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Suicides by ingestion of pure caffeine powder. New challenge for public health?

Jozef Sidlo[1,2], Jan Sikuta[1,2], Henrieta Sidlova[3], Lubos Niznansky[1,2]

1 Institute of Forensic Medicine, Faculty of Medicine, Comenius University, Bratislava, Slovakia.
2 Institute of Forensic Medicine, Health Care Surveillance Authority, Bratislava, Slovakia.
3 Institute of Pathology, Faculty of Medicine, Slovak Medical University, Bratislava, Slovakia .

Correspondence to: Jozef Sidlo, Assoc. Prof. MD. CSc. MPH
Institute of Forensic Medicine, Faculty of Medicine, Comenius University
Sasinkova 4, 811 08 Bratislava, Slovakia
TEL.: +421904819241; FAX: +421220856556; E-MAIL: jozef.sidlo@fmed.uniba.sk

Jozef Sidlo and Lubos Niznansky contributed equally to this work.

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Abstract

OBJECTIVES: Intentional or unintentional caffeine abuse due to excessive intake of energy beverages is frequent. Fatalities due to caffeine intoxication are presented rarely. Over the last years, cases of caffeine ingestion for purposes of committing suicide have been reported in scientific literature.
DESIGN: The aim of this case study is to report a fatal case of a 26-year-old man who intentionally ingested pure caffeine powder.
METHODS: Standard autopsy, microscopic examination and toxicological examination using screening method, TLC, GC, and GC/MS were performed.
RESULTS AND CONCLUSIONS: The presence of caffeine only at the concentration of 362 ug/mL in blood and 187 ug/mL in urine was revealed. The cause of death was cardiac arrest most likely due to ventricular dysrhythmia. The concentration of caffeine determined in the femoral blood of the decedent was three times higher than the lethal concentrations reported in other published case studies. Based on the investigated circumstances, the manner of death was evaluated as a suicide.

Abbreviations:

TLC	- thin layer chromatography
GC	- gas chromatography
GC/MS	- gas chromatography/mass spectrometry
PIN	- personal identification number

INTRODUCTION

Caffeine (1,3,7-trimethylxanthine) is a natural alkaloid that acts as a stimulant of the central nervous system and the heart rate (Holmgren *et al.* 2004). Caffeine is consumed through classic drinks, over-the-counter and prescription medications, herbal medicines, dietary supplements and food products sold to suppress appetite. Caffeine consumption has increased in recent years. This is especially true among young people – students and athletes who consume it in a concentrated form as energy drinks or as 100% caffeine anhydrous powder used in high doses for self-preparation of beverages (Hoyte *et al.* 2013). Caffeine is absorbed rapidly and completely when it is consumed orally. Clinical effects are identifiable within 15 minutes, and peak plasma concentrations are attained within 15–45 minutes after ingestion. O'Connell and Zurzola (1984) found out peak plasma concen-

CASE REPORT

Fig. 1. Fine rim of the whitish powder on the margin of the stomach content on the face of deceased.

trations of 2.5–6.8 ug/mL (mean 4.0 ug/mL) within 20–40 min after administration of a single 130 mg oral dose in 36 subjects. In adults, the plasma half-life is reported to be 2–10 hours (mean 4 hours) (Moffatt *et al.* 2011). During elimination, approximately 85% of a dose is excreted in urine within 48 hours, about 1% as unchanged drug. Clinically, caffeine intoxication presents with a headache, stomachache, nausea, vomiting, fever, hyperventilation, dizziness, anxiety, tinnitus, tremor, and agitation (Rudolph & Knudsen, 2010). Rhabdomyolysis has been described even in the subtoxic concentrations (Phillips *et al.* 2012). In humans, blood caffeine concentrations higher than 25 ug/mL are considered toxic (Perkovič Vukčevič *et al.* 2012), higher than 100 ug/mL is considered lethal (Musgrave *et al.* 2016; Winek *et al.* 2001). In overdose cases, hypertension, hypotension, arrhythmia, altered level of consciousness, rigidity, and spasms have been reported (Kerrigan & Lindsey, 2005; Thelander *et al.* 2010). The immediate cause of death is often attributed to ventricular dysrhythmia/fibrillation (Avci *et al.* 2013; Berger & Alford, 2009), which was also found in an experimental rat study (Strubelt & Diederich, 1999). Chronic ingestion of alcohol and medications may prolong the half-life of caffeine by approximately 72%, thus contributing to its toxic effects (Sepkowitz, 2013). Some fatalities may result from heightened and prolonged caffeine levels attributable to various substances metabolized through the same metabolic pathway (Sepkowitz, 2013; Hodek *et al.* 2015; Bostikova *et al.* 2015). However, fatal cases due to only caffeine intoxication are rare and not often reported in the literature (Bonsignore *et al.* 2014). The aim of this case report is to provide details of a fatal case of a 26-year-old man who intentionally ingested pure caffeine powder, where only caffeine was present in the blood and urine.

CASE HISTORY

The body of a man was found on the floor in a prone position in his room in the afternoon after he had not arrived at work that day. His face was covered with a coat of the stomach content of black colour containing a fine rim of the whitish powder (Figure 1). In the room was found a plastic bag of white-blue colour with pressure cap containing white powder labelled "Caffeine, 100 g, Myprotein.co.uk, Nutrition fit for you, BBD: 04/2015, BATCH: 1104207, MANU: 07/10/11" (Figure 2). On the table was found a farewell message "It was not me ...", a PIN code and a credit card (Figure 3). Any other toxic substances, drugs or ingredients for self-preparation of high energy drinks containing caffeine were not found in the apartment.

AUTOPSY FINDINGS

The autopsy of the deceased (height 190 cm, weight 90 kg) was conducted the next day after death.

Macroscopic findings

The external examination didn't reveal such characteristic signs of violence to suggest the intervention of another person, fight, or self-defence. At autopsy, the decedent was found to have cerebral oedema, passive congestion, and pulmonary oedema (Figure 4), diffuse bleeding from the stomach mucosa and incipient atherosclerotic changes of the coronary arteries. Subsequently, complete microscopic examination of samples removed from the brain, lungs, heart, liver, pancreas,

Fig. 2. Plastic bag with caffeine powder.

spleen and kidneys and toxicological examinations of femoral blood and urine were performed.

Microscopic findings

Microscopic examination of the organ samples confirmed macroscopic findings and revealed mild perivascular fibrosis and signs of hypertrophy of solitary myocardial fibres, mild chronic passive congestion, and mild hepatic steatosis and acute passive congestion, and arteriolosclerosis of the spleen. Neither macroscopic nor microscopic examination revealed pathological changes that could have been considered as the cause of death.

Toxicological findings

Toxicological examination revealed only presence of caffeine at the concentration of 362 μg/ml in blood and 187 μg/ml in urine. Caffeine was determined by GCMS analysis (Varian, Ion trap mass spectrometer). Chromatographic separation was carried out on DB-5MS 30m × 0.25mm x 0.25μm film thickness capillary column. Before the analysis by GCMS, blood was deproteined. Caffeine from blood and urine was extracted in alkaline pH two times with diethyl ether. GCMS and thin layer chromatography confirmed, that no other drugs including ethanol were presented in the blood and urine.

The powder seized in the bag (Figure 2) was analyzed at the Institute of Forensic Sciences of the Police Force. Analyses performed revealed that a white-blue plastic bag with pressure cap included 86.51g of white powder containing 100% caffeine free of contaminants which creates a presumption that a man ingested about 13g of pure caffeine.

CAUSE OF DEATH

Based on the results of the autopsy examination and toxicological analyses, the immediate cause of death – cardiac arrest most likely due to abnormal heart rhythm resulting from intoxication (overdose) of caffeine was determined.

DISCUSSION

Cases of clinically significant intoxications in healthy adults have been described following the intake of a large number of energy drinks. Ingestion over

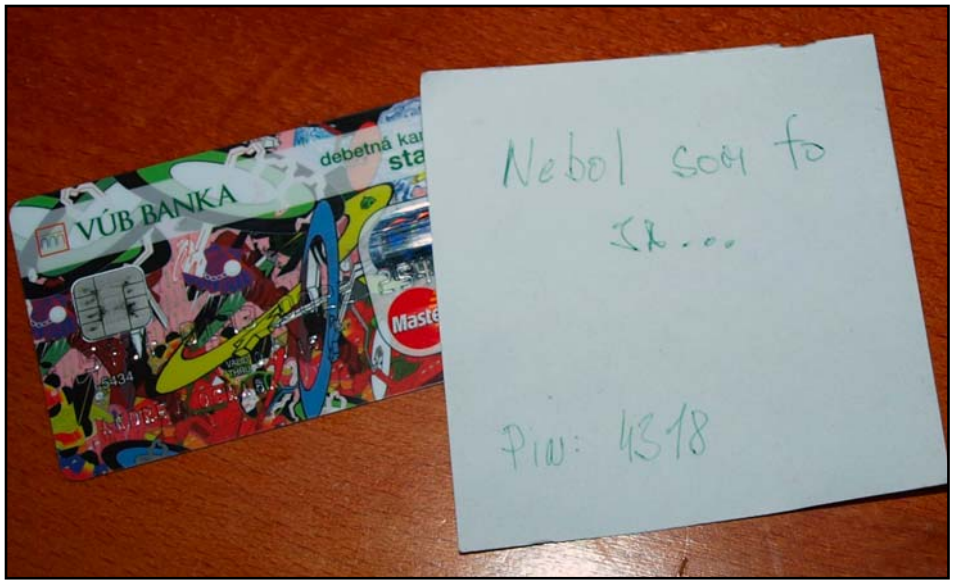

Fig. 3. Credit card and paper with farewell message and PIN code.

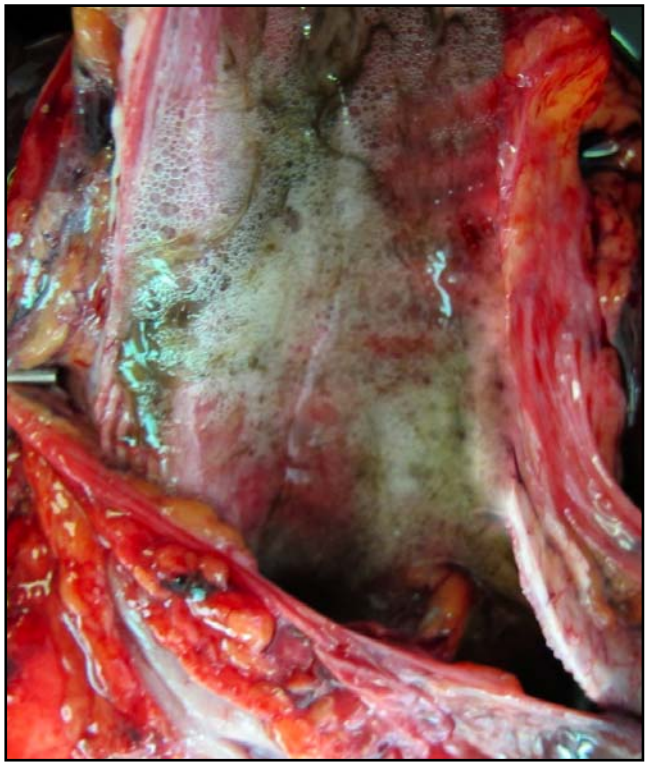

Fig. 4. Edematose fluid in the trachea.

a brief time of 3-10 g of caffeine might be lethal (Holmgren *et al.* 2004; Szpak & Allen, 2012). To reach the dose of 3 g of ingested caffeine, a person would need to drink a large number of highly caffeinated beverages within a few hours (Garriot *et al.* 1985; Musshoff *et al.* 2004; Riesselmann *et al.* 1999). Severe acute iatrogenic intoxication has been reported after overdose with intradermal caffeine injection within mesotherapy in which its lipolytic effect is used. The concentration of caffeine in blood plasma reached 85 ug/mL (Winek *et al.* 2001). Correlations between blood levels and clinical effects are difficult to establish due to inter-individual variability, tolerance, and/or pre-existing disease states. Blood caffeine concentrations within 80 - 100 ug/ml are considered lethal in humans. Results of the analysis show that the concentration of caffeine 362 ug/mL in blood is one of the higher of lethal cases. However, there are some cases, where caffeine concentrations in the blood were up to 343 ug/mL (Cannon *et al.* 2001). In some of those cases, the concentration of caffeine in the urine was from 43,2 to 136,7 ug/mL, lower than the caffeine concentration 187 ug/mL in the urine sample of this case study. This comparison confirms that the measured concentration of caffeine in the blood was lethal. Fatalities in adults are reported following ingested doses of 5 - 50 g, even though recovery after ingestion of 30 g has been described. As mentioned above ingestion over a short time of 3-10 g of caffeine may be lethal. This is consistent with this case study, considering 13 g of pure caffeine was missing from a plastic bag shown in Figure 2. Fatalities following ingestion of huge amounts of pure caffeine anhydrous or caffeine pills have occasionally been described in the literature. The lethal concentration of 80–100μg/mL in the blood can theoretically be reached after ingestion of 50–100 caffeine tablets containing 100 mg of pure caffeine (Jabbar & Hanly, 2013). The result of a large recent meta-analysis study shows that caffeine, despite being widely used, is very rarely used for suicide (Silva *et al.* 2014; Zeleny *et al.* 2015). A recently published study reports average caffeine concentrations in post-mortem blood from 51 cases of caffeine-related poisoning deaths in relation to the manner of death according to medical examiner reports. Twenty-six (51%) of cases were evaluated as suicides with an average blood caffeine concentration of 203μg/mL (Jones, 2017). In the most of studies where caffeine is considered as the reason of death/suicide, drugs other than caffeine were presented in the blood. Table 1 summarizes the most frequently cited published cases of lethal caffeine-related overdoses from the point of view of age, sex, blood caffeine concentration, type and concentration of co-ingested substances, amount and form of caffeine ingested and manner of death. From the table, it is apparent that studies where only caffeine was present in the blood are very rare.

CONCLUSION

The caffeine concentration determined in the decedent's blood in this case study was three times higher than the lethal concentration reported in the scientific literature. In addition, blood caffeine concentration in our case was nearly two times (1.8×) higher than average concentration in the cases of suicides in the previously cited studies. Moreover, caffeine was ingested as pure caffeine powder and was present in the body without interactions with other drugs, whereby in this case study, from the point of view of the manner of death, seems to be unique. Based on the investigation into the circumstances – findings at the place where the decedent was found, the case was concluded that caffeine had been consumed as a tool to commit suicide. The social history revealed that the man working in a bank had had no financial responsibility, personal conflicts or problems at work, so the meaning of a farewell message "It was not me..." remained unclear. Based on the preceding facts, the young man's motive for committing suicide most likely will remain undetermined.

DECLARATIONS OF INTEREST

None.

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Tab. 1. Overview of selected published cases caffeine-related deaths according to age, gender, toxicology, form and amount of caffeine used and manner of death

Author (Year)	Age	Gender	Blood caffeine concentration (µg/mL)	Other detected substances/ concentration	Caffeine form/amount ingested	Manner of death
Holmgren (2003)	54	F	173	Orphenadrine 2.2 µg/g Thioridazine 1.1 µg/g	Caffeine (100 tablets á 100 mg)	Undetermined
Holmgren (2003)	47	F	200	Ephedrine 4.8 µg/g	"Letigen" (100 tablets Caffeine/ Ephedrine á 200/20 mg)	Undetermined
Riesselmann (1999)	19	F	220	Theophylline 2 mg/L	"Guarana" (1 pack ? capsules á 44 mg caffeine)	Undetermined
Banerjee (2014)	52	M	49	Lidocaine 2.3 mg/L	Caffeine (30 tablets unspecified)	Undetermined
Banerjee (2014)	42	F	33	Ethanol 0.3 g/L	Unknown	Undetermined
Banerjee (2014)	37	F	73	Ethanol 0.1 g/L	Unknown	Undetermined
Banerjee (2014)	39	F	90	Acetaminophen 520 mg/L Butalbital 75 mg/L	"Fioricet" (to 90 tablets Butalbital/Acetaminophen/ Caffeine á 50/325/40 mg)	Undetermined
Banerjee (2014)	44	M	80	Levetiracetam 16 mg/L Citalopram 0.1 mg/L	"Stay Awake" (? tablets á 200 mg caffeine)	Undetermined
Banerjee (2014)	50	F	320	–	"NoDoz" (59 pills á 200 mg caffeine)	Undetermined
Kanstrup (2003)	31	F	180	Ephedrine 2.8 mg/kg	"Letigen" (? tablets Caffeine/ Ephedrine á 200/20 mg)	Undetermined
Magdalan (2017)	20	F	613	–	Pure caffeine (? g powder)	Undetermined
Kerrigan (2005)	39	F	192	Ibuprofen trace	Caffeine (? injection unspecified)	Accidental
Kerrigan (2005)	29	M	567	Phenytoin 7 mg/L	Dietary supplement (unspecified)	Accidental
Magdalan (2017)	27	M	140	–	Pure caffeine (45 g powder)	Accidental
Holmgren (2003)	21	M	210	Venlafaxine 0.5 µg/g	Caffeine (200 pills á 100 mg)	Suicide
Holmgren (2003)	31	M	153	–	Caffeine (approx. 100 tablets unspecified)	Suicide
Bonsignore (2014)	31	M	170	Ethanol 0.24 g/L Salicilic acid 169 mg/L	Pure caffeine (100 tablets á 100 mg)	Suicide
Riesselmann (1999)	81	F	190	Salycilic acid 360 mg/L Acetaminophen 700 mg/L	Unknown	Suicide
Jabbar (2013)	39	M	350	–	Pure caffeine (12 g powder)	Suicide
Banerjee (2014)	43	F	320	–	"Jet Alert" (? pills á 200 mg caffeine)	Suicide
Banerjee (2014)	57	M	220	–	"NoDoz" (? tablets á 200 mg caffeine)	Suicide
Kanstrup (2003)	39	F	400	Ephedrine 24 mg/kg	"Letigen" (132 tablets Caffeine/ Ephedrine á 200/20 mg)	Suicide
Yamamoto (2015)	18	F	290	–	Sleep inhibitor (258 tablets á 200 mg)	Suicide
Aknouche (2017)	48	M	401	Nordiazepam 188 ng/ml Sertraline 31 ng/mL Fluoxetine 48 ng/mL	Pure caffeine (100 g powder)	Suicide
Jantos (2013)	25	F	141	Ethanol 2.66 g/L	"Stacker 4" (? capsules á 300 mg caffeine)	Suicide
This case	26	M	362		Pure caffeine (13 g powder)	Suicide

Abbreviations: M - male, F - female, ? - unknown number/amount

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