Forensic Science International 262 (2016) e15–e20

Contents lists available at ScienceDirect

Forensic Science International

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

Case Report

Intravenous and oral suicidal e-liquid poisonings with confirmed nicotine and cotinine concentrations

Karina Sommerfeld [c,*], Magdalena Łukasik-Głębocka [a,b], Maksymilian Kulza [d], Artur Drużdż [e], Paweł Panieński [a], Ewa Florek [d], Barbara Zielińska-Psuja [c]

[a] Poznan University of Medical Sciences, Department of Emergency Medicine, Przybyszewskiego Street 49, 60-355 Poznan, Poland
[b] Department of Toxicology, Raszeja Hospital, Mickiewicza Street 30, 60-834 Poznan, Poland
[c] Poznan University of Medical Sciences, Department of Toxicology, Dojazd Street 30, 60-631 Poznan, Poland
[d] Poznan University of Medical Sciences, Department of Toxicology, Laboratory of Environmental Research, Dojazd Street 30, 60-631 Poznan, Poland
[e] University School of Physical Education in Poznan, Department of the Rehabilitation in Internal Disease, Królowej Jadwigi Street 27/39, 61-871 Poznan, Poland

ARTICLE INFO

Article history:
Received 24 August 2015
Received in revised form 29 February 2016
Accepted 8 March 2016
Available online 19 March 2016

Keywords:
E-liquid
Nicotine
Cotinine
Serum concentration
Poisoning

ABSTRACT

The increasing availability of e-cigarettes is a potential toxicological concern. E-cigarettes appeared on the Polish market in 2006, and since 2009 they have been widely available with a new source of nicotine, the so-called e-liquid. In this paper two cases of suicidal oral and intravenous poisonings with the e-liquid are described. The clinical courses of these poisonings are presented. Nicotine and cotinine concentrations in the patient's blood were determined using high performance liquid chromatography with diode array detection. In the course of intoxication patient No. 1, classic symptoms of acute nicotine poisoning without convulsions were observed. Nicotine and cotinine concentrations measured in serum were 0.096 and 4.4 mg/L, respectively. The case of patient No. 2, admission with no typical symptoms of nicotine poisoning was identified, except unconsciousness and slow respiration. Nicotine and cotinine concentrations in the serum at the time of No. 2 admissions were determined to be 0.8 and 1.3 mg/L, respectively. With the increasing number of e-liquid poisonings cases, it should be aware that these products can be a readily available source of poison.

1. Introduction

Electronic cigarettes, commonly referred to as e-cigarettes, are electronic systems dispensing nicotine in the form of aerosol. Developed by a Chinese pharmacist Hon Lik in 2003, they were created parallel to the nicotine replacement therapy and were meant to be used as a source of nicotine alternative to conventional tobacco products. An e-cigarette consists of two major parts: a power supply system which includes a battery and a light-emitting diode imitating cigarette glow, and a system generating aerosol from a solution containing nicotine (the so-called liquid, e-liquid or juice), located in a removable container referred to as cartridge. Most e-cigarette models can be refilled by their users with liquids of different composition and nicotine content, sold in packaging of 20–100 mL. The most common nicotine solvents, i.e. the so-called e-liquid bases include: propylene glycol (of the lowest viscosity), a mixture of glycerol and propylene glycol, or – in older systems – glycerol (of increased viscosity). Some e-liquids are also based on polyethylene glycol or ethanol [1–3].

For several years, new nicotine products (e-cigarettes, nicotine patches) are present on the Polish market. They are supposed to have a less adverse effect to the human than traditional tobacco products. Smokers are increasingly more interested in them, since the large-scale anti-smoking campaigns run in many countries have lead to stricter laws governing the use of traditional cigarettes. These preparations are easily available. All of them, regardless of their form and declared effects on human health, contain nicotine. Most of e-liquids have a nicotine content of up to 18 mg/mL, however some manufacturers offer products with a higher nicotine content, i.e. 20, 24 and even 36 mg/mL [1,2]. Due to the easy availability of e-liquids containing nicotine, this substance could be used as well for suicidal purposes.

* Corresponding author. Tel.: +48 61 8472081x150; fax: +48 61 8470721.
E-mail addresses: karina.sommerfeld@gmail.com (K. Sommerfeld), madzikuska@op.pl (M. Łukasik-Głębocka), fhmmax@gmail.com (M. Kulza), adruzdz@op.pl (A. Drużdż), ppanienski@ump.edu.pl (P. Panieński), ewaflorek@ump.edu.pl (E. Florek), bzielin@ump.edu.pl (B. Zielińska-Psuja).

http://dx.doi.org/10.1016/j.forsciint.2016.03.005
0379-0738/

Nicotine is an alkaloid that causes many biological effects, the intensity of which depends on the dosage. Nicotine shows its effects through nicotinic receptors, located mainly in the autonomic nervous system. Depending on the concentration, it exerts a twofold effect on the nervous system – low doses have a stimulating effect, while high doses block nicotine receptors. Typical symptoms of a mild nicotine poisoning include nausea and vomiting, pale skin due to vasoconstriction, tremor, sweating, dizziness, tachycardia and increased blood pressure. In the course of acute poisoning confusion, convulsions, bradycardia and hypotension are observed. In severe poisoning, muscle weakening can lead to respiratory muscle paralysis and death [4].

After absorption, nicotine easily penetrates biological membranes, including the blood–brain barrier. It undergoes rapid biotransformation mainly in the liver (75%) to a number of metabolites, including cotinine, which has a long half-life (15–19 h) compared to nicotine (2–3 h) [5,6]. Cotinine, a major metabolite of nicotine in humans (55–92%) is created in the process of oxidation of the pyrrolidine ring to an iminium ion with the participation of aldehyde oxidase [4]. In people with fast metabolism, however, trans-3-hydroxycotinine is the main metabolite [7]. Cotinine is in terms of quantity one of the most stable metabolite of nicotine and its concentration is directly proportional to the amount of nicotine absorbed. The rate of metabolism and the rate of elimination of cotinine from circulation, reaching approximately a 10 times higher blood concentration than nicotine. The level of cotinine in the blood of smokers reaches the average value of 250–300 ng/mL [4,8]. Cotinine, as a product of decomposition, is pharmacologically inactive, it accumulates and is eliminated much more slowly ($t_{0.5}$ = 20–30 h) than nicotine [7,9].

Despite significant toxicity, nicotine is hardly ever the cause of serious and fatal poisonings. According to the literature, a dose of 30–60 mg or 0.8–1.0 mg/kg of body weight is potentially lethal for an adult [10–12]. These values may seem on the low side, since only a few cases of fatal poisoning with a potentially lethal dose of nicotine (in various forms) have been reported, while there have been cases when patients survived after consuming much higher doses of this alkaloid, reaching up to 4.0 g [13–16,21]. There have been reports of fatalities among children who ingested as little as a teaspoon of a very diluted e-liquid [12,17,18].

In the literature there are few cases of e-liquids poisoning reported, while nicotine intoxications by ingestion of the tobacco extracts are well described [14,19]. Nicotine poisonings due to intravenous injection are very rare. Hagiya's case reported in 2010 presents the female intravenously injected 5 mL of cigarette soakage solution, Thornton shows intravenous intoxication with e-liquid [16,17]. Between 2010 and 2012 a several dozen of nicotine oral and inhalation accidental exposures, mostly in children were identified without serious complications [12]. Only one fatality resulting from a suicidal ingestion of concentrated liquid nicotine intended for e-cigarette use was reported in 2015 [19].

The article presents two cases of suicidal nicotine poisonings by different routes – oral and intravenous. The poisonings were confirmed by determining the nicotine and cotinine concentrations in serum using high performance liquid chromatography with diode array detection (HPLC-DAD).

1.1. Case history No. 1

A 21-year-old woman (height – 166 cm, weight – 62 kg) was admitted to the Department of Toxicology 1.5 h after drinking 30 mL of base liquid for e-cigarettes called *Dirty Neutral Base*, with a nicotine concentration of 12 mg/mL, as stated on the label. An analysis of the leftover e-liquid transported along with the patient revealed that it contained 12.4 mg/mL of nicotine. Therefore, the patient had ingested a total of 372 mg of nicotine, i.e. 6.0 mg/kg body weight. About 15 min after e-liquid ingestion the patient vomited profusely. She experienced abdominal pain, motor agitation anxiety and dyspnea. Approximately 1 h after ingestion the woman was found by her boyfriend, who was concerned about her condition, including, confusion, persistent vomiting and panting breath. The clinical symptoms are presented in Table 1 (case No. 1).

During the ambulance transportation, because the patient's blood pressure dropped to 70/40 mmHg, so she was infused with 500 mL of 0.9% sodium chloride (NaCl) and oxygen was administered through a mask. On admission to hospital, 1.5 h after the poisoning, the patient was conscious, but periodically confused, restless and talkative. She was vomiting. A physical examination revealed pale skin and normal muscle tone, but the patient was not able to fully open her eyes, the upper eyelids set at the level of half the irises. No pathological neurological symptoms were found. What drew attention was extremely noticeable. Pronounced symptoms included: panting breath (respiratory rate – 30/min), bradycardia (heart rate – 42/min) and hypotension (blood pressure – 90/55 mmHg). The pupils were narrow, of equal size, showing a delayed response to light. Epigastric and central mesogastric pain persisted on palpation. The performed laboratory tests revealed a leukocytosis of 13.0 G/L (normal range: 3.8–10.0 G/L), low potassium levels of 2.55 mmol/L (normal range: 3.5–5.0 mmol/L), and a small alkalosis in the arterial blood gas analysis (pH 7.51; pCO_2 20.2 mmHg; pO_2 125 mmHg; HCO_3^- 20.0 mmol/L; BE −6.8 mmol/L; sO_2 98.2%). The level of electrolytes (sodium, magnesium, ionized calcium), the activity of alanine and aspartate aminotransferases, and creatine kinase, as well as serum creatinine levels were normal. The blood glucose level (non-fasting) was 150 mg/dL. The electrocardiography (ECG) showed a regular sinus rhythm of 42/min. The patient was admitted to the toxicological intensive care unit. The fluid therapy was continued – the patient was given a quick transfusion of 1000 mL of 0.9% sodium chloride and 500 mL of 6% hydroxyethyl starch (HES) solutions, and subsequent fluid infusions were used to supplement potassium. Due to still persistent hypotension (75–80/30–50 mmHg), norepinephrine in the form of continuous infusion, initially at a dose of 0.086 μg/kg/min, ultimately of 0.258 μg/kg/min was administered. The patient's heart rate spontaneously accelerated to 58–60/min. Due to persistent vomiting reflex and epigastric pain, metoclopramide 10 mg and omeprazole 40 mg were administered intravenously, followed by ondansetron 4 mg intravenously.

About 2.5 h after admission or 4 h after the poisoning, the patient was pale, conscious, but anxious, heart rate 60/min, blood pressure 90/50, respiratory rate 20/min, the pupils were narrow, of equal size, with delayed response to light. Vomiting and eyelids muscle weakening were still observed. The laboratory tests performed at that time revealed normal arterial blood gas parameters (pH 7.371; pCO_2 37 mmHg; pO_2 166 mmHg; HCO_3^- 21.8 mmol/L; BE −3.2 mmol/L; sO_2 98.2%) and a normal potassium level of 4.22 mmol/L. The electrocardiography (ECG) showed a regular sinus rhythm of 60/min. In the following hours the patient was gradually calming down.

About 12 h after the poisoning, the patient was conscious, calm, in full logical contact. Her respiratory rate was 16/min, heart rate 74/min, blood pressure 115/70 mmHg during a norepinephrine infusion at a dose of 0.258 μg/kg/min. The paleness of skin persisted. The patient was able to fully open her eyes, the pupils dilated to about 4 mm and properly responded to light. The vomiting reflex subsided. The laboratory tests performed at that point revealed persisting leukocytosis (13.8 G/L) and normal arterial blood gas parameters. The concentrations of sodium, potassium, glucose, creatinine, lactates, and C-reactive protein in the blood were normal. The urine was alkaline (pH 8.0). After a psychological and psychiatric consultation, the patient left the