HHS Public Access

Author manuscript

Biol Psychiatry. Author manuscript; available in PMC 2018 March 12.

Published in final edited form as:

Biol Psychiatry. 2017 April 01; 81(7): e51–e52. doi:10.1016/j.biopsych.2016.08.013.

Can Naloxone Be Used to Treat Synthetic Cannabinoid Overdose?

Jermaine D. Jones, **Michelle L. Nolan**, **Roshni Daver**, **Sandra D. Comer**, and **Denise Paone**

Division of Substance Abuse (JDJ, SDC), New York Psychiatric Institute/College of Physicians and Surgeons of Columbia University, New York; Public Health/Preventive Medicine Residency Program (RD), Bureau of Alcohol and Drug Use Prevention, Care and Treatment (JDJ, MLN, RD, DP), New York City Department of Health and Mental Hygiene, Long Island City, New York

To the Editor

Synthetic cannabinoids, commonly known as K2 or Spice, have emerged as a recreational drug and an inexpensive alternative to cannabis (1). Currently, there is no antidote for synthetic cannabinoid overdose/overintoxication, and clinical care typically only includes symptom management. However, naloxone, a drug used to treat opioid overdose, might prove beneficial (2,3). Naloxone is a nonselective opioid antagonist increasingly used by medical personnel and laypersons to reverse overdose due to the use of opioid analgesics and heroin (4).

Why might an opioid receptor antagonist affect a drug that acts on the cannabinoid receptor? Studies show that opioid and cannabinoid receptors are colocalized in multiple brain regions where they may exist as heterodimeric systems. Both receptors also have cross-modulatory pharmacologic effects, including cross-agonism, -antagonism, -sensitization, and -tolerance (5,6). Accordingly, several studies suggest that opioid receptor antagonists might counter the effects of cannabinoid agonists (2,7).

In April 2015, synthetic cannabinoid-related emergency department visits increased dramatically in New York City. In response, the New York City Department of Health and Mental Hygiene conducted a public health investigation to gain a better understanding of the circumstances, presenting symptoms, and severity of synthetic cannabinoid overdose. Twenty-seven medical charts were identified from citywide emergency department records and reviewed; 15 met the eligibility criteria for inclusion: patient was admitted to the hospital April 10–20, 2015, and synthetic cannabinoid use was documented in the medical record. The medical chart review identified four cases with documentation of improved symptomology after the administration of naloxone (Table 1). In each of these cases we

Address correspondence to Jermaine D. Jones, Ph.D., Columbia University, College of Physicians and Surgeons, Division on Substance Abuse, 1051 Riverside Dr., New York, NY 10032; jonesje@NYSPI.Columbia.edu.

Disclosures

SDC has received compensation (in the form of partial salary support) over the past 3 years from investigator-initiated studies supported by Reckitt-Benckiser Pharmaceuticals, Schering-Plough Corporation, Johnson & Johnson Pharmaceutical Research & Development, Endo Pharmaceuticals, and MediciNova and has also served as a consultant to Grunenthal USA, Guidepoint Global, Mallinckrodt, Neuromed, Orexo, Pfizer, and Salix. All other authors report no biomedical financial interests or potential conflicts of interest.

found evidence of increased responsiveness and/or normalized vital signs after naloxone administration. These four cases were of particular interest because there was no evidence of recent opioid use (either by self-report or in drug toxicology) that would account for symptom improvement after naloxone administration.

In New York City, first responders have been trained to administer naloxone in instances of suspected opioid use or respiratory depression. Although these cases tentatively suggest that the administration of naloxone led to symptom improvement, this conclusion should be made with caution. In each of these cases a number of treatment interventions may have been used aiding in resolution of adverse symptoms. In addition, little is known about the time course of synthetic cannabinoid overdose, and symptoms may have improved without medical intervention. Finally, in two of the four cases there is evidence of alcohol use. Opioid antagonists also block alcohol-mediated effects, which may account for some degree of symptom improvement (8).

Another interesting finding from these cases is the shared clinical presentation of synthetic cannabinoid overdose to opioid overdose (9). The co-occurrence of symptoms such as loss of alertness, unconsciousness, and decreased respiratory measures may further demonstrate the interrelatedness of endogenous opioid and cannabinoid systems and may add credibility to the potential utility of naloxone in cases of synthetic cannabinoid overdose. Again, we stress caution in drawing conclusions from only four cases. In addition, because synthetic cannabinoids include hundreds of different chemical compounds, their chemical composition and resultant neuropharmacology is varied. Therefore, the efficacy of naloxone to improve symptoms after synthetic cannabinoid use may vary depending on the exact synthetic cannabinoid compound(s) involved. Despite these limitations, these case results provide a basis to initiate further investigation into how clinicians might address the adverse health consequences of a class of drugs with no presently known antidote.

Acknowledgments

This study was supported by the New York City Department of Health and Mental Hygiene and the National Institute on Drug Abuse Grant No. R01DA035207.

References

1. Castaneto MS, Gorelick DA, Desrosiers NA, Hartman RL, Pirard S, Huestis MA. Synthetic cannabinoids: Epidemiology, pharmaco-dynamics, and clinical implications. Drug Alcohol Depend. 2014; 144:12–41. [PubMed: 25220897]
2. Justinova Z, Tanda G, Munzar P, Goldberg SR. The opioid antagonist naltrexone reduces the reinforcing effects of Delta 9 tetrahydrocannabinol (THC) in squirrel monkeys. Psychopharmacology (Berl). 2004; 173:186–194. [PubMed: 14668977]
3. Rosenbaum CD, Carreiro SP, Babu KM. Here today, gone tomorrow…and back again? A review of herbal marijuana alternatives (K2, Spice), synthetic cathinones (bath salts), kratom, Salvia divinorum, methoxetamine, and piperazines. J Med Toxicol. 2012; 8:15–32. [PubMed: 22271566]
4. Substance Abuse and Mental Health Services Administration. SAMHSA Opioid Overdose Prevention Toolkit. Rockville, MD: Substance Abuse and Mental Health Services Administration; 2016. HHS Publication No. SMA16-4742
5. Robledo P, Berrendero F, Ozaita A, Maldonado R. Advances in the field of cannabinoid–opioid cross-talk. Addict Biol. 2008; 13:213–224. [PubMed: 18482431]

6. Scavone JL, Sterling RC, Van Bockstaele EJ. Cannabinoid and opioid interactions: Implications for opiate dependence and withdrawal. Neuroscience. 2013; 248:637–654. [PubMed: 23624062]

7. Haney M, Ramesh D, Glass A, Pavlicova M, Bedi G, Cooper ZD. Naltrexone maintenance decreases cannabis self-administration and subjective effects in daily cannabis smokers. Neuropsychopharmacology. 2015; 40:2489–2498. [PubMed: 25881117]

8. O'Brien CP, Volpicelli LA, Volpicelli JR. Naltrexone in the treatment of alcoholism: A clinical review. Alcohol. 1996; 13:35–39. [PubMed: 8837932]

9. Doyon, S. Opiods. In: Tintinalli, JE.Kelen, GD.Stapczynski, JS.Ma, OJ., Cline, DM., editors. Emergency Medicine: A Comprehensive Study Guide. 6. Vol. Chapter 167. New York: McGraw-Hill; 2004. p. 1071-1075.

			Presenting Vitals (EMS)				Final Vitals (ED)					
Reported Drug Use	**Drug Toxicology**	**BAC (mg/dL)**	**HR/beat/min**	**O_2 Sat, %**	**RR, breaths/min**	**BP, mm Hg**	**HR, beats/min**	**O_2 Sat, %**	**RR/breaths/min**	**BP, mm Hg**	**Outcome**	**Mental Health Hx**
Can	Negative (amphetamine and cannabis were not tested)	NR	116		6	128/80	60	98	19	127/74	Discharged	SCZD
Can	Not performed	0		80	16	114/73	61	100	16	99/54	Admitted	None
Can, alcohol	Negative	18	141	87	30		89	98	16	106/59	Admitted, left AMA	Alcohol abuse
Can, alcohol	Negative	46						95			Admitted	None

F, female; HR, heart rate; Hx, history; M, male;

Biol Psychiatry. Author manuscript; available in PMC 2018 March 12.