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New psychoactive substances abuse and its clinical consequences - the case report

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Abstract
Introduction: The meteoric rise of new psychoactive substances' use has been a public health problem for at least few years. Their presence was noticed by EU authorities around 2005. First cases of NPS poisoning in Poland appeared shortly thereafter, in 2008. Due to great variety of used substances and lack of information about them, precise diagnosis and targeted treatment remain a significant problem. Hereby, we present a patient with multi-drug poisoning related to NPS abuse and discuss new psychoactive substances that are often found in such cases.
Aim of study: To discuss most common new psychoactive substances and their health effects on the basis of the case report
Results: A 28-year old patient was admitted to the Department of Toxicology and Cardiology with symptoms suggesting acute intoxication with psychoactive substances. The patient had a history of drug abuse. A few pouches containing unidentified psychoactive substances were found near the patient. On admission, his condition was serious- he was unconscious and required mechanical ventilation. Tachycardia and aspiration pneumonia were present as well.The applied therapy focused on restoring acid- base homeostasis, electrolyte balance and mitigating toxic influence of detected drugs, with preventive antibiotic administration used as well. His general and psychological condition improved with treatment, and he was discharged from the department after ten days, with continuation of the therapy in ambulatory setting.
Conclusions: An increasing amount of patients present cases of polysubstance abuse, whose treatment may prove especially difficult. Such cases require extensive therapy to prevent debilitating complications. A focus on drug regulation and patient education could diminish the number of such cases in the future.

Keywords: new psychoactive substances; drug abuse; poisoning

Introduction

From at least a few years, public health officials and media warn about two related phenomena: the rise of new psychoactive substances and prescription drugs abuse epidemic [1],[2]. While a flood of new, synthetic drugs proved to be challenging for regulators [3] , abuse of prescription drugs increased at the same time as well [4],[5],[6] ,[7]. In 2005, Council of Europe defined new psychoactive substance (NPS) as 'a new narcotic or psychotropic drug, in pure form or in preparation, that is not controlled by the United Nations drug conventions, but which may pose a public health threat comparable to that posed by substances listed in these conventions' [8]. First cases of NPS poisoning in Poland appeared shortly thereafter, in 2008. The annual amount of acute intoxication’ cases grew through 2015, after which it stabilized on a lower level. Due to great variety of used substances and lack of information about them, precise diagnosis and targeted treatment remain a significant problem [9]. UN report from 2013 underlines the difficulties in regulation of designer drugs, with producers often one step ahead of monitoring agencies [10]. Some researchers suggested new regulatory approaches to control this market, including a shift from regulating specific substances to broad standards on NPS use, monitored and enforced with support of non-government sector [11]. Hereby, we present a patient with multi-drug poisoning related to NPS abuse.

Case description

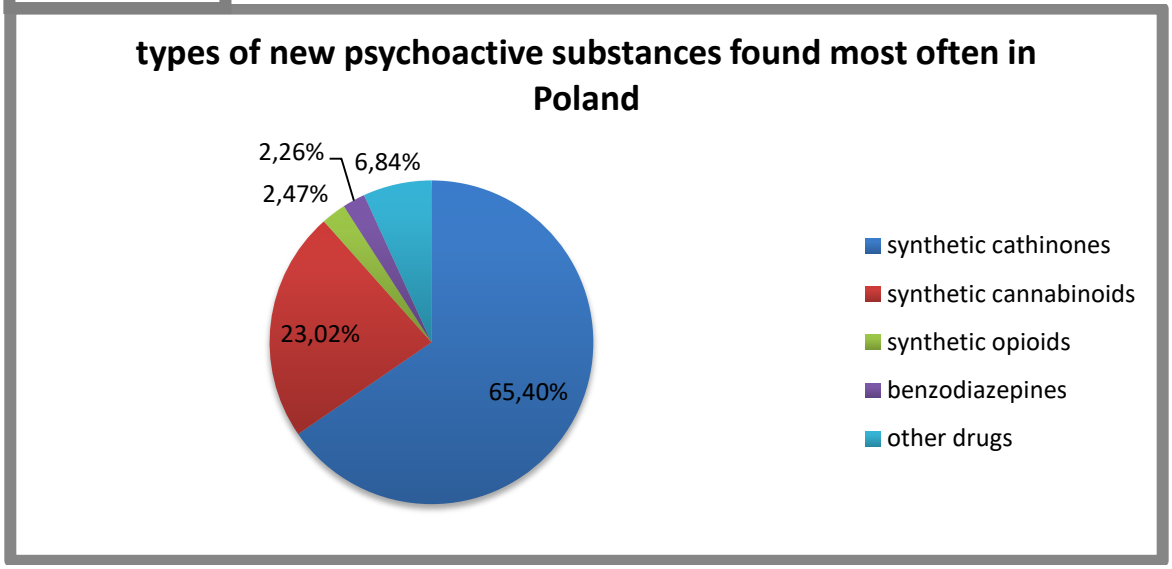
A 28-year old patient was admitted to the Department of Toxicology and Cardiology with symptoms suggesting acute intoxication with psychoactive substances of some kind. The patient had a history of drug abuse. The patient’s parents (who called an ambulance) reported

that he has admitted to using unspecified drugs before losing consciousness and collapsing on the floor. The emergency team found a few pouches with tablets and herbs in the patient's vicinity, carrying paper labels like "4F-MPH" (methylphenidate derivative), "Bromazepam" and "Flunitrazolam" (benzodiazepines), "mild cuddler" (an NPS containing probably synthetic cannabinoids). The patient had to be intubated during transport to the hospital because of progressive respiratory failure and vomiting. On admission, the patient's condition was serious- he was unconscious and required mechanical ventilation, which was continued for three days. Tachycardia was also present at 120 beats per minute. Blood pressure was within reference range at 120/80 mmHg. The chest x-ray revealed inflammatory changes in the lower lobe of the right lung- deemed to be an aspiration pneumonia, in typical localization. Computer tomography of the head showed large perivascular space in lentiform nucleus, possibly requiring differential diagnosis with post- stroke lesion. Initially, the patient had mild acidosis and anemia, although both parameters improved with treatment. Rhabdomyolysis, possibly related to oxygen deficiency or effects of ingested substances, was noticed as well. Leukocytosis, high levels of C-reactive protein (from 25 to 39 mg/l) and creatine kinase (ca 750 to 3918 U/l) were present throughout the patient's hospital stay, but, in time, they subsided a little as well. Toxicological examination revealed traces of methylphenidate and methamphetamine. The patient was screened for benzodiazepines presence in blood serum, with positive outcome at 140,5 ng/mL (cutoff value 50 ng/mL). The applied therapy focused on restoring acid- base homeostasis, electrolyte balance and mitigating toxic influence of detected drugs, with preventive antibiotic administration (clindamycin) also used. After assisted ventilation ceased to be needed, sputum culture was set up. It revealed *Klebsiella pneumoniae* lung infection, which was successfully treated with antibiotics. The consolidation visible in right lower lobe receded after lung infection treatment. The patient had been consulted by a neurologist and a psychiatrist. On the first day of hospitalization, our patient was partially disoriented, had formal thought disorders, inappropriate affect and cenesthetic hallucinations (he asked to be relieved of "electric shocks"); he was treated with tranquilizer. The medical history of our patient showed patterns of substance abuse since at least 10 years. His general and psychological condition improved with treatment, and he was discharged from the department after ten days, with continuation of the therapy in ambulatory setting.

Discussion

Severe acute poisonings, similar to those described in this case, are encountered more often in recent years. Although we are past the 2015 peak in NPS-related emergencies, they have become part of drug abuse reality [9]. The greatest therapeutic problems are: the sheer speed at which new substances are designed and produced, and scarce information about what was actually ingested by the patient [9,10]. Quite often, the patient neither knows nor cares what drugs he actually uses [12, 13]. Below we present a short characteristic of the most common substances encountered in designer drugs in 2018, along with their possible effects and methods of treatment. "New drugs" usually contain substances from the following groups: synthetic cathinones, synthetic cannabinoids, synthetic opioids and benzodiazepines [chart 1]. Out of them, synthetic cathinones and cannabinoids are by far the most common, accounting for 65,4% and 23,02% of all substances found in NPS, respectively [13].

Chart 1 [13]



Synthetic cathinones are stimulants, with mode of action and effects on organism broadly similar to cocaine or amphetamine [13]. They enhance neurotransmission in dopaminergic and adrenergic pathways, usually by noradrenaline and dopamine reuptake inhibition. Some of them affect serotonin levels as well, similarly to MDMA (the serotoninergic mechanism is also responsible for some of the most serious poisoning' symptoms) [9]. Generally, their effects include stimulation, euphoria or mood lift, and increased cardiovascular activity. Hallucinations are also observed in some cases. Other effects are presented in Table 1. The most popular substances from this group are: 4-CEC, HEX-EN, N- propylpentedrone, N-ethylpentylone, NEP, 4-CMC, α-PHiP, 4-CL-α-PVP. 4F- MPH, the substance our patient probably ingested, is one of new stimulant drugs as well. Negative symptoms in acute stimulant poisoning manifest differently depending on whether serotonergic or dopaminergic system is more affected. If the drug is predominantly dopaminergic, most symptoms will be manifestation of increased sympathetic system activation- arousal, aggression, increased heart rate and hypertension .

If serotonergic system is the one disrupted, hallucinations and disorientation will be observed, alongside myoclonic twitches and jerks and other symptoms of nervous system impairment. Mixed symptoms from both toxidromes are very common [9]. The influence of new stimulants on various organs is provided in detail in Table 1.

Table 1 [9]

Affected system	Most common symptoms
mental state	arousal, aggression, delusions, hallucinations, anxiety, suicidal thoughts, depression, attention and memory deficits, insomnia
nervous system	dyskinesia, myoclonus, convulsions, nystagmus
circulatory	tachycardia, heart arrhythmias, chest pains, heightened blood pressure
respiratory	tachypnoe, dyspnea, cough
gastrointestinal tract	nausea, vomiting
integumentary system	aching muscles and joints, muscle spasms
other	hyperhidrosis, hipertermia, priapism

Somatic symptoms usually recede after a few hours, but psychological problems can persist for weeks or months [9]. All of the aforementioned new stimulants/cathinones precipitate described symptoms to some degree, but some of them have especially dangerous side effects, for example: 4-CEC and 4-CMC can cause renal failure, NEP and 4-CMC can induce asystolia and HEX-EN is associated with cases of respiratory failure [13].

Treatment of acute stimulant' poisoning should include meticulous monitoring of patient's condition and stabilizing blood pressure, heart rate, respiratory function, body temperature, acid-base homeostasis and, obviously, his mental state. Patients can be given benzodiazepines if their arousal or aggression preclude therapeutic action. They are often dehydrated and require iv infusion of some sort. If rhabdomyolysis is present as well, dialysis should be performed to avoid renal insufficiency development [9].

Synthetic cannabinoids, the second most common drug family found in NPS, are derivatives or analogues of tetrahydrocannabinol (THC), the narcotic substance found in marijuana. This is one of the most prolific group of NPS, with over 150 identified substances and new ones popping up every year [9]. All of these substances have more pronounced effects than marijuana, mainly because they are full agonists of cannabinoid receptors, unlike THC which acts partially agonistic to C1/C2 receptor. Most of these substances are deemed to have stronger addiction potential than marijuana, compounded by mental health issues that develop in some long- term users.

Reported results of their ingestion include feeling relaxed, more open, energized, euphoric. But there are adverse effects as well- anxiety, nausea, vomiting, irritability and aggression, distorted perception, delusions or memory disorders. They can cause acute psychosis and permanent brain damage. Hallucinations are five times more likely to develop after using synthetic cannabinoids compared to plain cannabis. This is caused by the fact that some of them (mainly chemicals from indole group) strongly activate serotonergic receptors, and can induce hallucinations or serotonergic toxidrome. Detailed description of synthetic cannabinoid poisoning symptoms can be found in Table 2.

Table 2 [9]

Affected system	Encountered symptoms
mental state	extreme arousal, anxiety, sedation, psychosis, cognitive impairment
nervous system	convulsions, ataxia, muscle twitching, coma, respiratory depression, tinnitus
circulatory system	increased heart rate and blood pressure, heart arrhythmia, orthostatic hypotension, myocardial ischemia
respiratory system	dyspnea, cough
urogenital system	anuria, oliguria, acute kidney injury
gastrointestinal tract	stomachache, nausea, vomiting
integumentary system	rhabdomyolysis, muscle pain
other	hypokalemia, xerostomia, xerophthalmia

There are many difficulties in treatment process. First, synthetic cannabinoids are not detectable by standard tests for THC traces in urine, which can contribute to diagnostic problems with poisoned patients. The leading varieties found in Poland in 2018 are 5F-ADB and FUB-AMB [13]. Most of the THC analogues sold contain other drugs and impurities, which may affect clinical presentation significantly. In large proportion of patients, at least some of mentioned symptoms will be present. Therapeutic process should focus on monitoring and stabilizing respiratory and cardiovascular system. Measuring body temperature is very important because of high hyperthermia risk. Benzodiazepines and iv fluids should be administered as well. Diuresis may be also needed, especially if rhabdomyolysis develops [9].

Conclusions

An increasing amount of patients present cases of polysubstance abuse, whose treatment may prove especially difficult. Such cases require extensive therapy to prevent debilitating complications. The explosion in manufacture and use of various new psychoactive substances after 2008 has contributed significantly to this phenomenon and strained international drug control system. Novel regulatory approaches, like generic regulations and temporary bans on NPS use, could prove helpful [10]. A constant focus on education and safety is needed as well [12].

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