CLINICAL PRACTICE

*Clinical Vignettes***Emergence of New Classes of Recreational Drugs—Synthetic Cannabinoids and Cathinones***Vikas Khullar, MD, Ankur Jain, MD, and Maryam Sattari, MD, MS*

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Designer drugs represent an increasingly popular form of recreational substance abuse, especially amongst young adults. The two classes of designer drugs that have recently risen to prominence are the synthetic cannabinoids and synthetic cathinones. These substances are not detected by conventional drug screening methods and can often be associated with serious health consequences, including seizures, renal failure and death. Thus, clinicians should be familiar with the signs, symptoms, and toxicities associated with the use of these substances, and maintain a high level of suspicion for synthetic drugs as an alternative means of “getting high.” We present a case of a 20-year-old college student who presented to the emergency department with altered mental status and severe agitation who later admitted to using bath salts. The goal of this article is to raise awareness about these new designer drugs, their clinical presentation, and management of their intoxication.

KEY WORDS: designer drugs; synthetic cathinones; bath salts; synthetic cannabinoids.

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INTRODUCTION

Drug abuse remains a major problem in the United States (U.S.) and has important potential health, social, and legal consequences.^{1,2} In recent years, many new “designer drugs” have been synthetically produced. These synthetic compounds contain modified molecular structures of illegal or controlled substances. The two classes of designer drugs that have risen to prominence are the synthetic cannabinoids and synthetic cathinones. These substances are often perceived as safe and can be purchased via the Internet, in stores specializing in tobacco or drug paraphernalia (“head” shops), convenience stores, adult book stores, gas stations,

truck stops, or from dealers. As of December 2010, 8,264 exposures to these substances were reported to U.S. Poison Centers, including their involvement in four deaths.³ These reports of overdose and adverse effects as well as their abuse potential have led to the emergency scheduling of several of these substances as Schedule I by the U.S. Drug Enforcement Agency (DEA).^{4,5} Schedule I status is reserved for substances with high abuse potential and no accepted use for medical treatments. Despite federal and state regulations to prohibit their sale and distribution, the illicit use of these drugs continues, especially amongst young adults.^{1,3} Given their increasing prevalence, healthcare providers must be familiar with these substances in order to recognize and manage the intoxication syndromes associated with them. In this article, we present a case of a 20-year-old male presenting with intoxication from bath salts and briefly discuss the background, effects, and clinical management of these designer drugs.

CASE PRESENTATION

A 20-year-old Hispanic man was brought to the Emergency Department by the police for altered mental status. Police reported that he appeared to be having hallucinations with rapid speech and threatened to use a knife to harm his girlfriend. No history could be obtained from the patient at the time of admission due to his extreme agitation. On examination, the patient was afebrile, heart rate was 120 beats per minute and blood pressure was 146/99 mmHg. He kept moving on and off the bed and was inattentive to questioning. The patient was noted to be shivering. However, the rest of the physical exam was unremarkable. Laboratory testing revealed an elevated serum creatine phosphokinase (CPK) level of 1,151 U/L (reference range 30–170 U/L). Serum toxicology screening was negative for ethanol, acetaminophen, and salicylate. Urine drug screening was positive for cannabinoids. The rest of laboratory investigations, including complete blood count, basic metabolic panel, liver function tests, and thyroid stimulating hormone (TSH) test, were normal. In the setting of elevated CPK, intravenous fluids were initiated. Lorazepam and haloperidol were administered as needed for agitation. Over

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the next 24 hours, CPK levels started to trend downwards and the patient became more alert, oriented, and less agitated. While he admitted to amphetamine use approximately eight months prior to presentation, the patient only endorsed the recent use of marijuana and inhaling bath salts. Over the next day, treatment was continued with both oral and intravenous hydration and the patient was discharged to a rehabilitation facility for further evaluation and treatment for substance abuse. Of note, the patient had had a similar prior presentation to our hospital a few months prior with similar signs and symptoms. Elevated CPK levels at that time were attributed to cocaine, but the patient denied cocaine use and his urine and serum toxicology screenings were entirely negative. Although unconfirmed, it is likely that this prior episode is the result of the use of “bath salts.”

DISCUSSION

Bath Salts

This patient’s acute psychosis is attributable to his reported ingestion of “bath salts.” Bath salts as a category have traditionally referred to substances viewed as inorganic salts such as Epsom, table salt, baking soda and Borax with cleansing properties, until 2010 when a new type of substance of abuse became available on the market under the same name.⁶ Bath salts in this category refer to synthetic cathinones, stimulants structurally related to amphetamines that have effects similar to cocaine and methamphetamine.⁷ They are also known by other street names, such as Bliss, Magic, Meow Meow, and Zoom (Table 1).^{8,9} Sold under

these intriguing names and under labels such as “not for human consumption,” “plant food,” and “insecticides,” these products have been able to avoid proper evaluation for safety by agencies such as the DEA and the U.S. Food and Drug Administration (FDA) and have become easy for young adults to obtain.¹⁰ The primary ingredients in these novel synthetic stimulants are beta-ketone amphetamine analogs, namely 3,4-methylenedioxy-*N*-methylcathinone (Mephedrone), 3,4-methylenedioxypyrovalerone (MDPV) and 4-methylmethcathinone (mephedrone).⁷ These beta-ketone amphetamine analogs are derivatives of cathinone, a naturally occurring amphetamine analog found in the “khat” plant (*Catha edulis*).¹¹ While khat chewing has been ongoing for hundreds of years in African and Arabian countries, use of its synthetic derivatives has only recently become popular in Europe and America.¹¹

Bath salts can be ingested orally, intranasally, intravenously, or rectally, and work by stimulating the release and inhibiting the reuptake of norepinephrine, serotonin, and dopamine.^{8,12} They produce stimulant effects similar to those of methamphetamine and methylene-dioxymethamphetamine (MDMA).^{12,13} The most common symptoms include hallucinations, paranoia, insomnia, agitation, and suicidal thoughts (Table 2 and 3).¹² These symptoms can mimic acute psychosis.¹³ Many associated symptoms have been reported (Table 2).¹⁰ Serious complications, such as rhabdomyolysis, renal failure, serotonin syndrome, seizure, suicides, homicides, and even death, have been associated with use of bath salts.^{6,13,14} Due to variable composition of bath salts, their pharmacokinetics are unpredictable, but psychiatric symptoms resolve in a matter of hours to days.¹⁵ The long-term use of bath salts can lead to tolerance, and abstinence is characterized by withdrawal and intense craving.¹⁰

Table 1. Street Names for Synthetic Cannabinoids and Synthetic Cathinones

Synthetic Cannabinoids (SCs)	Synthetic Cathinones
Armageddon	Arctic Blast
Aroma	Bath Salts
Aztec Gold	Bliss
Black Mamba	Blue Silk
Cloud 9	Cloud Nine
Demon	Drone
Dream	Energy-1
K2	Ivory Wave
Mad Hatter	Lunar Wave
Mr. Nice Guy	Magic
Spice	Meow Meow
	Ocean Burst
	Pure Ivory
	Purple Wave
	Red Dove
	Snow Leopard
	Stardust
	Super Coke
	Tranquility
	Vanilla Sky
	White Dove
	White Knight
	White Lightening
	Zoom

Synthetic Cannabinoids

Synthetic cannabinoids (SCs) refer to a variety of herbal/chemical mixtures that function as cannabinoid receptor agonists and mimic the effect of delta-9-tetrahydrocannabinol (THC), the active ingredient in cannabis. These substances include either THC or THC-like compounds, and were originally developed for potential medicinal purposes and to study cannabinoid receptor pharmacology.^{16–20} SC products first emerged in Europe in 2004 as “Spice,” and in the U.S. in 2008 as “K2.” Today, SC products are distributed worldwide under countless trade names, such as “Aztec Gold,” “Black Mamba,” “Cloud 9,” and “Mad Hatter” (Table 1).^{16–20} These products are generally marked with disingenuous labels such as “not for human consumption” or “herbal incense” and often packaged in colorful wrappers designed to appeal to teens, young adults, and first-time drug users.¹¹ They are often inhaled via a pipe or rolled into a cigarette.²¹

SCs appear to be three to five times more potent than traditional marijuana, and therefore are more likely to be

Table 2. Signs and Symptoms Associated with Synthetic Cannabinoids and Synthetic Cathinones

Signs and Symptoms	Synthetic Cannabinoids	Synthetic Cathinones
Psychiatric		
Addiction	+	+
Aggressive behavior	+	+
Agitation	+	+
Anxiety	+	+
Delusions		+
Dysphoria	+	
Euphoria	+	
Hallucinations	+	+
Homicides		+
Insomnia		+
Listlessness	+	
Loss of inhibitions	+	
Paranoia	+	+
Psychosis		+
Relaxation	+	
Self-mutilation		+
Suicidal thoughts/suicides		+
Withdrawal	+	+
Cardiovascular		
Cardiac arrhythmias	+	
Chest pain	+	+
Hypertension	+	+
Myocardial infarction	+	
Myocarditis		+
Palpitations	+	+
ST segment abnormalities	+	
Tachycardia	+	+
Transient ischemic events	+	
Neurologic		
Altered mental status	+	+
Dystonia	+	
Headaches		+
Inability to speak	+	
Loss of consciousness	+	
Myoclonus		+
Seizures	+	+
Transient ischemic attacks	+	
Tremors		+
Others		
Acute kidney injury	+	+
Death		+
Diaphoresis		+
Hyperthermia		+
Injected conjunctivae	+	
Mydriasis		+
Nausea	+	
Rhabdomyolysis	+	+
Serotonin syndrome	+	+

associated with sympathomimetic effects and hallucinations.^{22,23} These products also have weak monoamine oxidase inhibition activity at large doses, which results in a risk for serotonin syndrome.^{16,24} Analysis of several “K2” products has suggested the presence of high concentrations of other chemicals, including vitamin E and clenbuterol, a potent β_2 -agonist.^{16,24}

SC use causes symptoms similar to marijuana use, such as altered mental status, tachycardia, and injected conjunctivae.^{17–20,25–27} Studies in adults have linked SCs to other cardiovascular, psychiatric, and neurological signs and symptoms (Table 2).^{17–21,26–28} There has also been a case report of severe rhabdomyolysis associated with SC use.²⁹ Recently, SCs have been associated with acute kidney injury (AKI) (acute tubular injury and acute interstitial nephritis) in young, previously healthy patients without pre-

Table 3. Key Points

- The synthetic cathinones (“bath salts”) and synthetic cannabinoids represent two new classes of designer drugs.
- Neither type of drug is detected using current toxicology screening methodologies.
- Signs of synthetic cathinone ingestion include hallucinations, paranoia, insomnia, agitation and suicidal thoughts.
- Signs of synthetic cannabinoid ingestion include altered mental status, tachycardia and conjunctival injection. Renal failure may result.
- Currently no antidotes to these substances are available and initial management is supportive and symptomatic.

existing renal disease.^{30,31} While all of the reported patients with AKI eventually recovered creatinine clearance, some required short-term hemodialysis. It is unclear whether these patients are at risk for long-term kidney sequelae, despite recovery of creatinine clearance. Other serious complications associated with SC use include cardiac arrhythmias, myocardial infarction, ST segment abnormalities on electrocardiogram, and seizures.^{16,20,26,28,32–37} The cardiac arrhythmias may be attributed to the β -agonist activity of clenbuterol.^{16,24} Case reports also suggest that tachyphylaxis can develop after only a few doses, leading to an increased risk of overdose with continued use.^{16,24,25} In addition to the above immediate toxicities, there is concern over long-term SC use, as chronic use of marijuana has been associated with increased rates of schizophrenia and possible memory loss.^{38,39}

Clinical Management

While clinical testing for designer drugs is currently under development, SCs and all of the chemical substances that constitute the various bath salts are not detected by conventional toxicology screening methods.^{40,41} In fact, toxicologists are only able to identify about 40 components (e.g. MDPV, mephedrone, methylone, naphyrone, methedrone, butylone, methcathinone, and ethylone) that constitute bath salts.⁷ Clinicians should hence maintain a high level of suspicion for patients who present with signs and symptoms suggestive of drug use, but have negative drug screening. Although there is not a specific toxidrome associated with these designer drugs, intoxication should be considered in patients without a psychiatric history who present with agitation, anxiety, and psychosis.⁷ Similarly, clinicians should be aware of the potential for unusual toxicities in users of designer drugs. For example, clinicians should inquire about SC use in cases of unexplained AKI, especially in otherwise healthy young patients.³¹

Currently, no antidote exists for bath salts or SCs. Initial treatment of suspected toxicity is symptomatic and supportive, including ensuring a secure airway, hydration, sedation, and monitoring for arrhythmia, myocardial ischemia, and electrolyte abnormalities.²³ Benzodiazepines can be used as needed for hallucinations, agitation and seizures. Intravenous diphenhydramine can be used for dystonia. Antipsy-

chotic agents should be used with caution in patients with intoxication since they have the potential to lower the seizure threshold.⁴¹ Intravenous fluids and electrolytes can be used to manage volume and electrolyte disturbances. If bath salts or SCs are suspected, a urine toxicology sample should be obtained to screen for other potentially ingested substances.⁴¹ After recovery, patients should be referred for psychiatric consultation, as many have a history of polysubstance abuse.^{12,37}

CONCLUSION AND RECOMMENDATIONS

Designer drugs are produced to elicit similar effects to controlled substances while circumventing drug laws. Despite the recent DEA restrictions placed on these compounds, they remain available on the Internet and at many convenience stores. The expectation of a more intense high than that induced by street drugs, easy access, affordability, and avoidance of detection by conventional drug tests all contribute to the growing abuse of designer drugs as alternatives to street drugs such as marijuana and cocaine. Clinicians should be familiar with these substances, the various signs, symptoms, and toxicities associated with their use, and maintain a high level of suspicion for synthetic drugs as an alternative means of “getting high.” Designer drug intoxication should be considered in patients who present with mental status changes, predominant sympathomimetic features, and negative toxicology screening. Currently, no antidotes to these substances are available and initial management is supportive and symptomatic.

Conflict of Interest: The authors declare that they do not have a conflict of interest.

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