMC4900770.
13. Sari I, Turkcuer I, Erurker T, Serinken M, Seyit M, Keskin A. Therapeutic plasma exchange in Amitriptyline intoxication: case report and review of the literature. Transfus Apher Sci. 2011;45(2):183–5. https://doi.org/10.1016/j.transci.2011.07.015. Epub 2011/08/30.
14. Strøm J, Sloth Madsen P, Nygaard Nielsen N, Bredgaard Sørensen M. Acute self-poisoning with tricyclic antidepressants in 295 consecutive patients treated in an ICU. Acta Anaesthesiol Scand. 1984;28(6):666–70. https://doi.org/10.1111/j.1399-6576.1984.tb02142.x. Epub 1984/12/01. PubMed PMID: 6524283.
15. Buchman AL, Dauer J, Geiderman J. The use of vasoactive agents in the treatment of refractory hypotension seen in tricyclic antidepressant overdose. J Clin Psychopharmacol. 1990;10(6):409–13. https://doi.org/10.1097/00004714-199010060-00005. Epub 1990/12/01.
16. Citak A, Soysal DD, Uçsel R, Karaböcüoglu M, Uzel N. Seizures associated with poisoning in children: tricyclic antidepressant intoxication. Pediatr Int. 2006;48(6):582-5. Epub 2006/12/16. https://doi.org/10.1111/j.1442-200X.2006.02276.x. PubMed PMID: 17168978.

Publisher's note