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Suicides under the influence of synthetic cathinones

Samobójstwa pod wpływem syntetycznych katynonów

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Abstract

The increased risk of suicide in cases of use of ethyl alcohol, pharmaceutical drugs, and classic illicit drugs is well known and extensively described in the literature. However, relatively little information can be found about suicides committed under the influence of new psychoactive substances, including synthetic cathinones. This study presents a forensic toxicological analysis of suicides committed by people under the influence of synthetic cathinones. The findings collected in the case files allowed to determine the surrounding circumstances, the cause of the suicide, and the manner in which it was committed. We analysed 16 cases of suicide by persons aged 19–48 years, who were under the influence of synthetic cathinones. The vast majority (over 87%, $n = 14$) were male. The most common method of suicide in the analysed cases was hanging ($n = 12$). The co-presence of ethyl alcohol in blood was found in seven cases (the maximum concentration was 2.2 mg/mL). We concluded that in every case of death, especially in young people dying by suicide, it is reasonable to perform chemical and toxicological testing for the presence of various intoxicants other than ethyl alcohol. The results of toxicological testing may be useful not only for the judiciary but also for psychiatrists and psychologists who work with people abusing and addicted to new psychoactive substances.

Keywords: new psychoactive substances, synthetic cathinones, intentional poisoning, suicide

Streszczenie

Podwyższone ryzyko popełnienia samobójstwa w przypadkach używania alkoholu etylowego, leków czy klasycznych narkotyków jest dobrze znane i opisane w literaturze. Stosunkowo niewiele informacji można znaleźć na temat samobójstw popełnionych pod wpływem nowych substancji psychoaktywnych, w tym syntetycznych katynonów. W niniejszej pracy dokonano analizy toksykologiczno-sądowej przypadków samobójstw popełnionych przez osoby będące pod wpływem syntetycznych katynonów. Zebrane w aktach sprawy ustalenia pozwoliły na poznanie okoliczności towarzyszących, ocenę przyczyny samobójstwa oraz sposobu jego dokonania. Analizowano 16 przypadków samobójstw osób w wieku 19–48 lat znajdujących się pod wpływem syntetycznych katynonów. Zdecydowana większość (ponad 87%, $n = 14$) to mężczyźni. Najpowszechniejszą metodą dokonania samobójstwa w analizowanych przypadkach było powieszenie ($n = 12$). Współobecność alkoholu etylowego we krwi stwierdzono w 7 przypadkach (maksymalne stężenie wynosiło 2,2 mg/ml). Z naszych badań wynika, że zasadne jest podejmowanie badań chemiczno-toksykologicznych na obecność różnych środków odurzających – innych niż alkohol etylowy – w każdym przypadku zgonu, zwłaszcza młodych ludzi w wyniku działania samobójczego. Wyniki analiz toksykologicznych mogą być przydatne nie tylko dla wymiaru sprawiedliwości, ale także psychiatrów i psychologów, którzy pracują z osobami nadużywającymi i uzależnionymi od nowych substancji psychoaktywnych.

Słowa kluczowe: nowe substancje psychoaktywne, syntetyczne katynony, zatrucie zamierzone, samobójstwo

INTRODUCTION

Suicide is a major public health problem worldwide. According to the World Health Organization (WHO), globally about 700,000 people die by suicide each year (World Health Organization, 2021), and it is estimated that the incidence of suicide attempts is even 10–20 times higher (World Health Organization, 2009). In 2019, more than one in every 100 deaths (1.3%) was due to suicide. More than half of global suicides (58%) occurred in individuals under 50 years of age. Most adolescents who died by suicide (88%) were from low- and middle-income countries. Suicide was the fourth leading cause of death in young people aged 15–29 for both sexes. A prior suicide attempt is the most important risk factor for suicide in the general population. It is estimated that about 20% of suicides worldwide are due to pesticide poisoning. Most of them occur in rural agricultural areas in low- and middle-income countries. Other common methods of suicide worldwide include hanging and the use of firearms (World Health Organization, 2021). The latest information published by the General Police Headquarters of Poland (Komenda Główna Policji, KGP) shows that in recent years the number of fatal suicides in Poland has exceeded 5,000 and stayed at a similar level (5,276 deaths in 2017; 5,182 in 2018; 5,255 in 2019; and 5,165 in 2020). Men commit suicide five times more frequently than women. In recent years, hanging has been by far the most common method of taking one's own life (over 4,000 cases). Statistics show that, in terms of the number of fatalities, it is followed by jumping from heights and in front of moving vehicles. In 2020, the greatest number of suicides in Poland was committed by people aged 60–64 (524 cases). Only one case was reported in the 7–12 age group, 106 cases involved the 13–18 age group, and 143 cases occurred in the over-85 age group. According to the KGP data, the total number of suicide attempts (including non-fatal ones) increased in Poland from 11,139 in 2017 to 12,013 in 2020 (Komenda Główna Policji, 2020).

Suicidal thoughts and tendencies are conditioned by many factors including individual psychological factors, social factors, and interpersonal relationships. The increased risk of suicide in cases of use of ethyl alcohol, pharmaceutical drugs, and classic drugs of abuse is well known and has already been widely described in the literature (Klimkiewicz et al., 2011; Orpana et al., 2021). Relatively little information, however, can be found on suicides committed under the influence of new psychoactive substances (NPSs), including synthetic cathinones (SCs) despite the fact that harmful use of psychoactive substances is considered to be one of the major risk factors for suicide (Kraemer et al., 2019; Marinetti and Antonides, 2013). The occurrence of mental disorders related to the use of psychoactive substances increases the risk of committing suicide two- or even threefold (Jarema, 2018). In a state of bliss under the influence of drugs, the user experiences visions and hallucinations that may distort their auto- and allopsychic

orientation. In recent years, KGP has provided statistical data on the use of so-called “legal highs” by people who attempted suicide: there were 31 such cases in 2017, 21 cases in 2018, 22 cases in 2019, and 15 cases in 2020 (Komenda Główna Policji, 2020). Unfortunately, these data do not specify what type of NPS was used, but the most common products on the illicit drug market are the already-mentioned SCs and synthetic cannabinoids.

In the years 2013–2019, the Department of Forensic Medicine and Forensic Toxicology of the Medical University of Silesia (Śląski Uniwersytet Medyczny w Katowicach, SUM) in Katowice reported at least several dozen cases of suicide by young people under the influence of NPSs. The aim of this study was to present cases of suicide committed by people under the influence of SCs along with the concentrations of these xenobiotics in the biological material. Based on the findings collected in the case reports, we were able to establish the circumstances surrounding the death and assess the cause of the suicide and the manner of its execution.

MATERIALS AND METHODS

The suicide cases investigated at the Department of Forensic Medicine and Forensic Toxicology of SUM in Katowice between 2013 and 2019 were analysed for the presence of SCs in the biological material secured during autopsy.

Certified reference materials and reagents

Certified reference materials were purchased from Cayman Chemical Company (Ann Arbor, MI, USA), Cerilliant (Round Rock, TX, USA), LGC Standards (Dziekanów Leśny, Poland), and Lipomed (Arlesheim, Switzerland). Other chemical reagents used in the analyses were of sufficient purity (HPLC – high-performance liquid chromatography – grade).

Biological materials – samples

The subject of the study were biological materials (including blood, urine, and vitreous body samples as well as liver and kidney biopsies) collected at the local unit during medico-legal autopsies in the years 2013–2019 and delivered to the Department of Forensic Medicine and Forensic Toxicology of SUM in Katowice. In each case, the above department received the decision of the police or the prosecutor's office to perform toxicological analysis for the presence of psychoactive substances. Most of the analysed cases concerned intoxication, including fatal intoxication, suicide, driving under the influence of psychoactive substances, and possession of drugs. The obtained results of toxicological analyses were compared with the data from protocols of biological material collection and data from prosecutor's and court files of completed cases. The case files were each time made available for analysis with the consent of the competent prosecutor's office or court.

Case number	Substance and concentrations in blood, urine, and vitreous humour [ng/mL]; in liver and kidney [ng/g]	Sex/age	Case description	Other drugs and concentrations in blood and urine [ng/mL], in alcohol [mg/mL]
1	4-MEC: 402 B, 1,030 VH	M/NA	Fall from height. The man was treated psychiatrically and for addiction, he took drugs	
2	Pentedrone: 213 B, 333 K	M/39	Hanging. He was addicted to drugs	Alcohol: 1.1 B
3	Pentedrone: 581 B, 9,712 U	M/35	Hanging	
4	Pentedrone: 238 B	F/NA	Hanging. She was addicted to drugs	
5	Pentedrone: 2,304 B, 7,798 U UR-144: 1.4 B	M/NA	Hanging. He was addicted to drugs. Before the incident, he smoked a joint and drank beer. He was agitated and aggressive	Alcohol: 0.4 B, 1.3 U
6	3-MMC: 1,811 B, 82 U	M/32	Hanging. He was addicted to drugs	Alcohol: 0.7 B, 0.6 U
7	α -PVP: 74 B, 1,670 U	M/37	Hanging	Amphetamine: 100 B, 650 U
8	α -PVP: 1,382 B, 1,010 VH	M/19	Hanging. The man allegedly took legal highs; there was white powder in the flat; he showed behavioural problems and was consulted in hospital the day before he hanged himself. In the past, the man was hospitalised for 10 days in a psychiatric hospital; he suffered from psychosis after taking psychoactive substances; he allegedly expressed suicidal intentions and took haloperidol and diazepam	
9	α -PVP: 84 B	M/35	Hanging with self-binding of the hands. The man did not receive treatment and did not abuse alcohol but had a history of drug problems. According to his family, he struggled with lack of work, family disagreements, and had a sense of being unappreciated by others	
10	α -PVP: 692 B	M/20	The man self-inflicted cutting wounds, damaging blood vessels. He left a death note	
11	N-ethylpentadone: 148 B	M/25	The man was struck by a train – he was walking along the tracks towards the train and did not respond to the sound signals. The man was treated for addiction; he escaped from his last rehab facility and was addicted to alcohol and legal highs	Alcohol: 2.2 B
12	4-CMC: 381 B, 632 U	M/23	Hanging. The man was addicted to alcohol and drugs. In the past, he declared his intention to commit suicide. Shortly before the suicide, he began vaping an e-cigarette, snorted white powder (traces of powder were found in his nose), appeared intoxicated, laughed for no reason, spoke little and nonsensically, vomited, and choked. In the morning, his friends found his body – his face was blue and there was a reddish yellow substance coming out of his mouth	THCCOOH: 15.1 B, 24.8 U, quetiapine: 70 B, 170 U, alcohol: 0.5 B
13	4-CMC: 112 B, 499 U	M/19	Hanging on the handle of a balcony window with shoelaces. The man was not treated psychiatrically or for addiction; according to his friends, he took drugs	
14	4-MEAP: 10 B, 122 U	M/48	Hanging	Alcohol: 0.4 B, 0.6 U
15	3,4-MDPPH: 70 B, 53 L, 112 K	F/36	Hanging on the door handle in a flat. The woman was addicted to alcohol and drugs. Before the incident, she hallucinated and was delusional and hyperactive	Alcohol: 2.2 B
16	3,4-MDPPH: 374 B, 1622 U	M/NA	Suicide – intentional poisoning by exhaust fumes	HbCO – 93%

M – male; F – female; NA – not available; B – blood; K – kidney; U – urine; VH – vitreous humour; L – liver; THCCOOH – 11-nor-9-carboxy-tetrahydrocannabinol; HbCO – carboxyhaemoglobin.

Tab. 1. Case reports and concentrations of synthetic cathinones (SCs) and other detected psychoactive substances in suicide cases with at least one identified SC (16 cases)

Analytical methods

The biological materials were analysed with preliminary methods (enzyme-linked immunosorbent assay, ELISA) and confirmatory reference methods (chromatography). The analytes were isolated from the matrix by acetonitrile precipitation as well as extraction with ethyl acetate. The primary method used in the study for the identification and quantification of NPSs, including SCs, was liquid chromatography coupled with a triple quadrupole mass spectrometer (LC-QqQ-MS) – Thermo

Scientific TSQ Quantum Access MAX. The analytes were separated in a Thermo Scientific C18 column (150 × 2.1 mm ID, 5 µm). The mobile phase was fed into the column in gradient mode in the form of a mixture of 0.2% formic acid solution in water (v/v) and 0.2% formic acid solution in acetonitrile (v/v). The mass spectrometer was operated in the positive ion detection mode using full scan acquisition and multiple reaction monitoring (MRM). The exact test procedure was described in a study detailing two cases of poisoning with an SC called PV8 (Pieprzyca et al., 2018).

Substance [number of identifications]	Concentration range [ng/mL]	Mean concentration [ng/mL]	Median concentration [ng/mL]
α -PVP [4]	74–1,382	558	388
3,4-MDPHP [2]	70–374	222	222
4-CMC [2]	112–381	246.5	246.5
Pentedrone [4]	213–2,304	834	409.5
4-MEAP [1]	10	-	-
3-MMC [1]	1,811	-	-
4-MEC [1]	402	-	-
<i>N</i> -ethylpentedrone [1]	148	-	-

Tab. 2. SC concentrations in the blood of suicide victims (16 cases)

RESULTS

The conducted tests revealed 16 cases of suicide by people under the influence of substances classified as SCs. They were mostly young people, aged 19–48 years, with a mean age of 30.66 and a median age of 33.5 years. In four cases, the user's age was unknown. The vast majority (over 87%, 14 cases) of SC users were male.

The most common method of suicide in the analysed cases was hanging ($n = 12$). There was also a case of a fall from height, a case of self-cutting and exsanguination, and a case of poisoning by exhaust fumes. In the analysed cases, the autopsy material revealed the presence of the following SCs (number of determinations in brackets): 4-methylethcathinone (4MEC) (1), pentedrone (4), 3-methylmethcathinone (3-MMC) (1), α -pyrrolidinopentiophenone (α -PVP) (4), α -ethylaminopentiophenone (*N*-ethylpentedrone) (1), 4-chloromethcathinone (4-CMC) (2), 4-methyl- α -ethylaminopentiophenone (4-MEAP) (1), and 3,4-methylenedioxy- α -pyrrolidinohexanophenone (3,4-MDPHP) (2). Detailed information from the case files of each case and the determined concentrations of the detected substances are shown in Tab. 1.

The determined blood concentration ranges of SCs are shown in Tab. 2.

The co-presence of ethyl alcohol in blood was found in seven cases (the maximum concentration was 2.2 mg/mL). In one case, amphetamine was found alongside α -PVP at a concentration of 100 ng/mL in blood and 650 ng/mL in urine (case No. 7), and in another case, synthetic cannabinoid UR-144 was found alongside pentedrone and ethyl alcohol at 1.4 ng/mL (case No. 5). In most cases, the suicide victims were addicted to drugs.

DISCUSSION

SCs are a group of psychostimulants that mimic the effects of amphetamine, cocaine, or ecstasy (MDMA). They are analogues of cathinone, naturally found in the leaves of the khat plant (*Catha edulis*). Although SCs appeared on the market relatively recently, they have become popular over the past decade, mainly due to their legality, low price, and limited detectability by rapid drug testing (Zawilska and Wojcieszak, 2013).

The effects of SCs are substance specific and may resemble those of cocaine, amphetamine, or MDMA, but are shorter lasting, which often prompts the user to take further doses. In general, it can be said that SC use induces signs and symptoms of central nervous system (CNS) stimulation in the form of psychomotor agitation, increased alertness, surge of energy, euphoria, excitement, increased empathy, ease of interpersonal communication, increased sensory perception, moderate sexual arousal, disturbed perception, and insomnia (European Monitoring Centre for Drugs and Drug Addiction, 2015). Users of SCs meet in online forums to discuss the dosage, effects, and ways of acquiring such substances. SCs exert their psychotropic effect by increasing the content of monoamines in the synaptic cleft, which is achieved in two ways: by blocking the reuptake of monoamines and by stimulating the release of noradrenaline, dopamine, and serotonin from the presynaptic neurons (Liechti, 2015). Studies using animal models and clinical observations indicate that SCs may induce physical and psychological dependence (De-Giorgio et al., 2019). The spectrum of adverse effects caused by SCs is broad and includes the following signs and symptoms: cardiovascular, mainly due to the sympathomimetic activity (tachycardia, palpitations, chest pain, hypertension, myocarditis, cardiac arrest); haematological (disseminated intravascular coagulation, thrombocytopenia, anaemia); neurological (insomnia, sleep disorders, nightmares, tremors, convulsions, hyperthermia, mydriasis, visual disturbances, paraesthesias, bruxism, involuntary limb movements, headaches, dizziness); and gastrointestinal (nausea, vomiting, abdominal pain) as well as other possible side effects (excessive sweating, hyponatremia, hyperkalaemia, hyperuricaemia, elevated creatinine and creatine kinase levels, metabolic acidosis, dry mouth, and weight loss with prolonged use) (Adebamiro and Perazella, 2012; Logan et al., 2017; Penders et al., 2012).

SCs exert a strong effect on the CNS and can therefore cause both acute and chronic mental disorders. The observations to date show that in cases of suicide committed under the influence of SCs, cognitive, mental, and perceptual signs and symptoms may be of greatest importance (Więckiewicz et al., 2020; Zawilska and Wojcieszak, 2013). Their detailed breakdown is shown in Tab. 3.

Cognitive	Mental	Perceptual
Disorientation Long-term cognitive decline Decrease in mental capacity Problems with associating names, places, and times	Irritability Aggressiveness Hyperactivity Anxiety Panic attacks Lack of motivation Social withdrawal Depression Suicidal thoughts	Paranoid delusions Auditory and visual hallucinations

Tab. 3. Cognitive, mental, and perceptual signs and symptoms induced by SCs

With chronic use, most SCs can lead to the development of a variety of psychiatric disorders that can manifest themselves both during the period of use and after withdrawal of these substances. Synthetic psychostimulants can cause, among others, psychotic disorders (clinical picture similar to schizophrenia and delusional disorders), affective and anxiety disorders, sleep disorders, delirium, and sexual dysfunctions (Schifano et al., 2017). SCs can also induce persistent mood disorders involving a prolonged lack of motivation and willingness to act accompanied by depressed mood as well as suicidal thoughts and tendencies (Schifano et al., 2020).

Our research revealed 16 cases of suicide of people who were under the influence of SCs at the time of death. The most common method of suicide in the analysed cases was hanging. There was also a case of a fall from height, a case of self-cutting and exsanguination, and a case of poisoning by exhaust fumes. In the analysed cases, the autopsy material revealed the presence of the following SCs: 4MEC, pentedrone, 3-MMC, α -PVP, *N*-ethylpentedrone, 4-CMC, 4-MEAP, and 3,4-MDPHP. Tab. 4 presents a comparison of SC concentrations determined in our research with the ranges published recently in a study by Adamowicz (2021).

In the analysed 16 cases, the concentration ranges of five SCs (3,4-MDPHP, 4-CMC, 4-MEAP, 3-MMC, 4-MEC) were high compared to the literature data and were within the lethal concentration ranges collected by Adamowicz (2021). The determined concentrations for α -PVP and pentedrone were within the concentration ranges recorded in both non-fatal and fatal cases. So far, α -PVP and

pentedrone have been among the most popular SCs, and the number of reported cases of use of these two substances is relatively high compared with other SCs (Adamowicz et al., 2016; Sykutera et al., 2015).

Suicidal behaviour is influenced by many interacting factors. Most often, it is impossible to single out one cause of suicide; instead, multiple factors should be considered. In the cases analysed above, people who committed suicide under the influence of SCs had problems with work and family disagreements, felt unappreciated, were irritable and hyperactive, suffered from hallucinations and delusions, and expressed a desire to die before taking their life. It should be noted that in cases of suicide, SC use was not the direct cause of death. On the one hand, users may have consumed SCs with the intention of committing suicide, but on the other hand they may have committed suicide due to the psychoactive effects of SCs, e.g. while being in a state of drug-induced narcosis.

Our findings suggest that a full toxicological investigation (including physical evidence discovered with the deceased, which may prove invaluable for further investigation) should be considered in each case of suicide by a young person. The results of toxicological testing may be useful not only for the judiciary but also for psychiatrists and psychologists who work with people abusing and addicted to NPSs.

CONCLUSIONS

The presence of NPSs on the illicit drug market, with little known or even unknown properties, poses a challenge

Substance	Blood concentration [ng/mL] in our cases	Blood-plasma/serum concentration [ng/mL] in non-fatal cases reported by Adamowicz	Blood-plasma/serum concentration [ng/mL] in fatal cases reported by Adamowicz
α -PVP	74–1,382	<1–606	1–>20,000
3,4-MDPHP	70–374	-	154
4-CMC	112– 381	1–75	<1–1,870
Pentedrone	213–2,304	<1–460	<5–8,794
4-MEAP	10	-	2–4
3-MMC	1811	<1–1,600	<1–1,600
4-MEC	402	28–353	6–17,300
<i>N</i> -ethylpentedrone	148	-	-

Tab. 4. Comparison of SC concentration ranges determined in 16 analysed suicide cases with the data presented by Adamowicz (2021)

not only to law enforcement services, but also to clinicians (psychiatrists, clinical toxicologists), and forensic and toxicology experts.

The use of and dependence on NPSs, including SCs, is a significant risk factor for suicidal behaviour. SC addicts are often characterised by the co-occurrence of a number of other suicide risk factors. In addition to depressive disorders, such people often also have serious social and financial problems. Individuals prone to impulsive behaviour are particularly vulnerable to the use and abuse of psychoactive substances.

The extension of the chemical and toxicological analysis to psychoactive substances other than ethyl alcohol, including NPSs, allowed to explain important circumstances surrounding the deaths of young people by suicide. Undertaking chemical and toxicological tests for the presence of various intoxicants other than ethyl alcohol in each case of death, especially in young people dying by suicide, is therefore fully justified.

Ethical approval

The research was commissioned by the Prosecutor's Office, and therefore no ethical approval was required.

Conflict of interest

The authors declare that they have no conflict of interest.

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