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CASE REPORT

Lactic acidosis due to voluntary e-liquid ingestion

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Summary This case reports an acute poisoning with ''e-liquid'' together with its clinical and biological consequences. Toxicological investigations in blood and urine samples highlighted the presence not only of nicotine and cotinine, but also of propylene glycol. For the first time, we describe here an acute poisoning with e-liquid, followed with clinical and biological manifestations due to propylene glycol and not nicotine toxicity.

Introduction

Electronic cigarettes, also known as ''e-cigarettes'', are currently widely used by smokers as smoking cessation help. Here, we describe an acute poisoning due to voluntary ingestion of ''e-liquid'' and its biological and clinical consequences.

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Case report

This case concerns a 44 years old man, 57 kg, with a medical history of Lyme disease, a former consumption of cannabis, and a current tobacco withdrawal. He deliberately drank a declared quantity of 30 mL of solvent contained in e-cigarette cartridges, currently called ''e-liquid''. According to the patient, the cartridges were from Poland, but their proper identification remained unknown. Two hours after ingestion (timing based on the patient's declaration), he was admitted to the emergency department. He was suffering from headache, nausea, abdominal pain, ventricular extrasystoles and tachypnea (29/min). Admission laboratory investigations included Na^+: 141 mmol/L, Cl^-: 105 mmol/L, K^+: 2.7 mmol/L, uremia: 0.48 g/L, serum creatinine: 10.9 mg/L, alcaline phosphatase: 58 U/L and creatine kinase (CK) 80 U/L. Liver chemistry was slightly disturbed, with increased aspartate aminotransferase (AST) (52 U/L) and normal alanine aminotransferase (ALT) (28 U/L). Eight hours after ingestion, a lactic acidosis associated to an elevated anion gap (23) was diagnosed, with arterial pH at 7.3 and blood lactate concentration at 11.4 mmol/L. The first toxicological investigations in urine samples were performed using a Drug-Screen-Multi 9TB device (Nal von Minden, Moers, Deutschland) and did not detect the presence of benzodiazepines, tricyclic antidepressants, barbiturates, cannabis, cocaine, amphetamines, ecstasy, methadone and opiates. During the following hours, he developed a muscular paralysis prevailing on the lower limbs, and a hypotonic anal sphincter. On the advice of the local Poison Center, he was admitted in Intensive Care Unit for full supportive medical care and additional toxicological investigations, especially determination of propylene glycol, nicotine and cotinine concentrations in biological samples. Propylene glycol (PG) analysis was performed using a GC-FID (Thermo Fischer Scientific, Villebon-sur-Yvette, France) equipped with a CP-SIL 8CB 25 m × 0.25 mm × 0.25 μm column (Varian, Middleburg, The Netherlands) after derivatization with phenylboronic acid and using 1,3-propanediol as internal standard. Data were analysed with Chromquest® software (Thermo Fischer Scientific). Nicotine analysis was performed with a UPLC-TQD (Waters®, Saint-Quentin-en-Yvelines, France), with cotinine-D3 as internal standard, after alcaline extraction with organic solvents. Chromatographic separation was processed with an Acquity® HSS C18 1.8 μm, 2.1 mm × 150 mm column (Waters®) with a gradient mixture of ammonium formiate pH 3/acetonitrile with 0.1% formic acid. Acquisition was performed with positive ion electrospray ionization in multiple reaction monitoring (MRM) mode, and data analysis with Masslynx® software (Waters®). Concerning the toxicological screening, after liquid-liquid extraction, urine (after hydrolysis) and blood samples were analysed using a UPLC-Q-TOF (Waters®, XEVO-G2-Q-TOF) fitted with an electrospray ionization source (ESI) operating under positive ion mode. Chromatographic separation was performed with an Acquity® HSS C18 1.8 μm, 2.1 mm × 150 mm column (Waters®). Methylclonazepam and beta-hydroxyethyltheophylline were used as internal standards. Mass spectra were acquired in MSE mode and data analysis was performed with Masslynx® software (Waters®). Fourteen hours after the supposed time of e-liquid ingestion, the concentration of PG was 300 mg/L in whole blood and 1230 mg/L in urine samples, and concentrations of nicotine and cotinine in blood were 21 and 102 μg/L, respectively. Lactic acidosis persisted (pH 7.3), with an anion gap remaining high (20.6). No other drug was detected. Perfusion of 4-methylpyrazole (1000 mg/day, 4 days) was started, as well as overhydration and alcalinization. At day 1, the blood concentration of PG was 294 mg/L, blood lactate concentration decreased (2 mmol/L), and AST (74 U/L), CK (2649 U/L) and lactate dehydrogenase (LDH) (266 U/L) increased. Blood gas values were also normalized. At day 2, PG blood level was 272 mg/L, AST: 139 U/L, CK: 6177 U/L and LDH: 339 U/L. On day 3, PG blood level was 33 mg/L, AST: 171 U/L, CK: 6742 U/L, LDH: 412 U/L and acid lactic normalized at 0.6 mmol/L. Nicotine and cotinine levels were 0.8 and 36 μg/L, respectively. The biological status improved on day 4, with AST: 145 U/L and CK: 5448 U/L. On day 5, PG was undetectable (< 30 mg/L), nicotine and cotinine levels were 0.7 and 8.1 μg/L, respectively, and levels of AST and CK were 97 and 2546 U/L, respectively. A breakdown of patient biological data is presented in Table 1. From a clinical point of view, the state of the patient gradually improved and neurological symptoms declined.

Discussion

Over the last few years, the use of electronic nicotine delivery systems (ENDS), currently called electronic cigarettes, can be considered as an alternative to smoking. Briefly, consumers, also called ''vapers'', breathe in vapor produced by the heating of a mixture of propylene glycol and glycerin, various flavourings and with or without different concentrations of nicotine. ENDS are experiencing booming sales, the global market for e-cigs being predicted to reach over $ 3.2 billion by 2015, and over $ 10 billion by 2017 [1]. Thus, an increase in e-liquid poisonings is observed. A great number of intoxications via various routes of exposure have already been reported by American Poison Centers [2]. Fortunately, these cases were not deleterious, except a death following a self-injection of e-liquid. In the present case, the absence or presence of nicotine, and its concentration, were unknown in the ingested product, and nicotine and cotinine levels in the patient blood samples appeared extremely low. This could be explained by an ingestion of an e-liquid with very low nicotine dosage, or ingestion of nicotine-free e-liquid by a smoking patient. Accordingly, previously reported nicotine levels in acute intoxications were far higher [3], and the nicotine blood concentration found for our patient (21 μg/L) is compatible with blood concentrations expected after a single cigarette smoking (5 to 30 μg/L). Furthermore, the patient did not present a typical nicotinic intoxication symptomatology (vomiting, diaphoresis, hypotension, seizures, respiratory failure). Here, the observed symptomatology and biological disturbances appear in accordance with propylene glycol intoxication. An ion and/or osmolar gap with or without lactic acidosis has been described in several PG intoxication cases, most of them being related to its use as a solvent in intravenous medications [4–12] or, less frequently, after oral ingestion of PG-containing products [13–15]. Plasma or serum concentrations of PG

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