Synthetic Cannabinoids

by Tyler Gilson, PharmD & UPCC Editorial Staff

Synthetic cannabinoids are not marijuana. These chemicals have a variety of serious effects as highlighted here in a few cases reported in the medical literature.

Case Examples

A 26-year-old man who had just smoked a synthetic cannabinoid, was brought to the emergency department 50 minutes after the sudden onset of right-sided weakness, dysarthria, and aphasia. A computed tomography angiogram revealed a clot in the left middle cerebral artery (MCA). The clot was lysed, and he improved clinically. His 19-year-old sister, who smoked the same product, also presented at the hospital with signs of stroke. Magnetic resonance imaging revealed a large infarct, also in the left MCA infarction, along with punctate infarcts, suggestive of an embolic event. She had a mildly elevated troponin without electrocardiogram (ECG) changes. She had persistent neurological injuries. In both siblings, there was no family history of blood clots, hypercoagulability, stroke, or stroke risk factors. Both of their ECGs and coagulation panels were negative. Both smoked spice (from the same supplier) just prior to the onset of their strokes. Toxicological analysis of serum from both patients was positive for JWH-018, a common synthetic cannabinoid, and negative for other compounds tested (AM-2201, JWH-019, JWH-073, and JWH-250).1

In another published series of patients, three separate 16-year-old boys presented with a history of 3-7 day durations of chest pain and were found to have ST segment elevation myocardial infarctions with troponins peaking at 12, 16, and 25 ng/mL. ECGs were performed in two of the boys and the results showed no myocardial injury. Cardiac catheterization performed in two of the boys showed no coronary occlusions. All three admitted to smoking spice in the days prior to presentation. Analysis of the urine of one of the boys was negative for JWH-018 and JWH-073.2

Background

Synthetic cannabinoids (Spice, K2, etc.) are designer drugs initially marketed as legal THC but in fact do not contain any THC. THC is tetrahydrocannabinol, the main psychoactive constituent of marijuana. The synthetic cannabinoids can cause effects that are very different from the usual euphoric effects of THC. Individuals using synthetic cannabinoids are typically young adults and adolescents.

What is in a Packet of Synthetic Cannabinoids?

Synthetic cannabinoids are sprayed onto the leaves of various dried herbs and plants. Producers of these products never use actual marijuana but other legal herbs. They are sold in small foil packets labeled as incense or aromatherapy and labeled “not for human consumption” in an attempt to avoid federal drug enforcement laws. They are marketed with many different names, such as K2, Spice Silver, Spice Gold, Spice Diamond, Spice Arctic Synergy, Spice Tropical Synergy, Spice Egypt, Mr. Smiley, Zohai, Eclipse, and Black Mamba. The exact synthetic cannabinoid(s) sold vary depending upon regulatory constraints and the availability of new cannabinoid compounds.

Synthetic cannabinoids may bind to either or both of the cannabinoid receptors: CB1 (type 1) and CB2 (type 2). THC binds to these same receptors. The CB1 receptor, found predominantly in the central nervous system, is primarily responsible for psychoactive effects. However, many synthetic cannabinoids have effects beyond these receptors and can cause cardiac effects, renal injury, and seizures. Synthetic cannabinoids are more potent than THC and have a longer half-life, leading to prolonged toxicological effects.3 Synthetic cannabinoids can elicit euphoric and dysphoric properties. The spectrum of adverse effects (cont. on pg. 3)
**Hepatotoxicity Associated with Herbal Supplements**

*by Emily Buxton, PharmD & UPCC Editorial Staff*

Drug-induced liver injury is an important cause of acute liver failure. While acetaminophen is the most common drug associated with acute liver failure, other drugs and certain herbal products and dietary supplements have also been associated with liver injury. Below we discuss a few noteworthy herbal preparations associated with hepatotoxicity. In addition to the plants described below, several other possible hepatotoxins that are noteworthy include Black Cohosh, Chaparral, Germander, Greater Celandine (*Chelidonium majus*), Green Tea (*Camellia sinensis*), and several other traditional Asian and Chinese herbal products.

**Kava**

*Kava (Piper methysticum)*, is a member of the pepper family. It is used to treat general anxiety similar to benzodiazepines. In the Pacific Islands, it is consumed as a beverage socially as well as part of religious or cultural ceremonies. Hepatotoxicity occurs within a week to as long as a year after use with elevated transaminases and the ALT/AST ratio >1.2 Histologic findings included necrotizing hepatitis and cholestatic hepatitis. In 2002, the FDA issued a Consumer Advisory warning consumers of the “potential risk of severe liver injury associated with the use of kava-containing dietary supplements.” Since that time, a hepatotoxic component of kava has been identified (flavokawain B).

**Pennroyal**

Pennroyal is a member of the mint family (*Lamiaceae*) and is used as an abortifacient and a menstrual stimulant/regulator. Hepatotoxicity and multi-organ system failure leading to death have been well described.

**Pyrrolizidine alkaloids**

Pyrrolizidine alkaloids are found worldwide in many unrelated families of plants. These alkaloids are metabolized to pyrroles that have strong alkylating properties that produce venous occlusion and hepatic sinusoidal obstruction syndrome (formerly hepatic veno-occlusive disease). Comfrey (*Symphytum sp*), Gordolobo yerba (*Senecio sp*), Heliotrope (*Crotalaria sp*), as well as borage, coltsfoot, and T’u-san-chi’I (*Gynura segetum*) are a few of the plants containing these alkaloids that have been associated with hepatotoxicity.

**Summary**

Clinicians should include dietary supplements in the differential of patients who present with acute or chronic liver disease. Suspected cases of dietary supplement-induced liver injury should be reported to the Drug-Induced Liver Injury Network (DILIN; https://dilin.dcri.duke.edu) and to the FDA’s MedWatch program (www.fda.gov/Safety/MedWatch).

**References**


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Metabolic Other Renal

that may mandate endotracheal intubation may require large doses of restraining agents to achieve the desired level of sedation. Severe agitation may result from the use of synthetic cannabinoid receptor agonists have primarily been identified through case reports (table). Physical dependence has been noted. Chronic users of synthetic cannabinoids can experience withdrawal symptoms, such as drug cravings, profuse sweating, nocturnal nightmares, tremors, and headaches.1

Table: Adverse Effects of Synthetic Cannabinoids1, 2, 4

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<td>Nausea</td>
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Treatment

Symptomatic and supportive care are the primary treatments for a patient exhibiting toxicity as a result of exposure to a synthetic cannabinoid. Benzodiazepines are the standard therapies for delirium and for stimulant effects such as agitation and tachycardia. Agitated patients who are at risk of harming themselves may need to be restrained chemically, only using physical restraints as a backup until sedative medications take effect. If an IV cannot be established, some chemical restraining agents can be used intramuscular (IM), such as midazolam, droperidol, and haloperidol. Once IV access is secured, the preceding agents may be continued intravenously. If these first line agents fail to resolve the patient’s agitation, either propofol or dexmedetomidine may be titrated intravenously to the desired level of sedation. Severe agitation may require large doses of restraining agents that may mandate endotracheal intuba-

Synthetic cannabinoids do not cross-react with routine urine toxicology tests that are intended to pick up marijuana metabolites. There are several laboratories that test specifically for some synthetic cannabinoids. The turnaround time for such tests is usually 7-14 days. In addition, the specific synthetic cannabinoids that laboratories can test are limited and often lag behind what compounds are available on the street.

Current Regulatory Status

In 2011, the Drug Enforcement Agency categorized five commonly used synthetic cannabinoids: JWH-018, JWH-200, JWH-073, CP-47,497, and cannabicyclohexanol, plus their salts and isomers, as Schedule I drugs according to the Controlled Substances Act on a temporary basis.2 In 2012, this classification was changed to permanent status. This classification makes selling and possession of synthetic cannabinoids illegal. In 2011, the Utah state legislature enacted Utah Code Ann. 58-37-4.2 (Listed Controlled Substances) and effectively added these same compounds to the list of controlled substances in Utah. This list has been amended annually since 2011 to include additional synthetic cannabinoids.5 Chemicals not specifically listed in the statute may still be illegal depending on how they are used. Utah Code Ann. 76-10-107 (Abuse of Psychotoxic Chemical Solvents) makes it a crime to use or possess “chemical substances capable of and used to cause intoxication, inebriation, excitement, stupefaction, or the dulling of the brain or nervous system as a result of the inhalation of its fumes or vapors.”

Summary

Synthetic cannabinoids present a challenge to emergency providers because of their severe toxicity and the inability of common drug screenings to detect them. Since there are no antidotes, aggressive supportive care remains the cornerstone of treatment. As regulations ban the currently available designer drugs, amateur chemists will continue to try to develop new designer drugs that are increasingly difficult to detect and have unknown effects and risks.

References


M-44 SODIUM CYANIDE

The United States Department of Agriculture, Animal and Plant Health Inspection Service, Bureau of Wildlife Services would like us to remind you that the M-44 sodium cyanide device is used in Utah. The ejeector device contains a capsule of sodium cyanide, which is baited with meat and placed in the ground. This device is used in specific situations to control coyotes, red foxes, gray foxes and wild dogs in order to protect livestock and endangered species and to prevent the spread of disease. This device is primarily used on private lands but may also be used on federal land in any county in the state. Areas where the M-44 sodium cyanide device is used are marked with signs. While human exposure to this device is extremely unlikely, be aware this device contains 91% sodium cyanide for which there is an antidote. Please report any exposure to this device to the Utah Poison Control Center at (800) 222-1222.
FDA Reminds the Public about the Potential for Life-Threatening Harm from Accidental Exposure to Fentanyl Transdermal Systems ("Patches")

The appropriate storage, use, application, and disposal of fentanyl patches (including Duragesic and generic products) is essential to prevent potential life-threatening harm from accidental exposure to the active ingredient, fentanyl. The FDA reviewed 26 cases of pediatric accidental exposures to fentanyl patches reported over the past 15 years. Ten of these resulted in death and 12 in hospitalization. Sixteen occurred in children two years old or younger. Young children are known to take improperly discarded patches from the trash or find improperly stored patches and place them in their mouths or stick them to their skin. Young children can also be exposed when held by someone wearing a partially detached patch, or by co-sleeping with an adult wearing a patch, when the patch dislodges from the adult and sticks to the child. Exposure of young children to a fentanyl patch, even a used patch, can lead to serious adverse events and even death. When disposing of fentanyl patch, the adhesive sides of the patch should be folded together and then the patch should be flushed down the toilet.

Christy Hunter, RN, ASN joined the UPCC staff as a Specialist in Poison Information in December of 2013. Christy graduated from Weber State University’s nursing program in 1999 at the age of 21. She has worked in various capacities as an RN, ranging from hospital to geriatric care, but she has always enjoyed pediatrics, recently concluding a 12-year employment in the Pediatric Intensive Care Unit at Primary Children’s Hospital. Caring for children has brought her tremendous gratification, and working at the UPCC lets her continue in this service. Christy was born at Cannon Air Force Base in Clovis, New Mexico, but her family has roots in Utah and she has spent most of her life there. As the second of five daughters, she spent most of her childhood with her family boating at Lake Powell, riding motorcycles, and terrorizing her sisters. Christy and Scott, her husband of 14 years, live in Clearfield with two loveable dogs — Daphne, a Great Dane, and Brutus, a mastiff — and two not-so-loveable cats. She enjoys spending time trying to talk her husband into adopting another dog, working in the garden, camping, boating at Bear Lake, and walking the dogs. Working at the UPCC has been a very exciting, but challenging experience. While she has an enthusiastic interest in toxicology, she doesn’t have much hands-on expertise; still every day at work she learns something new and gains knowledge and confidence. Her most gratifying calls involve children that can be managed safely at home, and providing a relief to their parents.