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Selected Topics: Toxicology

A COMMON SOURCE OUTBREAK OF SEVERE DELIRIUM ASSOCIATED WITH EXPOSURE TO THE NOVEL SYNTHETIC CANNABINOID ADB-PINACA

Michael D. Schwartz, MD,* Jordan Trecki, PHD,† Laura A. Edison, DVM, MPH,‡ Alaina R. Steck, MD,§ Justin K. Arnold, DO,§ and Roy R. Gerona, PHD||

*Centers for Disease Control and Prevention, National Center for Environmental Health, Office of Environmental Health Emergencies, Atlanta, Georgia, †Drug Enforcement Administration, Office of Diversion Control, Drug and Chemical Evaluation Section, Springfield, Virginia, ‡Centers for Disease Control and Prevention, Epidemiology Program Office, Atlanta, Georgia, §Georgia Poison Center, Atlanta, Georgia, and ||Department of Laboratory Medicine, University of California–San Francisco, San Francisco, California

Reprint Address: Michael D. Schwartz, MD, Centers for Disease Control, National Center for Environmental Health, Office of Environmental Health Emergencies, 1600 Clifton Road, MS F-09, Atlanta, GA 30333

☐ **Abstract—Background: Since 2009, synthetic cannabinoid (SC) use has emerged as a growing public health threat in the United States (US). Several outbreaks of unexpected, severe toxicity linked to SC use have been reported since 2012. Reports of varied and significant morbidity after SC use are expected to increase because newer compounds enter the marketplace more frequently as manufacturers attempt to circumvent regulatory efforts. Case Report: We report a cluster of 7 patients who experienced a spectrum of anxiety, delirium, psychosis, and aggressive behaviors after smoking the same SC-containing product at a party. An 8th patient with the same exposure source presented with delayed onset seizures. Biologic samples were analyzed for novel, newly identified SCs belonging to the FUBINACA family of compounds. A previously unknown SC, N-(1-amino-3, 3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1H-indazole-3-carboxamide (ADB-PINACA) was identified in biologic samples from 7 of the individuals. ADB-PINACA was identified in the SC-containing product ("Crazy Clown") seized by law enforcement and identified as the product smoked by the 8 patients in the reported cluster. Why Should an Emergency Physician Be Aware of This?: The information compiled using this cluster of cases, and a similar reported outbreak of altered mental status in Colorado, implicating the same SC (ADB-PINACA) and brands of SC-containing products, aided the US Drug Enforcement Administration in its temporary scheduling of ADB-PINACA and three other SCs. In this outbreak, close cooperation between public health and law enforcement allowed for a rapid intervention, which halted the outbreak by interrupting the common source and accelerated regulatory efforts to prevent further morbidity and mortality. Published by Elsevier Inc.**

☐ **Keywords—synthetic cannabinoid; delirium; ADB-PINACA; cluster; outbreak; spice; K2; DEA scheduling**

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INTRODUCTION

Synthetic cannabinoids (SCs) are a newly emerging public health threat. SCs ("Spice," "K2") collectively constitute >50 individual synthetic compounds that are part of this new designer drug epidemic. SCs typically are dissolved in a solvent, applied to dried plant material

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or herbal potpourri, and smoked as an alternative to marijuana. SC-containing products are marketed commercially as "herbal incense" and labeled "not for human consumption," both designations suggesting legitimacy. Users smoke SC-containing products expecting to evade standard urine drug screening and to experience a more intense psychoactive effect than with marijuana. The SCs tested so far are more potent than delta-9-tetrahydrocannabinol (THC), and reports of sympathomimetic effects and seizures from smoking SCs are more numerous than similar reported effects from smoking marijuana (1–3). Reports of cases and outbreaks of unpredicted, severe toxicity have increased as the number of SCs introduced to the market has risen. Seizures are one of the most common unpredictable toxicities reported after SC exposure (4–10). Chest pain and cardiovascular toxicity after SC use have also been reported (11,12). Two of the authors (MDS, RRG) have reported on a nationwide outbreak of acute kidney injury (AKI) associated with use of the novel SC XLR-11 (13). The recent outbreaks reported in Georgia and Colorado are the first involving clusters of cases with altered mental status and agitated delirium associated with a specific compound (14–16). Recently, the Arkansas K2 Consortium published a report of an isolated case of fatal psychosis after SC exposure (17).

CASE REPORT

Initial Epidemiological and Law Enforcement Investigation

On August 22, 2013, a hospital in Brunswick, Georgia called the Georgia Poison Center seeking management recommendations for 7 patients who presented simultaneously after smoking an SC-containing product at a party. The patients were not known to have any medical history, and all had been well previously on the day of presentation. On the evening of admission, all patients had been at the same party and smoked the same product. Glynn County (GA) police noted that this index cluster of 7 patients had been smoking a new shipment of "Crazy Clown," a synthetic incense made in Colorado and purchased from a smoke shop in Brunswick, GA. Emergency Medical Services (EMS) were called after 3 of the patients began behaving aggressively and transported all 7 patients to the emergency department (ED). The patients underwent laboratory evaluation with complete blood count, comprehensive metabolic panel, creatinine phosphokinase (CPK), coagulation profile, arterial or venous blood gas, and venous lactate.

Upon identifying the source of the implicated product smoked by the case patients, law enforcement personnel removed all Crazy Clown product from the smoke shop. Analysis of the product inventory by the Georgia Bureau of Investigation Crime Laboratory identified the novel pentyl indazole SC N-(1-amino-3,3-dimethyl-1-oxobutan-2-yl)-1-pentyl-1H-indazole-3-carboxamide (ADB-PINACA) in samples of Crazy Clown (18).

Individual Case Descriptions

Case 1. Patient 1 was a 25-year-old male who was markedly agitated and combative upon EMS arrival. He required chemical sedation and intubation to control his extreme agitation. First documented vital signs were heart rate (HR), 130 beats per minute (bpm); blood pressure (BP), 142/56 mm Hg; respiratory rate (RR), 20 breaths per minute (mechanically ventilated); and oxygen saturation (SpO_2), 100%. His initial laboratory results were significant for an anion gap 15 mEq/L, venous lactate 3.13 mmol/L, and CPK 920 IU/L. All other results were within normal limits. He was admitted to the intensive care unit (ICU) and continued to have intermittent tachycardia and hypertension until hospital day (HD) 3, when he was extubated. Although he was initially confused after extubation, his mental status rapidly improved, and the hospital discharged him in his baseline state of health on HD 5.

Case 2. Patient 2 was a 24-year-old male who also was confused and agitated upon initial EMS evaluation. He required sedation and intubation for management of violent behavior. Initial vital signs were HR 132 bpm, BP 128/88 mm Hg, RR 22/min (mechanically ventilated), SpO_2 98%, and temperature, 98.9°F. His initial laboratory results were within normal limits, without acidosis or elevated CPK. Approximately 7 h after presentation, his vital signs had normalized. He was admitted only briefly to the ICU and was extubated 15 h after presentation. Once fully alert, this patient signed out against medical advice (AMA), declining further evaluation.

Case 3. Patient 3 was a 30-year-old male who was reported to be the most severely combative and aggressive of these 7 patients. EMS administered haloperidol and lorazepam and intubated him shortly thereafter. En route to the ED, he suffered a witnessed cardiac arrest and was resuscitated by paramedics. He had regained spontaneous circulation by the time he arrived in the ED. Vital signs upon arrival were HR 93 bpm, BP 118/69 mm Hg, RR 16/min (mechanically ventilated), SpO_2 99%, and temperature 98.9°F. Initial electrocardiogram (ECG) showed an anterior ST-elevation myocardial infarction, for which he was promptly transferred to the cardiac catheterization suite. Cardiac catheterization demonstrated complete occlusion of the left anterior descending, and the patient underwent successful balloon angioplasty. He was admitted