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Case Report

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Ingestion of Synthetic Street Drug "25-I" (25I-NBOMe) Causing Type B Lactic Acidosis and Multi-Organ Dysfunction

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Abstract

25I-NBOMe (25-I) is a novel synthetic agonist of the 5-HT2A receptor. It is used recreationally for its psychedelic properties similar to LSD. Side effects include altered mental status, sympathomimetic symptoms, serotonin syndrome and multiple organ injury. We report a case of delayed type B lactic acidosis after ingestion of 25-I. A 16-year-old male presented after being found obtunded. He developed seizures requiring endotracheal intubation. He developed a lactic acidosis about 30 hours after ingestion, peaking at 8.5 mEq/L 38 hours post-ingestion. Concurrently the patient had an elevated mixed venous saturation and decreased arterial-venous oxygen content difference, indicating a type B lactic acidosis. Thiamine, L-carnitine, and coenzyme Q-10 were initiated to treat the metabolic derangement and promote oxygen utilization. Additional treatments included n-acetylcysteine and plasmapheresis. This treatment strategy resulted in reduction in lactate and other markers of organ injury. Arterial-venous oxygen content difference increased to normal levels. The patient made a full recovery. Type B lactic acidosis has been reported previously in a variety of diseases, but never after 25-I ingestion. A novel approach of vitamins and co-factors to support mitochondrial function, n-acetylcysteine and plasmapheresis was employed to treat the lactic acidosis and multi-organ dysfunction successfully.

Keywords: Mitochondrial dysfunction; Thiamine; Carnitine; Plasmapheresis; Type B lactic acidosis; 25-I

Introduction

The new synthetic street drug, 25-I (25I-NBOMe or 2-(4-iodo-2,5-dimethoxyphenyl)-N-[(2-methoxyphenyl)methyl] ethanamine), is a full agonist of the serotonin 2a (5-HT2a) receptor. 25-I, known as "Smiles," "synthetic LSD," or "Nbomb" has gained popularity due to its low cost and easy portability. It is administered on paper tabs placed in the mouth and is used recreationally for its psychedelic properties. It can present with sympathomimetic and serotonergic symptoms [1-3]. Reported adverse effects include multi-organ failure, hypertension, tachycardia, aggression, hallucinations, seizures, hyperthermia, acidosis, and acute kidney injury [1, 2, 4]. Among the 12 reported cases in the medical literature, three have died [1-5]. There are multiple deaths reported in media and Internet sources [6]. Patients described in the literature have been treated with supportive care alone as there are no established treatment regimens. We report a case of late-onset multiple organ dysfunction and type B lactic acidosis following 25-I ingestion treated with a novel approach of vitamins for mitochondrial support, plasmapheresis, and pharmacologic reduction of free radicals.

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Case Report

A 16-year-old male was found obtunded outside of a drug house. In the emergency department he was febrile, tachycardic, and hypertensive, with a Glasgow coma score of 7. He developed seizures requiring benzodiazepines and intubation.

He was given benzodiazepines and dexmedetomidine for agitation and suspected serotonin syndrome. An epinephrine drip was briefly required for hypotension. Lactate level initially peaked at 2.6 mEq/L 16 h post-ingestion. He also became hemodynamically stable and creatinine decreased from 1.45 to 1.04 mg/dL.

The patient then developed a new lactic acidosis about 30 h after admission, which rose to 8.5 mEq/L (Fig. 1). Initial mixed venous saturation (S_vO_2) was normal (46-72%) but later unexpectedly rose to 93%; this coincided with peak lactate. At this time he had an arterial total O_2 concentration (TO_2c) of 19 mL O_2/dL blood (vol%), and an elevated venous TO_2c of 17.8 vol%; the arterial-venous oxygen content difference ($AVDO_2$) was therefore 1.2 vol%, much lower than expected (Fig. 2), indicating impaired oxygen utilization. The patient developed multiple organ dysfunction, including hypotension, oliguria and increases in creatinine and hepatic

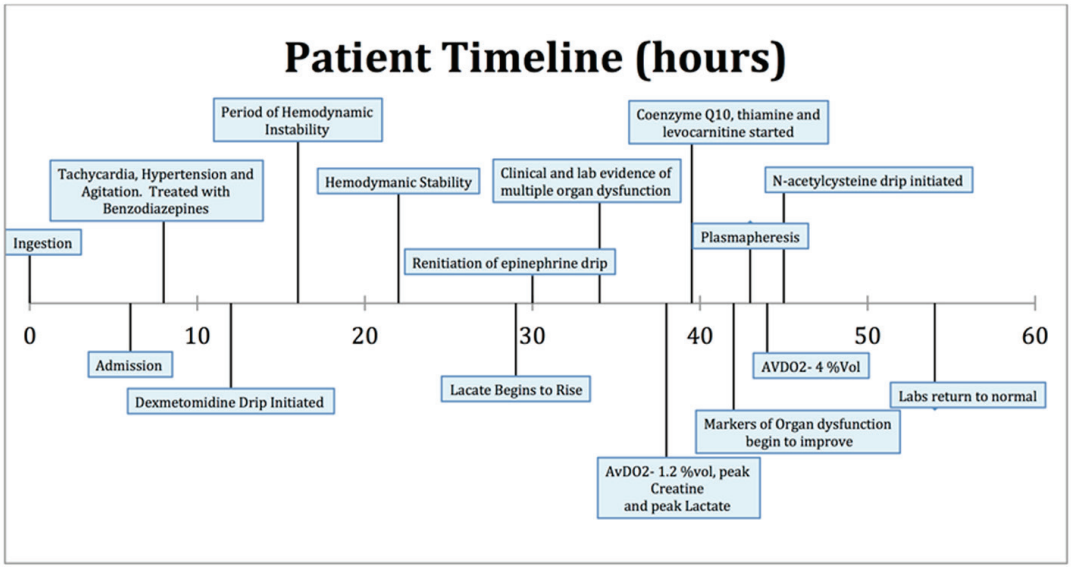

Figure 1. Timeline of major patient events over first 60 h of admission.

transaminases. This change was presumed to be caused by a defect in aerobic metabolism, despite adequate substrate delivery. To manage this metabolic uncoupling, thiamine 100 mg daily, levocarnitine 100 mg/kg/day divided every 8 h, and coenzyme Q-10 (CoQ-10) 120 mg every 8 h were given for 14 days. Additional treatments included N-acetylcysteine (NAC), per acetaminophen toxicity protocol, and one session of plasmapheresis with 2 L 5% albumin and 2 L fresh frozen plasma as replacement.

Subsequently, lactate levels and S_vO_2 returned to physiologic levels, 60-76% by 60 h after ingestion. Other markers of organ injury and dysfunction also improved.

The patient's serum levels of 25-I were 25.1 pg/mL before plasmapheresis and 30.6 pg/mL after. The concentration of 25-I in the pheresis fluid was 20.1 pg/mL. 25-I was also detected in the urine at admission [7]. He made a full recovery and admitted to taking 25-I.

Discussion

Our patient's presentation of hypertension, tachycardia and altered mental status was consistent with previous reports of 25-I ingestions [2-4]. However, the late development lactic acidosis and multi-organ dysfunction has not been reported. This second phase of illness was successfully managed with a novel combination treatment strategy to target metabolic uncoupling and promote drug clearance with plasmapheresis.

Lactic acidosis is most often caused by inadequate substrate delivery, type A lactic acidosis, with cardinal features of poor perfusion and low S_vO_2. Our patient had a high S_vO_2 and no signs of hypoperfusion, suggesting adequate substrate delivery with decreased oxygen uptake by tissues; the low $AVDO_2$ is congruent with this. The patient had signs of end-organ dysfunction, rising creatinine and transaminases, oliguria and hypotension. This is most consistent with type B lactic acidosis, caused by a defect in the aerobic metabolism pathway leading to anaerobic metabolism, decreased ATP production and lactic acidosis [8]. The heart, liver and kidney are all metabolically active organs that are at risk of injury in the setting of decreased ATP production.

Treatment of type B lactic acidosis focuses on restoring normal mitochondrial function and addressing the mechanism [8, 9]. We used a cocktail of vitamins and co-factors based on established treatments of mitochondrial disorders associated with lactic acidosis [9, 10]. Thiamine, vitamin B1, is a co-factor in multiple steps in amino acid and carbohydrate metabolism, including the conversion of pyruvate to acetyl-CoA. Acetyl Co-A can then enter the citric acid cycle. Levocarnitine aids in the transport of long chain fatty acids in the mitochondria where they are broken down into acetyl-CoA. Co-Q10 is part of the oxidative phosphorylation chain in the mitochondria. These vitamins support aerobic metabolism in the mitochondria.

Free-radical mediated injury may occur as a consequence of mitochondrial dysfunction [10]. To mitigate this, we treated with the free-radical scavenger NAC, using dosing standards for acetaminophen-associated liver injury. Plasmapheresis was used to clear any drug that was potentially protein bound. It is not known how 25-I is bound or metabolized.

In the literature on 25-I intoxication, there are no similar reports of late-onset type B lactic acidosis. The exact cause of this patient's metabolic failure and most appropriate management regimen were unclear, so multiple approaches were employed. The patient may have had an active metabolite of 25-I. Despite a relatively high level of 25-I in the urine at the time of presentation (2.28 ng/mL), the low level of 25-I at the time of lactic acidosis support this theory.

As detection of 25-I is not on standard drug screens, it should be part of the differential diagnosis for a patient presenting with a clinical picture similar to our patient. Testing using mass spectroscopy is used on a research level at a few

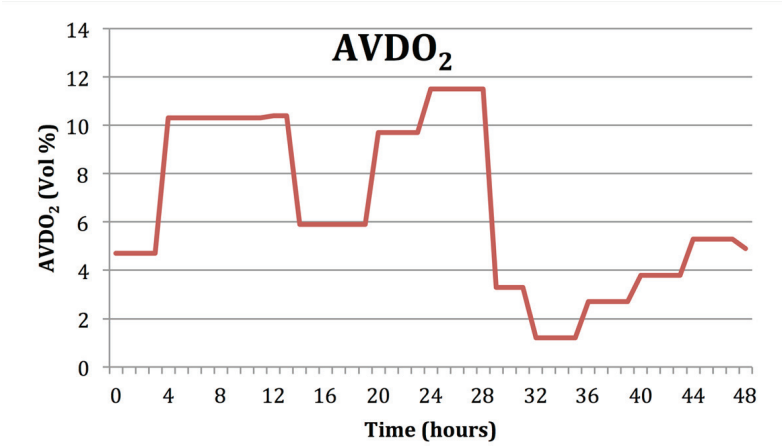

Figure 2. Arterial-venous oxygen difference over first 48 h of admission.

select centers [1, 3, 4, 7].

We present a case of 25-I ingestion causing type B lactic acidosis successfully managed with vitamins to support mitochondrial function, plasmapheresis for toxin removal, and NAC to scavenge free radicals all in an attempt to reverse the mitochondrial uncoupling process.

Acknowledgement

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Conflicts of Interest

The authors report no conflicts of interest.

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