



Case Report

Complex suicide with homemade nicotine patches

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ABSTRACT

Suicide by self-poisoning is rather common around the world. This paper presents an exceptional complex suicide in which nicotine was applied in the form of self-made patches soaked with an extraction from fine-cut tobacco. In addition, the 51-year-old suicide victim took a lethal dose of diphenhydramine. Toxicological analysis also revealed the presence of tetrazepam in subtherapeutic concentrations. The scene of death suggested an autoerotic accident at first, as the body was tied with tapes, cables and handcuffs. As a result of the entire investigations, the fatality had to be classified as a suicidal intoxication by nicotine and diphenhydramine.

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1. Introduction

Nicotine is a very toxic alkaloid that acts as a stimulant for the central nervous system but is also used as a pesticide. It can be extracted from tobacco, containing amounts of 0.5–8.0% by weight. Recipes for its extraction from tobacco are easily found on the Internet [1,2].

Nicotine can be absorbed following inhalation, ingestion or dermal contact. It is biotransformed to inactive metabolites such as cotinine, primarily by the liver. About 5% of the absorbed nicotine are not modified and excreted in urine within 24 h [3,4].

Nicotine binds to nicotine-acetylcholine receptors and effects stimulant and depressant reactions: Low doses stimulate the neural and cardiovascular systems, whereas high doses have a depressive effect. Overdoses can depress respiration and cause death by respiratory failure [5–9]. The ingestion of 40–60 mg nicotine, corresponding to 0.5–1 mg/kg [10], is assumed to be lethal [3].

Deaths related to nicotine uptake, regardless of the absorption route, without any competing cause of death, have been previously

described in the literature [1,11–14]. Those cases refer to the intentional ingestion of nicotine-containing solutions [1,13,14], misuse of nicotine patches for substitution therapy with concurrent cigarette smoking [11] or an overdose through nicotine injection due to failed nicotine tests [12]. Fatal outcomes have also been described after ingestion of nicotine-like substances such as anabasine or imidacloprid [15–18]. Most cases of nicotine toxicity resulted from the oral intake of nicotine-containing mixtures, such as pesticides, and misuse of substitutive patches by children. Toxic dermal absorption has previously been described in tobacco harvesters [19,20]. A recent review of previously published fatal cases of acute nicotine poisoning was presented by Cokery et al. [1]. The victims either ingested nicotine alone [1,13] or both nicotine and alcohol [21]. The review also includes fatalities after nicotine injections [12,22].

Once the organism is used to nicotine, an interruption of the uptake evokes abstinence symptoms. Therefore, transdermal nicotine systems (nicotine patches) are widely used in substitution therapy after cessation of smoking. The absorption of nicotine through the skin is gradual and slow, without the rapid enhancement in the brain that occurs after inhalation [4]. During continuous transdermal application, with the skin acting as a reservoir, the half-life of nicotine is up to 12 h, while after injection a half-life of only 1–2 h was determined [10].

Some drugs may affect the transdermal absorption of nicotine from patches. Sympathomimetic diet pills or decongestants can decrease its penetration through the skin by vasoconstriction whereas vasodilatation induced e.g. by antihypertensive medications, nitrates [23] or alcohol can accelerate its absorption.

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Transdermal application may result in toxic concentrations of nicotine. Three fatalities relating to the misuse/abuse of commercial nicotine patches are described in the literature [4,11,24]:

- A 31-year-old woman committed suicide by fixing 18 commercial transdermal nicotine patches (7 mg dose) to various parts of her body before pulling a plastic bag over her nose and mouth [4]. Death was attributed to asphyxia. Nicotine and cotinine concentrations were measured in different samples including cardiac blood, femoral vein blood and urine. The nicotine concentration in femoral blood was 460 ng/ml. In comparison to this, the authors determined a plasma nicotine concentration of about 8 ng/ml after application of a single patch of 7 mg. A ratio for the whole blood and plasma concentration was not given.
- Solarino et al. [24] reported on another suicide by nicotine absorption following dermal exposure as well as ingestion of nicotine, tramadol, diphenhydramine, and paracetamol. In that case, intoxication was mainly due to tramadol, which was measured in concentrations more than twenty times above the therapeutic limit. The peripheral nicotine blood concentration was 600 ng/ml. Diphenhydramine, a substance with sedative and antiemetic properties, was within the therapeutic range.
- Sanchez et al. [11] published a case of nicotine poisoning in a 32-year-old man. Only one nicotine transdermal patch was found on his body, when the medical staff started resuscitation. According to his relatives the man had abused patches while continuing his smoking habit. The man died four days after the incident in an intensive care unit; during the survival time, blood samples were taken and analyzed for nicotine. The plasma nicotine concentrations were extremely high.

Nicotine intoxications after dermal application without fatal outcome are also described in the literature [10,23,25–28]: an 8-year-old child was exposed to a life-threatening dose of nicotine due to a homemade remedy that is traditionally used for eczema in Bangladesh [25]. Blood analysis, 12 h after the onset of symptoms, showed a plasma nicotine concentration of 89 ng/ml. Although this value does not seem particularly high, the child showed severe symptoms.

The clinical signs of nicotine intoxication are only moderately characteristic. Among others, nicotine produces an increase of heart rate and blood pressure as well as vascular constriction. Typical symptoms are nausea, vomiting, and agitation. The condition is easily misinterpreted and related, for example, to an epileptic seizure or acute meningitis [2,25].

In the following, we present a complex suicide using homemade nicotine patches in combination with the oral application of diphenhydramine. To our knowledge, this is the first case involving non-commercial patches.

2. Case report

2.1. Case history

A 51-year-old man was found dead in his apartment after he had not been seen alive for several days. The entrance door was locked, and the blinds were closed. The man was found lying on his bed in a supine position with a blanket covering the body up to the neck. After removal of the blanket, the police found two electric cables running across the abdomen. The cables were attached to each other and knotted to the bed frame. Neither of these cables was connected to an electrical outlet. A pair of handcuffs, one cuff covered with plush, was affixed to the right wrist and to the cables (Fig. 1). The tying primarily suggested an autoerotic accident.

Once undressed, a large black plastic sheet was discovered on the abdomen, the edges of which were fixed to the skin with adhesive strips. The front sides of both thighs also showed several



Fig. 1. Handcuffs and cables at right wrist.

plasters (12 in total) of a dark brown color. Below the sheet on the abdominal skin, there were soaked compresses containing dark brown particles with a sweet tobacco smell. The same material was applied to the inner surface of the plasters on the thighs (Fig. 2). A glass containing similar brownish material was found on a table next to the body.

2.2. Autopsy findings

2.2.1. External examination

Autopsy was performed four days after discovery of the body (weight 68 kg, height 169 cm). The external examination yielded



Fig. 2. Anterior aspect of the body after removal of the clothes and the plastic sheet which originally had covered the abdomen (now positioned between trunk and left forearm). Two compresses soaked with brownish fluid have remained in place on the right abdominal wall. Initially, 12 plasters were fixed to the thighs.

resolved rigor mortis and minor signs of putrefaction. There were no injuries visible.

2.2.2. Internal examination

Autopsy did not reveal any pathology that could explain death. The inner organs showed only slight signs of putrefaction. The lungs were heavy and congested with blood. The bladder contained 350 ml urine. In the stomach, there were about 300 ml of black to dark brown liquid, mixed with small particles reminding of fine-cut tobacco and some small corny fragments. Moderate general arteriosclerosis was observed. No signs of trauma were noticeable.

2.3. Histological examination

Histological investigation confirmed moderate chronic emphysema in combination with blood congestion of the lungs and minor autolysis of the organs. Pulmonary sections were not only stained with hematoxylin-eosin and Berlin blue, but also with Fat Red 7B [29,30] in order to visualize so-called smokers cells (smokers macrophages). The substantial presence of predominantly intraalveolar macrophages containing brownish-reddish pigment inclusions corroborated the assumption that the deceased had been a heavy smoker. No siderophages could be detected in the pulmonary sections.

2.4. Toxicological analyses

Various samples (cardiac serum, peripheral serum, urine, gastric contents and a plaster removed from a thigh) were subjected to toxicological examination. Analyses were performed either with GC–MS or LC–MS/MS. The screening included 700 licit and illicit drugs and metabolites, such as analgesics, sedatives, antidepressants and other psychoactive drugs [31]. The results are indicated in Table 1.

The nicotine concentrations were in the toxic range in cardiac serum and especially in serum from a peripheral vein. Nicotine could also be detected in the gastric contents and in urine. High concentrations of its metabolite cotinine were determined in the serum samples and in urine. In addition, diphenhydramine could be identified in the body fluids. Its concentration measured in the serum from a femoral vein amounted to approx. 7600 ng/ml, so that toxic and potentially lethal effects have to be assumed [32].

The analyses also yielded a subtherapeutic serum concentration of tetrazepam. Methadone was determined in urine only.

By HS–GC–FID, ethanol was detected in peripheral venous blood in a concentration of 0.14 g/kg and in urine (0.29 g/kg).

2.5. Case synopsis

According to the autopsy findings and toxicological analyses, death was caused by a mixed intoxication with nicotine and diphenhydramine in the additional presence of a low concentration of tetrazepam. In conformity with the police investigations the fatality was categorized as suicide.

3. Discussion

Table 2 relates our toxicological results to former publications. Particular attention was paid to intoxications by transdermal application of nicotine.

The very few results brought out from previous cases allow no accurate comparison. Their analysis is also complicated by the fact that some values were determined in whole blood, while others refer to serum or plasma. No data with regard to a serum to blood ratio are available. In the current case, we speculate that the concentrations of nicotine in serum were high enough to cause toxic effects.

The concentrations measured in the present case in peripheral serum were higher than those observed in heart serum. Kemp et al. [4] found the opposite. They assumed postmortem redistribution and also took into account the localization of the patches: In their case, the patches were mostly attached to the thoracic skin. This localization can be regarded as a possible explanation for the observed inverse ratio. Furthermore, application of the patches to the thoracic skin may be accompanied by slightly faster transdermal absorption [10]. Accordingly, in the current case, the higher nicotine concentration in the peripheral venous blood may be explained by the location of the patches on both thighs and the abdomen. Further interpretation could only be confirmed by later analysis of other cases.

Due to the appearance of the stomach contents, attention was also paid to the nicotine concentration in this compartment. As shown in Table 2, the value was about 10 times higher than in serum. The morphology of the particles found in the gastric contents suggested a concomitant oral uptake of fine-cut tobacco. Altogether, the stomach contents contained only about 0.72 mg nicotine so that the oral uptake can be regarded as insignificant. Even so, the contribution of oral intake cannot be totally dismissed

Table 1
Toxicological results.

Sample type	Substance	Concentration in ng/ml	Method
Cardiac serum	Nicotine	190	GC–MS
	Cotinine	1900	GC–MS
Peripheral serum	Nicotine	310	GC–MS
	Cotinine	1600	GC–MS
	Diphenhydramine	Approx. 7600	LC–MS/MS
	Tetrazepam	82	LC–MS/MS
	Methadone	Not detected	GC–MS
Urine	Nicotine	1300	GC–MS
	Cotinine	3700	GC–MS, LC–MS/MS
	Diphenhydramine	Detected	GC–MS, LC–MS/MS
	Tetrazepam	Detected	GC–MS, LC–MS/MS
	Methadone	Detected	LC–MS/MS
Gastric content	Nicotine	2400	GC–MS
	Cotinine	Detected	GC–MS
	Diphenhydramine	Detected	GC–MS
	Tetrazepam	Detected	GC–MS
Plaster extract	Nicotine	Detected	GC–MS

Table 2

Toxicological results of the present case related with data from previously published reports. C/N, cotinine/nicotine. NA, not available.

Literature	Sample type	Nicotine (and cotinine) concentrations [ng/ml] – C/N ratio	Particularities
1. Kemp et al.	Cardiac blood Peripheral blood Urine Gastric content Vitreous Liver Brain	1400 (1300) – 0.92 460 (NA) – 2900 (7600) – 2.62 80 (20) – 0.25 270 (NA) – 2000 (3800) – 1.9 800 (900) – 1.13	18 × 7 mg/h patches, asphyxia (plastic bag)
2. Solarino et al.	Peripheral blood Urine	600 (2000) – 3.33 – (detected) –	25 × 7 mg/h patches + oral nicotine, tramadol, diphenhydramine and paracetamol intake
3. Sanchez et al.	Serum (11 h after cardiac arrest) Serum (57 h after cardiac arrest)	3700 (NA) – 1200 (NA) –	1 patch + continuous smoking
4. Davies et al.	Serum (12 h after onset of symptoms) Urine (12 h after onset of symptoms)	89 (1430) – 16.06 1120 (6960) – 6.19	Homemade paste against eczema
Presented case	Cardiac serum Peripheral serum Urine Gastric content Tape extract	190 (1900) – 10 310 (1600) – 5.16 1300 (3772) – 2.9 2400 (detected) – detected (NA) –	Plastic sheet on stomach with compresses + 12 tapes on thighs + diphenhydramine + tetrazepam

here. To the best of our knowledge, no other results of stomach content analyses are available in the pertinent literature for comparison.

The medical history of the deceased remained unknown. Although no information could be obtained whether the person was a smoker or not, histological investigations proved the presence of so-called smokers cells in the lung tissue. Smoking in adults (average of 33 cigarettes per day) has been previously found to result in serum nicotine concentrations of 10.5–50 ng/ml and cotinine concentrations between 94 and 444 ng/ml [33]. Measured peak blood concentrations, 2–8 h after application of a single nicotine patch, ranged between 3.5 and 23 ng/ml depending on the type of the transdermal nicotine system [10]. Due to the skin acting as a reservoir, nicotine may be released into the blood stream even several hours after the removal of the patch. As well, no significant metabolism is known to occur in the skin itself after dermal application of nicotine [10].

Moriya et al. measured nicotine and cotinine levels in blood and urine samples from autopsy cases [34,35]. In their first study [34], postmortem concentrations of nicotine (and cotinine) measured in smokers ranged between 4.4 and 205 ng/ml (31.3 and 938 ng/ml) in blood and between 158 and 7290 ng/ml (68.9 and 4620 ng/ml) in urine respectively. Hafezi and al. previously analyzed cotinine levels in the urine of one hundred consecutive autopsies of drug abuse victims [30]. The GS-MS results revealed urine cotinine concentrations between 732 and 8181 ng/ml. Considering these previous reports, the current results suggest that our suicide victim was a heavy smoker. Furthermore, the high amounts of both nicotine and cotinine found in blood and urine (high cotinine/nicotine ratios) indicate an acute-upon-chronic intake of nicotine, with toxic concentrations that could have played a role in the death process. High cotinine/nicotine ratios in smokers are based on the different half-lives of these two substances (nicotine from 24 to 84 min (average of 40 min), cotinine approx. 16 h) [3]. Inhalation of cigarette smoke is known to activate liver enzymes, causing enzymatic induction and a faster metabolism of nicotine. Furthermore, the increasing tolerance of smokers with regard to the nicotine effects has to be considered [10].

To the best of our knowledge, the case presented here is the first suicide with handmade nicotine patches described in the literature. Recipes for the extraction of nicotine from fine-cut tobacco can easily be found on the Internet [1,2]. However, in all previous cases with self-made nicotine extracts, the agent had been applied orally.

Diphenhydramine is used as a sedative and antihistaminic drug but also as an antiemetic. It is interesting to notice that other suicides by nicotine intoxication also involved the uptake of diphenhydramine. When taken orally, nicotine has significant emetic properties whereas the antiemetic diphenhydramine prevents vomiting. In our case, diphenhydramine was detected in a concentration explaining death by itself [32]. It remains unclear, whether the antiemetic effect of diphenhydramine was intended. Alternatively, diphenhydramine may have been chosen as a second toxic agent to ensure the fatal outcome.

The fact that the deceased was found tied at the scene pointed to an autoerotic accident at first. The literature is abundant with reports on erotic practices involving bondage [36–39], but self-tying is also seen in fictitious assaults [40] and in suicides (e.g. by hanging [41,42], drowning [43–45] and railway collision [44]).

Another issue to be considered is whether suicidal intoxication with more than one agent already justifies categorization as a planned complex suicide, as most medical laypersons have no knowledge about the pharmacological mechanisms of actions and potential interactions of the substances applied [46]. However, the situation is different if at least one of the toxic agents used is not a medical drug but a substance known as poison to the general public. In the case presented here, the non-therapeutic toxic agent nicotine was used in combination with the pharmaceutical preparation diphenhydramine. Consequently, a categorization as planned complex suicide seems justified.

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