Clinical Presentation of Intoxication Due to Synthetic Cannabinoids
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Clinical Presentation of Intoxication Due to Synthetic Cannabinoids

abstract

Synthetic cannabinoids are relatively novel substances of abuse. The use of these compounds among adolescents and young adults has been increasing, making it important for pediatric providers to be familiar with the presenting signs and symptoms of intoxication. We describe three case presentations of reported synthetic cannabinoid intoxication and provide a brief discussion of these compounds. *Pediatrics* 2012;129:e1064–e1067

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KEY WORDS
cannabinoids, intoxication, substance abuse, K2, Spice

ABBREVIATIONS
CB1 and CB2—cannabinoid brain receptors 1 and 2
ED—emergency department
IV—intravenous
THC—Δ9-tetrahydrocannabinol

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Over the past several years, recreational use of synthetic cannabinoid compounds has been increasing in the United States. Until recently, these compounds (known colloquially as “K2,” “Spice,” “Aroma,” “Mr. Smiley,” “Zohai,” “Eclipse,” “Black Mamba,” “Red X Dawn,” “Blaze,” and “Dream”) were available at gas stations, convenience stores, and on the Internet. They are now classified as schedule 1 controlled substances.1

Symptoms of synthetic cannabinoid toxicity are similar to the euphoric and psychoactive effects of marijuana with additional sympathomimetic symptoms, including diaphoresis, agitation, and restlessness.2 Despite their similarity to marijuana, synthetic cannabinoids do not result in a positive toxicity screen for Δ9-tetrahydrocannabinol (THC).2–4 Recognition of the signs and symptoms of intoxication of synthetic cannabinoids and a high index of suspicion are necessary to diagnose toxicity. We report three patients with suspected synthetic cannabinoid intoxication and provide a discussion of these relatively new compounds.

PATIENT PRESENTATIONS

Case 1

A 16-year-old girl, transferred from an outside hospital for altered mental status, was refusing to speak after being out with her boyfriend. The patient presented awake with her eyes open, but was not responding to verbal or painful stimuli. The boyfriend reported that they had been smoking marijuana containing “K2.” At the outside hospital, the results of a complete blood cell count, basic metabolic panel, and head computed tomography were normal. A urine toxicology screen was positive for THC. She was transferred to our emergency department (ED) for additional management.

On arrival, the patient was noted to be catatonic. She was lying supine on the stretcher with her eyes open. Her heart rate was 105 beats per minute, her respiratory rate was 18 breaths per minute, and her blood pressure was 118/73 mm Hg. Her skin was warm, and her pupils were equal, round, and reactive to light. Her conjunctivae were normal. She was noted to have vertical nystagmus. Her oral mucosa was moist, and the results of her cardiac, abdominal, and pulmonary examinations were normal except for sinus tachycardia. Her upper extremities had normal tone, but her lower extremities were slightly rigid and flexed. She was unresponsive to verbal and painful stimuli, including a sternal rub, a supraclavicular pinch, and application of pressure to her fingernails.

She was treated with a single dose of 50 mg of intravenous (IV) diphenhydramine, after which she began to move her lips in an apparent attempt to speak. She was then treated with lorazepam 2 mg IV twice. At that point, the patient began to speak slowly. She was observed overnight, during which time she slowly recovered her motor and verbal functions. In the morning, she was able to eat and ambulate and was discharged from the hospital.

Case 2

An 18-year-old boy was brought to the ED after he was found to be agitated and diaphoretic at a party. According to emergency medical services personnel, he was in an altercation with another person at the party, after which he began to complain of headache, dizziness, and diaphoresis. In the ED, the patient was found to be uncooperative, restless, and aggressive.

On examination, his vital signs included a temperature of 37.0°C, a heart rate of 131 beats per minute, a respiratory rate of 24 breaths per minute, a blood pressure of 131/89 mm Hg, and an oxygen saturation of 98% on room air. He appeared diaphoretic and anxious. His pupils were 3 to 4 mm, equal, and sluggishly reactive. His conjunctivae were mildly injected. His mucous membranes were moist. His capillary refill time was <2 seconds. His cardiac, abdominal, and pulmonary examination results were normal, except for his sinus tachycardia. The results of a limited neurologic examination were normal. Laboratory studies, including a urine toxicology screen and serum ethanol levels, had negative results. Serum electrolytes were within normal limits.

He continued to be aggressive and agitated and was given a dose of lorazepam 2 mg IV. On repeat questioning, he reported smoking “Spice.” The patient was given 50 mg of diphenhydramine IV and was admitted to the hospital. Over the next several hours, he returned to baseline and was discharged from the hospital.

Case 3

A 16-year-old previously healthy boy presented to the ED with altered mental status. He was a resident in a group home, brought in by his case worker, when she noticed that his face seemed “frozen” and his speech was slowed. The case worker also reported that he was agitated and that he referred to things that were not actually present. The patient reported smoking “Spice” ~5 hours before. He claimed to have bought the product from a local convenience store. Upon arrival in the ED, the patient was agitated and was dysarthric with pressured speech. He appeared dys- tonic. He was alert and able to answer simple questions, but seemed confused.

His vital signs included a temperature of 37.0°C, a heart rate of 62 beats per minute, a respiratory rate of 12 breaths per minute, blood pressure 110/52 mm Hg, and oxygen saturation of 100% on room air. His conjunctivae were injected. His cardiac, pulmonary, and abdominal examinations were unremarkable. His skin was warm and dry. His upper and lower extremities were hypertonic and hyperreflexic with normal strength.

After the initial assessment, he received a normal saline bolus of 1000 mL and 4 mg of lorazepam IV. The results of his laboratory tests included a negative
urine toxicology screen and a negative expanded serum toxicology screen. He had a normal complete blood cell count and basic metabolic panel. After 3 to 4 hours he began to return to his baseline and was discharged at his baseline neurologic status.

**DISCUSSION**

The American Association of Poison Control Centers reported that 4500 calls involving synthetic cannabinoid toxicity had been received since 2010.\(^5\) Commercially available synthetic cannabinoids are a blend of plant and herbal materials including bay bean, blue lotus, lion's tail, lousewort, Indian warrior, dwarf skullcap, maconhbrava, pink lotus, marshmallow, red clover, rose, Siberian Motherwort, vanilla, and honey.\(^6\) The botanical ingredients are sprayed with an active chemical ingredient, such as JWH-018, which produces the toxicity of synthetic cannabinoids.\(^2\) The origin of this compound is traced to Dr John W. Huffman, an organic chemist at Clemson University, who synthesized analogs and metabolites of THC to study cannabinoid receptors in the mid-1990s.\(^2\) (The designation JWH refers to the initials of Dr Huffman.) Popularity of JWH-018 and some of the other compounds in its group, such as JWH-073, as drugs of abuse was bolstered by a 2008 report by the German media that this product could produce a marijuana-like high, but could not be detected on routine drug screens.\(^2\) Although quantitative assays that are capable of detecting synthetic cannabinoids are commercially available, their routine use in emergency department settings is time inefficient and cost prohibitive.

Smoking and oral ingestion are the most common routes of consumption. When inhaled, as little as 1 mg of JWH-018 can produce intoxication because of its agonist activity at the cannabinoid brain receptors, CB1 and CB2.\(^2\)\(^7\) This compound is a full agonist at the CB1 brain receptor site and therefore produces a more intense effect than THC, which is only a partial agonist.\(^7\) In addition, the affinity of JWH-018 for the CB1 receptor is five times greater than that of THC.\(^8\) The more intense inhibition of the \(\gamma\)-aminobutyric acid neurotransmission in the brain by JWH-018 compared with THC may be associated with symptoms of paranoia, agitation, anxiety, and even convulsions.\(^9\)\(^10\) Synthetic cannabinoids may also increase serotonin receptor activation and inhibit monoamine oxidase, resulting in a serotonin syndrome.\(^2\)

Formulations of synthetic cannabinoids sold to consumers may also include \(\beta_1\) agonists, which can produce associated hypertension, palpitations, tachycardia, anxiety, and irritability.\(^2\)

The dystonic reactions noted in the first and third case are unusual side effects. However, there is no consistency in the composition of K2, and therefore the side effect profile is variable. It is also possible that the dystonia observed was actually a combination of catatonia and catalepsy combined with agitation. Dystonia from synthetic cannabinoids would be a curious phenomenon, because the effects of THC on the basal ganglia actually have been studied in the treatment of dystonia.\(^12\)

No antidote is presently available for synthetic cannabinoid intoxication; however, the symptoms are usually short acting and self-limited.\(^13\)\(^14\) Treatment of agitation and restlessness with benzodiazepines is an acceptable and effective intervention.\(^13\)\(^14\) Diphenhydramine has been used with some success in reversing dystonic reaction and muscle rigidity.\(^2\) Because of the prevalence of multidrug ingestions among substance abusers, it is recommended that laboratory studies include electrolytes, electrocardiogram, urine drug screen, blood alcohol level, and serum acetaminophen/salicylate levels.\(^2\) Given the high affinity of these compounds for their receptor sites and high potency, their effective dose is small, making the amount of excreted metabolites low. This makes the detection of these compounds difficult.\(^6\)\(^15\)

The potential for multiple long-term effects, including immunomodulation and carcinogenicity, memory loss, psychiatric complications, and dependence, has been described.\(^16\) Given the sensitivity of the developing brain and association between early cannabis use and psychosis, adolescent use of these new synthetic cannabinoids is particularly concerning. Recognition of the signs and symptoms of patients with synthetic cannabinoid ingestion can help physicians who treat adolescents be better prepared to diagnose and manage patients presenting with this toxicity.

Our case series has a few limitations. In the first case, K2 use is based on an indirect statement from the patient’s boyfriend, and could not be independently verified by the patient. Synthetic cannabinoid products often contain other active and inactive ingredients, which makes identifying the specific agent as the cause of the presenting symptoms difficult. Furthermore, clinical presentation of acute ingestion is often due to multiple substance use, and is rarely a pure presentation of a single substance.

**REFERENCES**


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