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CASE REPORT

Attempt of scopolamine-facilitated robbery: an original case of poisoning by inhalation confirmed by LC–MS/MS and review of the literature

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Abstract

Purpose Scopolamine, an alkaloid found in certain plants, has become a drug of use for recreational and predatory purposes. We present here the case of an attempted scopolamine-facilitated robbery, via inhalation, with full recovery of the victim. We also performed a review of toxicological findings for scopolamine poisoning cases in available scientific literature.

Methods Whole blood and urine samples were collected 4 h after the assumed poisoning. Concentrations of scopolamine were determined in both samples by a validated and accredited method using liquid chromatography–tandem mass spectrometry.

Results Scopolamine was the only substance found in both whole blood and urine samples, at 7 and 510 ng/mL, respectively.

Conclusions Scopolamine poisoning remains rare, as its half-life is short; blood and urine should be collected as soon as possible for toxicological analysis. This case is, to our knowledge, the first described case of inhaled scopolamine robbery attempt, with quantitative toxicological findings.

Keywords Scopolamine · Drug-facilitated robbery · Inhalation of scopolamine · LC–MS/MS · Review of the literature

Introduction

The use of scopolamine, an alkaloid found in certain plants, has been reported to be used to incapacitate people for criminal gain. Preparations containing scopolamine are known in South America as *Burundanga* and in Asia as *Devil's breath,* and are usually made from *Datura* leaves or berries. They are mostly used to facilitate robbery or sexual assaults [1]. In Europe, scopolamine seems to be used mostly for recreational purposes, sometimes with lethal outcome [2]. As the scopolamine plasma half-life is short [3], it is rapidly cleared from the body, and most reports do not have analytical confirmation of its presence. We present here a case of attempted scopolamine-facilitated robbery, which occurred in Paris, France, in December 2017. Analytical confirmation was obtained in whole blood and urine, and we compared our results with others in scientific literature.

Case history

A 58-year-old man, with no previous medical problems, started to be agitated a few minutes before meeting his sister for dinner. He was incoherent and gradually lost consciousness. Clinical evaluation by mobile emergency and intensive care unit revealed disturbance of consciousness with clonic movements, bilateral mydriasis, hypertension and tachycardia. He was brought to a neurological emergency room for a cerebral scan which showed no disorders and ruled out a stroke. As his condition did not improve, he was admitted to hospital where his Glasgow coma scale (GCS) was evaluated at 13/15, with probable hearing, visual hallucinations and bilateral mydriasis. He was afebrile and hemodynamically

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stable; routine physical examinations and electrocardiography were unremarkable. As a toxic cause was suspected, blood and urine were sampled. The patient regained full consciousness 5 h after his admission and was discharged after 24 h with a normal neurological examination. He was examined in our service upon judicial requisition 48 h after this episode, and explained that he was waiting for his sister on the street when an unknown man tried to apply a piece of cloth on his face. As the patient stepped back, the man blew a strong odor powder contained in the cloth on his face. He then has no recollection of what happened until his awakening in the hospital a few hours later. None of his belongings were stolen, probably thanks to his sister's arrival. The patient recalled inhaling the powder, but was not able to tell us if any got into his mouth.

Methods of toxicological analysis

The reference standards of scopolamine and atropine were purchased from Sigma-Aldrich (Paris, France). Blood and urine samples were drawn 4 h after the assumed poisoning and were sent to the expert toxicological laboratory of Garches, in the suburb of Paris. Toxicological analysis on whole blood and urine consisted of an alcohol (ethanol) analysis with gas chromatography–flame ionization detection, and a general screening on whole blood and urine using gas chromatography–mass spectrometry (GC–MS) and liquid chromatography–tandem mass spectrometry (LC–MS/MS). The urine sample was also screened by cloned enzyme donor immunoassay (CEDIA) immunoassay tests (Indiko; Thermo Fisher, Les Ulis, France) for different drugs: amphetamines, barbiturates, benzodiazepines, buprenorphine, cocaine metabolites, cannabinoids, methadone and opiates.

Concentrations of scopolamine were determined in both whole blood and urine samples by a validated and accredited (COFRAC, comité français d'accréditation) method using LC–MS/MS (LC–MS/MS TSQ Vantage; Thermo Fisher) derived from a previously published method in hair [4]. Briefly, a basic (1 M carbonate buffer, pH 9.7) liquid-liquid extraction was carried out on 1-mL sample by a mixture of hexane/ethyl acetate (1:1, v/v) after addition of internal standard (IS, ketamine-D_4; LGC Standards, Teddington, UK). After agitation and centrifugation, the organic phase was conserved and then evaporated to dryness. The residue was reconstituted in 80 µL of mobile phase, and 10 µL were injected into an 1.9-µm Hypersil GOLD PFP column (200 × 2.1 mm; Thermo Fisher). The mobile phase was a gradient of acetonitrile and the solution of 2 mM NH_4COOH + 0.1% formic acid (pH 2.9) starting from 20% of acetonitrile to 90% in 10 min at a flow rate of 300 µL/min. The ionization of both compounds was achieved in positive electrospray mode, and quantification in multiple reaction monitoring (MRM) mode, using the transitions *m/z* 304.1 –> 102.5 and 137.6 for scopolamine and *m/z* 242.1 –> 128.6 and 223.7 for ketamine-D_4.

Table 1 Precisions and accuracies of the method evaluated at three QC levels in whole blood

QC concentrations (ng/mL)	0.6	2.0	15
CV intraday %	5.6	5.2	3.5
Accuracy intraday %	101–107	95.2–101	97.7–106
CV interday %	8.1	7.0	10.5
Accuracy interday %	103	98.2	102

QC quality control, *CV* coefficient of variation

Validation parameters of the method with whole blood and urine

For the whole blood matrix, seven calibration curves obtained over a period of 2 weeks were constructed for the study of linearity. The calibration curves included a blank sample and nine calibration standards (CSs) over the concentration range: 0.05 ng/mL [lower limit of quantification (LLOQ)] to 20.0 ng/mL [upper limit of quantification (ULOQ)]. Quantification was achieved by plotting the peak area ratios of scopolamine to the IS versus concentration followed by linear regression analysis, which was the best-fitting model as shown by the back-calculated concentrations of the 63 CSs (seven curves with nine CSs), with all < 15% except 4. All correlation coefficients ranged from 0.997 to 0.999. The limit of detection of the method was set at 0.01 ng/mL.

Accuracy (measured value/nominal value) and precision (coefficient of variation, CV) were determined for three quality control (QC) levels (0.6, 2.0 and 15 ng/mL). For the intraday assay, six replicates of each QC level were processed on the same day. For the interday assay, each QC level was processed six times by day during three different days over a period of a week. The values obtained were analyzed using analysis of variance (ANOVA), which separated the intraday and interday standard deviations, corresponding to CVs. An accuracy within the range 85−115% of the nominal values and a precision with a CV of ± 15% were required. Results obtained for the method are shown in Table 1, showing that the method was accurate, precise and reproducible for quantification of scopolamine.

Recoveries and matrix effects were evaluated at 2.0 and 15 ng/mL in 6 different samples. For scopolamine, recoveries were 69 and 72%, and matrix effect was +6 and +4% in whole blood, respectively. Recoveries and matrix effects of IS were 79 and +1%, respectively.

The validation experiments were also conducted for urine matrix. The validation data for urine were comparable to those for whole blood, and thus were acceptable for quantification of scopolamine in the urine sample.

Results

Ethanol was negative in whole blood and urine. No other drugs of abuse were found in urine. Scopolamine was the only psychoactive substance found in both whole blood and urine samples, at 7 and 510 ng/mL (1/50 diluted upon measurement), respectively. Atropine was not detected in whole blood or urine (limit of detection 0.01 ng/mL).

Discussion

Scopolamine, also known as hyoscine is a tropane alkaloid found in plants belonging to the family of Solanaceae like *Datura stramonium, Brugmensia, Atropa belladona* (deadly nightshade) or *Hyoscyamus niger* (black henbane) [5]. Scopolamine is a non-selective competitive inhibitor of muscarinic receptors for acetylcholine, and scopolamine poisoning causes an anticholinergic syndrome. Most common central symptoms of anticholinergic encephalopathy are agitation, confusion, hallucination, convulsions and even coma. Peripheral effects are atropine-like signs including mydriasis, dry skin and mouth, urinary retention, hyperthermia, hypertension and tachycardia. The symptoms usually regress within two days with no sequelae other than anterograde amnesia of the event, but some fatal cases have been noted [2, 3, 6]. Treatment should be symptomatic, with use of supportive therapies. In severe cases, cholinergic drugs as physostigmine or rivastigmine have been used successfully as antidotes to treat the central nervous system depression symptoms [7, 8]. Due to its anticholinergic properties, scopolamine has a number of uses in medicine, in treatments of postoperative nausea, motion sickness and as a palliative. Therapeutic blood-level concentrations of scopolamine vary from 0.3 to 19 ng/ml [9]. Apart from its medical uses, scopolamine has been used for centuries in rituals, based on its hallucinogenic effect. Such preparations are known as *Burundanga* in South America or *Devil's Breath* in Asia and can lead to involuntary overdose [10]. Involuntary poisonings in drug adulteration have been reported, such as scopolamine sold as cocaine in Barcelona in 1991 [11], heroin adulterated with scopolamine on the East Coast of the United States in 1995 [12] or an epidemic of poisonings caused by scopolamine sold as Rohypnol™ tablets in Norway in 2008 [7]. Accidental poisonings can also occur in food confusion or food contamination by *Datura* leaves [13, 14], and in ingestion by an unattended child [15]. The use of scopolamine is also reported from criminal intent, as in our case, because of its submissive effect on victims. Scopolamine is usually added to a drink [16, 17] or food [6], and there even were reports of scopolamine added to moisturizing creams [18]. There are a few reports of poisonings by ingestion of a powder containing atropine and scopolamine, called Asthmador®, marketed in the middle of the twentieth century as an asthma medication [19].

Scopolamine has a short plasma half-life, which varies between 2 and 4 h after oral administration [20]. In one pharmacokinetic study in humans, the nasal absorption rate of scopolamine was found to be pH- and dose-dependent with a time of maximum concentration (*T*max) between 26.7 ± 5.77 min (0.4 mg, pH 4.0) and 6.25 ± 2.50 min (0.2 mg, pH 9.0) [21]. Scopolamine is metabolized by the liver, and pathways are still unclear, but metabolites could be used to improve the detection window in intoxications [22]. Its excretion seems to be mostly renal, and about 5% of an oral dose is excreted in the urine as unchanged compound, 30% being under glucuronide form [20]. These pharmacokinetics data explain why there is limited toxicological evidence in suspected scopolamine poisonings.

Table 2 shows the concentrations of scopolamine in human samples published in the past literature, which have been listed chronologically. All the past scopolamine poisonings were caused by oral ingestion; there is no date for inhalation of scopolamine. When the scopolamine concentrations in blood/serum are compared with those in urine, the levels in the former are much lower than those in the latter (one or two orders of magnitude lower), except those in fatal cases [2, 6]. Because the result for blood analyses may be negative (below the detection limit) occasionally, the sampling of urine is absolutely necessary for scopolamine analysis.

Our samples were drawn 4 h after poisoning, and our concentrations are in range of those reported in medical literature (Table 2). Unfortunately, we could not obtain a sample of the powder used in this case, because the assailant has not been apprehended by the police. In France, scopolamine is used in human medicine but is only available in patches or injectables. An oral form of scopolamine is available in veterinary medicine under the name Scopalgine®. We assume that the assailant used either crushed tablets of Scopalgine® or bought a product containing scopolamine online.

Conclusions

Scopolamine poisoning remains rare in France, whether it is accidental, criminal or of recreational purposes. Nevertheless, many plants contain toxic alkaloids, and emergency physicians need to be aware of this kind of poisoning. As scopolamine's half-life is short, blood and urine should be collected as soon as possible for toxicological analysis. If this has not been done, a hair sample should be analyzed [4].

Table 2 Concentrations of scopolamine in medical literature

Study	Route of administration	Outcome and details of case	Interval between exposure and sampling	Type of sample	Detection/quantification	Results
Present study	Inhalation	Present case	4 h	Whole blood	LC–MS/MS	7 ng/mL
				Urine	LC–MS/MS	510 ng/mL
Desachy et al. 1997 [23]	Oral	Full recovery (voluntary ingestion of *Datura* seeds)	6 h	Blood (serum)	GC–MS	16 ng/mL
				Urine	GC–MS	499 ng/mL
			18 h	Blood (serum)	GC–MS	<5 ng/mL
				Urine	GC–MS	37 ng/mL
	Oral	Full recovery (voluntary ingestion of *Datura* seeds)	6 h	Urine	GC–MS	415 ng/mL
			18 h	Urine	GC–MS	2042 ng/mL
Balikova 2002 [24]	Oral	Full recovery (30 people poisoned with « herbal tea » during meditation)	Mean interval: 6 h	Blood (serum)	GC–MS	13 ng/mL (mean concentration in serum of 12 intoxicated people of the 21 tested)
Cohen et al. 2003 [10]	Oral	Full recovery (voluntary ingestion of *Datura* leaves infusion)	Unknown	Urine	HPLC–UV	300 ng/mL
Boumba et al. 2004 [2]	Oral	Deceased (voluntary ingestion of *Datura* seeds)	Unknown	Whole blood	GC–MS	200 ng/mL
				Urine	GC–MS	Not detected
Marc et al. 2007 [25]	Oral	Full recovery (voluntary ingestion of *Datura* flowers and leaves)	2 h	Blood (serum)	LC–MS/MS	1.4 ng/mL
			26 h	Blood (serum)	LC–MS/MS	1.0 ng/mL
				Urine	LC–MS/MS	8 ng/ml
			43 h	Blood (serum)	LC–MS/MS	Traces
Vallersnes et al. 2009 [7]	Oral	Involuntary absorption (fake Rohypnol pills)	3 h	Blood (serum)	UPLC–MS/MS	0.79 ng/mL
			5 h	Blood (serum)	UPLC–MS/MS	0.45 ng/mL
Papoutsis et al. 2010 [26]	Oral	Full recovery (food confusion)	20 h	Urine	GC–MS	32.4−186.4 ng/mL (extreme values)
Ricard et al. 2012 [4]	Oral	Chronic voluntary ingestion	Unknown	Hair	LC–MS/MS	1.0−1.3 pg/mg
Nikolaou et al. 2012 [13]	Oral	Full recovery (voluntary ingestion)	4 h	Blood	GC–MS	Not detected
				Urine	GC–MS	32.7 ng/mL
Gomila et al. 2016 [17]	Oral	Full recovery (drug-facilitated robbery)	24 h (approximately)	Urine	GC–MS	899 ng/mL
Le Garff et al. 2016 [3]	Oral	Deceased (drug-facilitated robbery)	Unknown	Vitreous humor	GC–MS	5 ng/mL
Lusthof et al. 2017 [6]	Oral	Deceased (voluntary ingestion of *Datura* seeds)	Unknown (> 4 days)	Heart blood	LC–MS/MS	300 ng/mL
				Femoral blood	LC–MS/MS	4.8 ng/mL
				Stomach contents	LC–MS/MS	20 mg/kg
	Oral	Full recovery (drug facilated robbery)	12 h	Urine	GC–MS	Traces
			79 days	Hair	LC–MS/MS	0.2−0.8 ng/mg
	Oral	Full recovery (drug-facilitated robbery)	23 h	Blood (serum)	LC–MS/MS	0.35 ng/mL
				Urine	GC–MS	Traces

This is, to our knowledge, the first described case of inhaled scopolamine robbery attempt, with quantitative toxicological findings.

Compliance with ethical standards

Conflict of interest There are no financial or other relations that could lead to conflicts of interest.

Ethical approval The analyses of toxic substances were requested by judicial authorities. The blood and urine (about 15 mL, respectively) were collected from the patient with his informed consent.

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