ToxIC Brief

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Synthetic Cannabinoids Cases Reported to the ToxIC Registry, August 1, 2018–January 31, 2019

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Synthetic cannabinoid (SC) metabolites are hard to test for and are constantly changing, making it difficult to understand their clinical effects in practice. Research findings have shown that even when patients report SCs as the drug ingested, the true substance may be unknown to the patient and adulterants or other substances may be present. To identify cases involving an SC, medical toxicologists talk with the patient and treating physician and review available medical records.

Between August 1, 2018 and January 31, 2019, 86 cases involving psychoactive substances were reported to ToxIC by medical toxicologists from across the United States. Ten (12%) cases were believed to involve SCs as the primary agent, all of which were used intentionally. The method of determination of synthetic cannabinoid use was not reported in the ToxIC Registry. The median age was 31.5 years, with a range of 16 to 52 years, and 90% of these cases involved males. The 10 cases occurred in 4 states, Texas (1), Indiana (1), New York (1), and Pennsylvania (7). Considerably abnormal vital signs included tachycardia (heart rate > 140), hypertension (systolic blood pressure > 200 or diastolic blood pressure > 120), and bradycardia (heart rate < 50). See Table 1 for a summary of clinical features. The most common symptom experienced was agitation (by 8 of 10). Fifty percent of patients required medical treatment for their synthetic cannabinoid toxicity; the remainder were observed without intervention. No deaths were reported.

Method

For this bulletin, the sentinel field was queried in January 2019 to identify synthetic cannabinoid cases reported between August 1, 2018 and January 31, 2019. The entire registry was then searched for substances identified by the detector, and all primary synthetic cannabinoid exposures were further searched for any additional novel cases not flagged by the detector. See the inaugural *ToxIC Brief* from October 2018 for a detailed description of information captured by the sentinel event detector for the ToxIC registry.

Selected Case Studies

Case studies for four cases selected to illustrate the variation in clinical presentation reported by medical toxicologists to the ToxIC registry between August 2018 and January 2019 are highlighted as follows.

Toxicology Investigators Consortium (ToxIC)

ToxIC is a toxico-surveillance registry and research network of physicians specifically qualified in the field of medical toxicology. A mandatory sentinel event detector field is used to flag novel and emerging exposures. Novel (or "new") psychoactive substances (NPS) are defined as substances of abuse that are not controlled by the 1961 Convention on Narcotic Drugs or by the 1971 Convention on Psychotropic Substances that may pose a public health threat.[1]

Medical toxicologists in 35 participating sites across the United States consult with medical facilities to diagnose and manage the adverse effects of exposure to natural toxins, drugs, and chemical substances, including drugs of abuse. Core information on these cases is provided to the American College of Medical Toxicology (ACMT) as part of the ToxIC Registry. Analytical confirmation, however, may not be part of the clinical consultation conducted and rarely has an impact on the treatment plan. As a result, specific toxicology results are not systematically included in the ToxIC Registry.

The ToxIC registry contains more than 65,000 cases providing a uniform array of reliable clinical data on patients. Approximately 8,000 cases are added each year. ToxIC is operated by the ACMT.

***ToxIC Briefs* are available at:**

www.ndews.org

NDEWS is funded under NIDA Cooperative Agreement DA038360 awarded to the Center for Substance Abuse Research (CESAR) at the University of Maryland, College Park (UMCP). Opinions expressed in this report may not represent those of NIH or NIDA.

Case 1: Male Age 44

A 44-year-old man used SCs to get high. In the emergency department (ED), he was agitated with altered mental status including delirium/psychosis. He was given benzodiazepines and intravenous fluid for his symptoms and admitted to the hospital floor. During his stay, his lab results were significant for an elevated troponin, suggesting myocardial injury/infarction. His EKG was also remarkable for prolonged QTc at 510 ms.

Case 2: Male Age 36

A 36-year-old man used SCs to get high. In the ED, his vital signs were significant for bradycardia (heart rate < 50). He did not require medical intervention for his symptoms.

Table 1: Clinical Features in Ten Synthetic Cannabinoids Cases Identified by Medical Toxicologists and Reported to ToxIC, Aug. 2018–Jan. 2019

	Case 1	2	3	4	5	6	7	8	9	10	Total w/ Symptom
Hypertension							X				**1**
Tachycardia							X				**1**
Bradycardia				X							**1**
Myocardial injury		X									**1**
QT prolongation		X									**1**
Agitation	X	X	X		X	X	X	X	X		**8**
CNS depression	X							X			**2**
Delirium/psychosis	X	X									**2**
Resp depression								X	X		**2**
Rhabdomyolysis (muscle breakdown)					X						**1**
Vomiting										X	**1**
TOTAL Symptoms	**3**	**4**	**1**	**1**	**2**	**1**	**3**	**3**	**2**	**1**	

Case 3: Male Age 32

A 32-year-old man used SCs to get high. In the ED, he was hypertensive (systolic blood pressure > 200 or diastolic blood pressure > 120), tachycardic (heart rate > 140), and agitated. He did not require medical intervention for his symptoms.

Case 4: Male Age 30

A 30-year-old man used SCs to get high. He was admitted to the intensive care unit (ICU). He experienced both agitation and central nervous system depression as well as respiratory depression during his ICU stay. He required intravenous fluid resuscitation for his symptoms.

Conclusions/Implications

The patients experienced a wide variety of clinical features impacting the cardiovascular, respiratory, musculoskeletal, and neurologic systems, as well as psychological state. Opposing clinical presentations (stimulatory versus depressant) were observed, both between patients and within single-patient presentations. Agitation, experienced by eight of the ten patients, was the most common symptom. The number of symptoms experienced ranged from one to four.

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SCs, often referred to as "spice" or "K2." have been detected as drugs of abuse since the early 2000s but have grown in popularity in recent years.[2] Although SCs, like marijuana, target the cannabinoid (CB) receptors, they do so with greater affinity, particularly for the CB1 receptor. The clinical effects of SCs, however, differ significantly from marijuana intoxication. As different chemical versions of SCs are continuously synthesized to evade detection, a wide variety of clinical presentations has emerged. Opposing cases of significant agitation and central nervous system depression, tachycardia and bradycardia, as well as respiratory depression and acute kidney injury have been reported in the literature.[2–5]

SCs are not detected in routine urine drug testing, and newer versions can be missed even in more sophisticated testing, making it difficult to get a reliable understanding of their clinical effects in practice. Even when patients report SCs as the drug ingested, the true substance may be unknown to the patient and adulterants or other substances may be responsible for observed clinical effects. In recent analysis of self-reported SC ingestion, researchers often detected other drugs of abuse in addition to or in place of SCs.[6] The findings from several reports with confirmatory analytic testing, however, show support for the variable nature of true SC toxicity noted in this publication.[3,7]

In most cases, as in this series, supportive care is sufficient treatment and patients often recover without long-lasting sequelae. Outbreaks of clinically significant bleeding, however, have occurred in patients using SCs found to have coagulopathy (bleeding abnormality) on laboratory work-up. Analytic testing has resulted in the detection of superwarfarin adulterants, and bleeding deaths have ocurred.[8] No such cases were reported in this series. Clinicians should, however, maintain a high index of suspicion in patients reporting SC use who present with bleeding events.

Limitations

ToxIC case accrual is limited to medical centers that have medical toxicologists on staff. Participating sites are in 21 states but do not represent a population-based sampling and cannot be used to produce prevalence estimates. The results are intended to be used for epidemiologic and descriptive purposes. Analytical confirmation is rarely obtained as such laboratory analysis is not generally part of the clinical consultation and rarely has impact on the treatment plan. Although all participating sites have been trained to use the sentinel event detector field, a drug that would be considered new or emerging by one investigator may be considered less novel by another. These results reflect a brief period of time and may not be representative of larger trends.

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