Fatal Intravenous Injection of Electronic Nicotine Delivery System Refilling Solution

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Introduction

The popularity of electronic cigarettes or electronic nicotine delivery systems (ENDS) is increasing. Data from the 2012 National Youth Tobacco Survey demonstrates a nearly 50 % increase in ENDS usage over the last year among middle and high school students [1]. Similar increases in usage have been seen in adults [2]. ENDS are devices which vaporize a nicotine-containing solution so it can be inhaled [3]. In many cases, these devices can be refilled with nicotine-containing solutions called “eLiquid” [3, 4]. Some of these solutions contain potentially fatal amounts of nicotine [5]. Users of ENDS have reported negative symptoms involving multiple organ systems [6]. Serious morbidity or mortality related to these devices has not yet been reported. We report a fatality associated with the intentional injection of eLiquid.

Case Report

A 29-year-old man was found down by his family members who called emergency medical services (EMS). He had a history of depression but was not taking any prescription medications. He was found with a suicide note indicating that he had intravenously injected himself with eLiquid. Per his wife, he was a smoker and had been attempting to quit by using ENDS. Cardiopulmonary resuscitation was initiated by EMS. He was initially asystolic but developed ventricular

fibrillation and was defibrillated twice. He was intubated in the field and given 1 mg of atropine, 0.5 ampules of sodium bicarbonate, and 1 mg of lidocaine. Upon arrival in the emergency department, he was unresponsive but in a sinus rhythm. He had a heart rate of 125 beats per minute, temperature of 36.4 °C, and a blood pressure of 158/93 mmHg. His physical exam was non-focal and atraumatic. No salivation, diaphoresis, or obvious bronchorrhea was seen. His pupils were 4 mm and fixed. An initial head CT was unremarkable. He then began to have full body, tonic-clonic seizure activity and was treated with 4 mg of lorazepam. He had no prior history of seizures. He was transferred to a tertiary care hospital but was noted to have further seizure activity during transport. An additional 3 mg of lorazepam was given without improvement. He was started on a propofol infusion and loaded with fosphenytoin and levetiracetam which finally controlled the seizure activity. The propofol was subsequently titrated off. He was initially found to have leukocytosis of 21.8 K/mm³ (range 4.5–11 K/mm³), a potassium of 2.4 mmol/L (range 3.5–5.2 mmol/L), blood sugar of 401 mg/dL (range 60–100 mg/dL), creatinine of 2.0 mg/dL (0.5–1.5 mg/dL), creatine kinase of 977 unit/L (range 8–150 unit/L), and a troponin I of 0.34 ng/mL (range 0.00–0.07 ng/mL). A urine drug immunoassay was positive for amphetamines. While receiving levetiracetam and fosphenytoin, he had multiple abnormal electroencephalographs which demonstrated burst-suppression activity consistent with hypoxic encephalopathy. By day 1 in the hospital, his creatinine and creatinine kinase improved to 0.7 mg/dL and 830 unit/L, respectively, and his troponin I peaked at 3.71 ng/mL. Therapeutic hypothermia protocol was initiated on arrival but he never regained consciousness. He was diagnosed with anoxic encephalopathy and declared brain dead in the hospital by day 5. An autopsy was not performed as he was an organ donor. Comprehensive serum drug testing done on specimens collected on presentation detected only

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lidocaine, nicotine, and nicotine's primary metabolite, cotinine. No amphetamines were detected. His serum nicotine was 2,000 ng/mL (normal range 5–90 ng/mL) and cotinine was 2,100 ng/mL (normal range 100–1,200 ng/mL). The actual product which he allegedly injected was not available for testing.

Discussion

Nicotine is a naturally occurring, highly toxic substance. Nicotine's oral LD₅₀ is commonly reported to be approximately 1 mg/kg though there is evidence to suggest that true LD₅₀ may be closer to 10 mg/kg [7]. Nicotine has a volume of distribution between 2–3 L/kg and is rapidly distributed to body tissues, most importantly the brain [8]. Nicotine intoxication causes multiple effects due to the ubiquity of nicotinic acetylcholine receptors. Stimulation of these receptors results in activation of both the parasympathetic and sympathetic nervous system in addition to the neuromuscular junction. Nicotine is primarily encountered in cigarettes and other tobacco products but is also available in transdermal patches, chewing gums, and now ENDS solutions. Nicotine-based insecticides were once commonly used in the USA, but due to their inherent toxicity have been removed [9].

Cigarette smoking typically results in nicotine and cotinine levels of 10–50 ng/mL and 250–300 ng/mL, respectively [8]. Nicotine patches and gums result in levels 30–70 % lower [8]. Studies on blood nicotine levels achieved with use of ENDS are conflicting with some suggesting very little nicotine may be absorbed while others document levels consistent with the lower end of cigarette smoking [10, 11]. Cotinine levels from ENDS used to appear similar to those of cigarette users [12].

Unintentional ingestions of nicotine, primarily in the form of cigarettes, are commonly associated with gastrointestinal distress but otherwise little morbidity or mortality [13]. Intentional ingestions of nicotine solutions can rapidly cause seizures, paralysis, respiratory arrest, and cardiovascular collapse [14, 15]. Though antemortem, the blood nicotine and cotinine levels detected in our case are consistent with prior reports of death from intentional nicotine exposures, which have primarily been oral exposures. One report documented postmortem blood nicotine and cotinine levels of 2,200 ng/mL, while another case reported blood nicotine levels of 3,700 ng/mL [16, 17]. A case series of two suicides by ingestion of nicotine-containing solutions found postmortem blood nicotine levels of 5,500 ng/mL and 1,100 ng/mL [14]. There is a paucity of reported intravenous nicotine exposure to which our case can be compared. Hagiay et al. described a 27-year-old woman who injected an estimated 5.7 mg of nicotine-containing solution and had sudden onset of gastrointestinal distress but recovered within 36 h [18]. Serial blood nicotine levels were documented to be below 5 ng/mL. This case is

complicated by the very small amount of nicotine reportedly injected and the subsequently very low blood levels. Another case details a 54-year-old man who died after injecting a nicotine insecticide [19]. Postmortem analysis of blood from his right subclavian vein found a nicotine level of 140,000 ng/mL, and it was estimated that he may have injected 2,000 mg of nicotine.

As the use of ENDS increases, it is reasonable to assume that the nicotine-containing solutions used to refill them, commonly called eLiquid, will also become more prevalent. The nicotine content of these products can vary [5]. One study found some eLiquid solutions to contain as much as 25 mg/mL of nicotine [20]. Even based on an oral LD₅₀ of 10 mg/kg, studies have found potentially fatal amounts of nicotine in these products, including one which contained 750 mg of nicotine [5, 21].

This case report has several limitations. Unfortunately, the amount of nicotine injected in this case is unknown as the solution the patient used was not available. Based on the antemortem blood nicotine level of 2,000 ng/mL and a Vd of 2.6 L/kg for nicotine, this patient may have injected over 400 mg of nicotine. This is likely a conservative estimate that does not take into account that nicotine has an elimination half-life of approximately 120 min, and 72 % is converted to cotinine [22, 23]. Though the patient's suicide note described intravenous injection, an injection site was not identified thus raising the possibility that this could have been an oral ingestion. Finally, there are multiple other chemicals in these eLiquid solutions, including propylene glycol [24]. It is possible that this might have caused or contributed to his cardiovascular collapse.

As the use of ENDS continues to grow, exposures to eLiquids and other associated nicotine-containing solutions may increase. This case highlights the potentially fatal results.

Conflict of Interest None.

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