



Contents lists available at ScienceDirect

American Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/ajem

Recreational drug toxicity with severe hyperthermia: Rapid onsite treatment and clinical course

Srikanth Reddi, MD^{a,*}, Matt S. Friedman, MD^b

^a Pulmonary and Critical Care Fellow, Division of Pulmonary and Critical Care Physiology and Medicine at Harbor-UCLA Medical Center, Torrance, CA, USA 90509.

^b Prehospital Care, Department of Emergency Medicine at Maimonides Medical Center, 4802 10th Ave, Brooklyn, NY, USA 11219.

ARTICLE INFO

Article history:

Received 13 June 2022

Received in revised form 5 August 2022

Accepted 22 August 2022

Available online xxxx

Keywords:

N-Methyl-3,4-methylenedioxyamphetamine

Toxicology

Illicit drug

Hyperthermia

Serotonin syndrome

Sympathomimetics

ABSTRACT

Electronic dance music festivals have gained notoriety in the critical care and emergency medicine fields due to an alarming incidence of hospitalizations and deaths related to the high prevalence of recreational drug use. Recreational drug use toxicity, in part related to sympathomimetic toxidromes, may cause hyponatremia, seizures, rhabdomyolysis, hyperkalemia, acidosis, coagulopathy, circulatory shock, multi-organ failure, and even death. This wide-ranging syndrome has been referred to as psychostimulant drug-induced toxicity. Rapid onsite diagnosis and treatment, with attention to the A-B-Cs of clinical emergencies, is essential to preserve life. We describe a patient presenting with the highest recorded core temperature in a survivor of psychostimulant drug-induced toxicity, and emphasize management principles of this life-threatening and increasingly prevalent condition.

© 2022 Published by Elsevier Inc.

1. Introduction

Electronic dance music festivals (EDMFs) have gained notoriety due to an alarming incidence of hospitalizations and deaths owing to the high prevalence of recreational drug use [1,2]. At least 68 deaths have been attributed to synthetic “club drugs” or entactogens at music festivals in the preceding 15 years prior to a 2015 analysis [3]. Literature regarding management of onsite complications remains sparse.

This case report stems from an EDMF in Los Angeles, California that took place in July 2021. The onsite medical facility established 30 cots in addition to one critical care area with two ice water immersion baths (Fig. 1). Staffing was present with the capability to provide medical care encompassing first aid through ACLS.

2. Case report

A 31-year-old male reported ingesting one pill containing 137.9 mg of MDMA, followed by a second pill containing 100 mg of MDMA a short time after (both doses and formulations remain unverified). Later during the event, he collapsed and was carried to the medical tent by his friends appearing toxic on presentation. Physical exam was notable for mydriasis, clonus, cool yet diaphoretic skin, and unresponsive mental

status. His blood pressure was 80/30 mmHg with a heart rate of 190 bpm in cardiac rhythm visualized on a LIFEPAK 15 portable cardiac monitor consistent with supraventricular narrow-complex tachycardia. Synchronized cardioversion was performed at 100 J without success; cardioversion was repeated 150 J, again without success. An ECG was not performed due to the patient's unstable vital signs, but adenosine 6 mg IV was presumptively administered, without response; 12 mg IV was next administered, again without resolution of his tachycardia. His rectal temperature was then found to be 42.5 °C (108.5 °F), and the medical team prepared the patient for immediate ice-water submersion in a previously prepared 200-gal horse water trough, which served as the ice water tub. Despite submersion, the patient's core temperature increased to 43.2 °C (109.7 °F). In this prehospital setting, three liters of cold normal saline was rapidly administered via peripheral and intraosseous access. He received 100 mg of rocuronium intravenously and a laryngeal mask airway was placed. Intravenous midazolam was administered every five minutes due to refractory hyperthermia. The patient was submerged for 40 min until he reached a temperature of 38.8 °C (102.0 °F). After removal from the ice bath, rapid sequence endotracheal intubation was performed using a second dose of rocuronium. The patient was transported to a tertiary care facility and admitted to the ICU with critical multiorgan dysfunction. His urine toxicology report on admission was presumptively positive for amphetamines and benzodiazepines; neither confirmatory nor serum toxicology studies were able to be sent at the time of admission. His hospital course was complicated by rhabdomyolysis and acute renal failure

* Corresponding author at: Division of Respiratory and Critical Care Medicine, Harbor-UCLA Medical Center, 1000 W. Carson Street, Torrance, CA 90509, USA.

E-mail address: sreddi@dhs.lacounty.gov (S. Reddi).



Fig. 1. Medical field tent used at the music festival.

(Fig. 2) requiring hemodialysis; organ dysfunction otherwise recovered over the subsequent weeks.

3. Discussion

The use of 3,4-methylenedioxymethamphetamine (MDMA), known as “Molly” in powder form and “ecstasy” in pill form, is common at EDMFs [4]. Sympathomimetic properties elevate core body temperature, while euphoric effects encourage increased physical activity and distract the user from dangerous hyperthermia [5,6]. Toxicity may also cause multiple-organ damage [6–8]. This syndrome has been referred to as psychostimulant drug-induced toxicity (PDIT) [9]. Our case highlights the highest recorded core temperature in a survivor of a sympathomimetic toxidrome, to our knowledge [10,11].

MDMA-induced hyperthermia is due to a variety of synergistic factors including release of the neurotransmitters; alpha-1 and beta-3 sympathomimetic effects; and indirect effects on mitochondrial uncoupling [7,8,11]. The commonality between the pathophysiology of MDMA-induced hyperthermia and serotonin syndrome has been noted [5,6]. If left untreated, core temperatures rising greater than 42.0 °C increase the risk of mortality [7,12]. Renal failure is precipitated by myoglobinuria-induced acute tubular necrosis [7]. Specific to EDMF, volume depletion and intense muscular activity leading to myocyte necrosis appear to be the most frequent contributing factors.

The benefit of prompt management cannot be overstated. Cooling methods should be prioritized and initiated in the prehospital field, prior to transport to the nearest capable receiving facility [2]. Classic toxicology teaching recommends reducing the core temperature below 40 °C within the first 30 min of care [13]. Cardiac arrest has been reported in several cases at EDMF when hyperthermia was not treated onsite early and aggressively with ice water immersion [4,10]. Our patient took nearly 40 min to cool, which is twice the normal duration in these authors' experience. Intravenous short-acting benzodiazepines may be utilized as adjuncts to treat the sympathomimetic effects of psychostimulants. Non-depolarizing neuromuscular blocking agents should be considered in refractory cases to break the cycle of heat generation [5,10].

Focus should simultaneously be trained on the patient's airway, breathing and circulation. It is prudent to avoid succinylcholine due to potential complications of hyperkalemia from myocyte necrosis. Ketamine is an option as an induction agent for intubation in these patients. As patients in critical condition often have metabolic acidosis from renal injury and organ ischemia, hyperventilation is recommended initially. Circulatory shock may ensue and should be treated early with volume resuscitation [8,10].

This case of PDIT resulting in the highest recorded core temperature in a survivor of sympathomimetic drug toxicity highlights the importance of early aggressive pre-hospital care. More research is needed in pre-hospital management of drug-induced toxicities at mass gathering events, though we acknowledge the barriers inherent in evaluating critical illness in an uncontrolled setting.

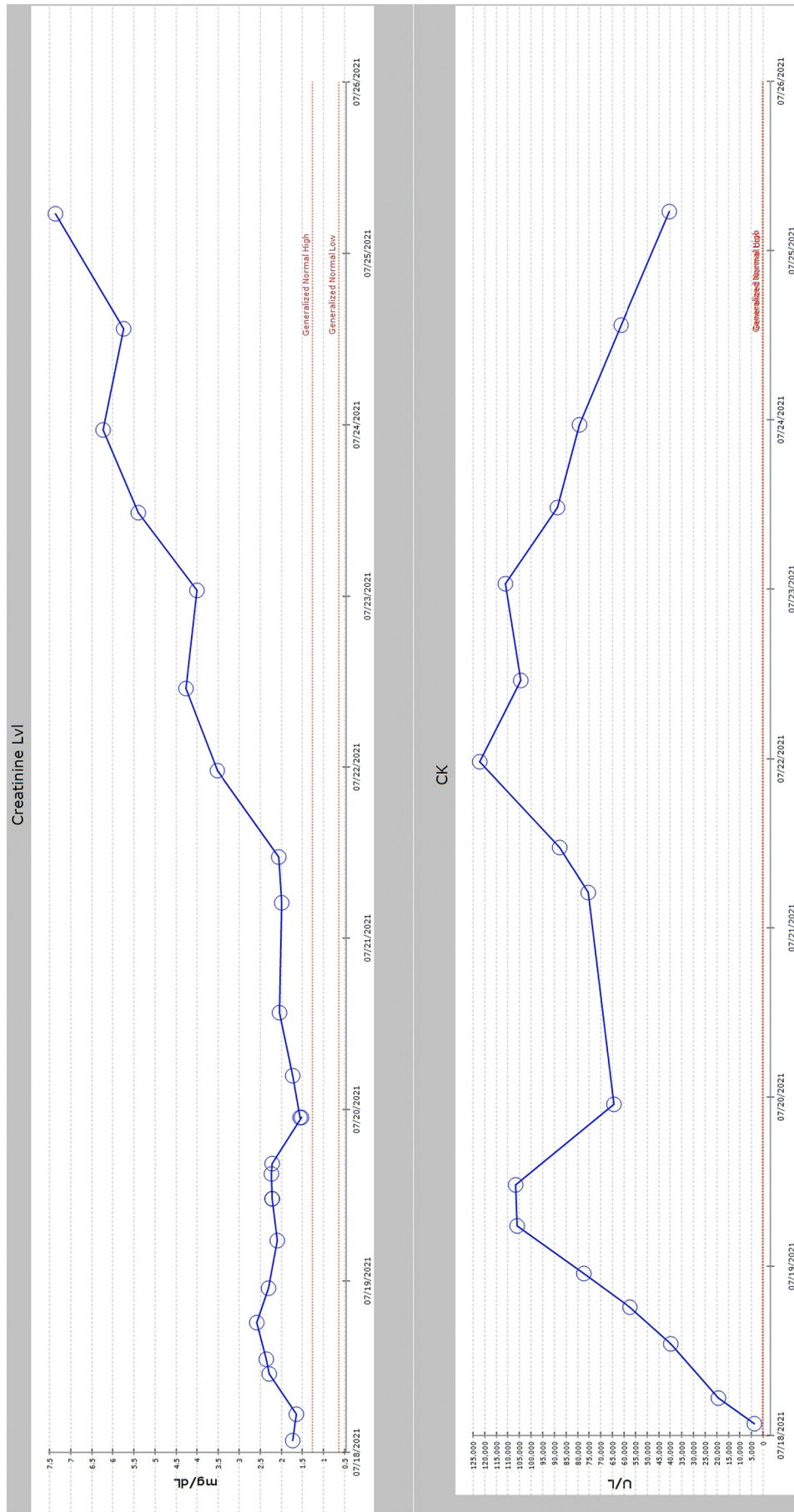


Fig. 2. Creatine kinase and creatinine trend.

CRedit authorship contribution statement

Srikanth Reddi: Writing – review & editing, Writing – original draft, Conceptualization. **Matt S. Friedman:** Writing – review & editing, Conceptualization.

Declaration of Competing Interest

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.
We have no conflicts of interest to disclose.

References

- [1] Friedman MS, Plocki A, Likourezos A, Pushkar I, Bazos AN, Fromm C, et al. A prospective analysis of patients presenting for medical attention at a large electronic dance music festival. *Prehosp Disaster Med.* 2017 Feb;32(1):78–82. <https://doi.org/10.1017/S1049023X16001187>. Epub 2016 Dec 16. PMID: 27978861.
- [2] Margolis AM, Leung AK, Friedman MS, McMullen SP, Guyette FX, Woltman N. Position statement: mass gathering medical care. *Prehosp Emerg Care.* 2021 Jul-Aug;25(4):593–5. <https://doi.org/10.1080/10903127.2021.1903632>. [Epub 2021 Apr 30. PMID: 33886431].
- [3] Turris SA, Jones T, Lund A. Mortality at music festivals: an update for 2016–2017 - academic and Grey literature for case finding. *Prehosp Disaster Med.* 2018 Oct;33(5):553–7. <https://doi.org/10.1017/S1049023X18000833>. Epub 2018 Oct 2. PMID: 30277196.
- [4] Ridpath A, Driver CR, Nolan ML, Karpati A, Kass D, Paone D, et al. Kunins HV; Centers for Disease Control and Prevention (CDC). Illnesses and deaths among persons attending an electronic dance-music festival - new York City, 2013. *MMWR Morb Mortal Wkly Rep.* 2014 Dec 19;63(50):1195–8. PMID: 25522087.
- [5] Hall AP, Henry JA. Acute toxic effects of 'Ecstasy' (MDMA) and related compounds: overview of pathophysiology and clinical management. *Br J Anaesth.* 2006 Jun;96(6):678–85. <https://doi.org/10.1093/bja/ael078>. Epub 2006 Apr 4. PMID: 16595612.
- [6] Liechti ME. Effects of MDMA on body temperature in humans. *Temperature (Austin).* 2014 Oct 31;1(3):192–200. <https://doi.org/10.4161/23328940.2014.955433>. PMID: 27626046; PMCID: PMC5008716.
- [7] Bora F, Yilmaz F, Bora T. Ecstasy (MDMA) and its effects on kidneys and their treatment: a review. *Iran J Basic Med Sci.* 2016 Nov;19(11):1151–8. PMID: 27917269; PMCID: PMC5126214.
- [8] Rusyniak DE, Tandy SL, Hekmatyar SK, Mills E, Smith DJ, Bansal N, et al. The role of mitochondrial uncoupling in 3,4-methylenedioxymethamphetamine-mediated skeletal muscle hyperthermia and rhabdomyolysis. *J Pharmacol Exp Ther.* 2005 May;313(2):629–39. <https://doi.org/10.1124/jpet.104.079236>. Epub 2005 Jan 11. PMID: 15644431.
- [9] Friedman MS, Saloum D, Haaland A, Drapkin J, Likourezos A, Strayer RJ. Description of adverse events in a cohort of dance festival attendees with stimulant-induced severe agitation treated with dissociative-dose ketamine. *Prehosp Emerg Care.* 2021 Nov-Dec;25(6):761–7. <https://doi.org/10.1080/10903127.2020.1837311>. Epub 2020 Nov 11. PMID: 33054495.
- [10] Armenian P, Mamantov TM, Tsutaoka BT, Gerona RR, Silman EF, Wu AH, et al. Multiple MDMA (ecstasy) overdoses at a rave event: a case series. *J Intensive Care Med.* 2013 Jul-Aug;28(4):252–8. <https://doi.org/10.1177/0885066612445982>. [Epub 2012 May 28. PMID: 22640978].
- [11] Mallick A, Bodenham AR. MDMA induced hyperthermia: a survivor with an initial body temperature of 42.9 degrees C. *J Accid Emerg Med.* 1997 Sep;14(5):336–8. <https://doi.org/10.1136/emj.14.5.336>. PMID: 9315942; PMCID: PMC1343106.
- [12] Grunau BE, Wiens MO, Brubacher JR. Dantrolene in the treatment of MDMA-related hyperpyrexia: a systematic review. *CJEM.* 2010 Sep;12(5):435–42. <https://doi.org/10.1017/s1481803500012598>. [PMID: 20880437].
- [13] Boyer EW, Shannon M. The serotonin syndrome. *N Engl J Med.* 2005 Mar 17;352(11):1112–20. <https://doi.org/10.1056/NEJMra041867>. Erratum in: *N Engl J Med.* 2007 Jun 7;356(23):2437. Erratum in: *N Engl J Med* 2009 Oct 22;361(17):1714. PMID: 15784664.