Research Article

Journal of Addiction Research

Behavioral Patterns of Psychiatric Patients Using Synthetic Cannabinoids

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Submitted: 04 Feb 2017; **Accepted:** 19 Feb 2017; **Published:** 23 Feb 2017

Abstract

Synthetic cannabinoids (SC) are analogs of natural cannabinoids that are chemically synthesized. These compounds are used frequently in the community as illicit substances. Literature review indicates that its use is increasing due to its easy accessibility despite it being placed under Schedule I of the Synthetic Drug Abuse Prevention Act of 2012. SC is readily found in most inner urban communities across the United States and its abuse is increasing at a high rate. Studies suggest that SC can result in medical and psychiatric manifestations including: vomiting, tachycardia, seizures, auditory hallucinations, aggressive behavior and an increase in impulsivity. The increase in prevalence compounded with the potentially devastating psychiatric sequelae raise concerns for mental health practitioners. While some literature exists that reviews the psychiatric manifestations of patients who use SC, there are no studies that review the presentation of patients of patients behavior's while intoxicated At this time SC drug screening is not readily available in most hospital centers and intoxication with SC is primarily based on a clinical evaluation, patient's self-report or collateral information. We conducted a retrospective case control study of patients who were admitted to the inpatient psychiatric service for a period of 7 months from who reported smoking SC. This paper will attempt to explore specific clinical risk factors of patients that use SC and the aggressive behavior of these patients while hospitalized as well as whether this increases duration of hospitalization and management on the unit In addition, we aim to bring to light the need for future investigations to better understand how to manage this difficult patient population.

Introduction

Synthetic cannabis is a designer drug in which herbs or other leafy materials are sprayed with lab-synthesized liquid chemicals to mimic the effect of tetrahydrocannabinol (THC), the psychoactive ingredient in the naturally grown marijuana plant (cannabis sativa). It acts as an agonist at cannabinoid receptors located throughout the brain therefore impacting mood, appetite, pain and immunity. Currently, there are over 700 researched cannabinoid (CB) receptors identified with CB1 and CB2 resulting in psychoactive effects [1]. The CB1 receptor is predominantly expressed presynaptically, modulating the release of neurotransmitters including GABA, dopamine, noradrenaline, glutamate and serotonin [1]. While SC use has been known to cause hallucinations and psychosis, the manner in which SC affects the release of these neurotransmitters is not fully understood and may entail abnormal dopaminergic transmission, serotonergic transmission and N-methyl-D-aspartate blockade, similarly to the drugs phencyclidine and Ketamine.

Like THC, the psychoactive ingredient in marijuana, SC binds to CB1 receptors located throughout many brain regions including the hypothalamus, the cerebral cortex and the cerebellum. When SC binds, it acts as a full agonist, therefore activating a CB1 receptor on a brain cell with maximum efficacy, rather than partially as with THC [2]. Subsequently, SC can potentiate psychoactive effects hundreds of times greater than that of THC. SC compounds are cannabinoid-like chemicals which were developed in research laboratories to study CB1/CB2 receptors. They were initially studied by researchers in hopes of potentiating medicinal use. Some of the few chemicals well known in studies include: JWH-018, JWH-073, JWH-081, JWH250, JWH-200, CP 47 497 and CP 47497. Although both THC and SC undergo Phase I metabolism by cytochrome P450, JWH-018 has been shown to have at least nine metabolites whose biological activity is currently undetermined, while THC has one known major psychoactive metabolite [3]. While natural cannabinoids have been shown to exhibit anticonvulsive activity, seizures caused by SC use are possibly due to the antagonism of other inhibitory networks such as GABA channels or the activation of excitatory networks such as glutamate receptors, Na^+ and Ca^{2+} channels [4]. Effects of SC use can include acute agitation, paranoia, depression, hallucinations and other perceptual disturbances, suicidal ideations, panic attacks, anxiety, psychosis, and a number of medical manifestations including nausea, vomiting, tachycardia, drowsiness, dizziness, hypertension, myocardial infarction, seizures, convulsions, kidney failure and death. Cardiovascular and CNS toxicity are reported to be related to the long term abuse-related effects of dependence and withdrawal. The cardiovascular symptoms, as well as drug-induced anxiety, agitation and panic attacks associated with SC use could

therefore be caused by activation of α1, β1 and β2 adrenoceptors. Activation of glutamate receptors and GABA channel blockade may also be responsible for anxiety due to SC use. Agitation and violent behavior, suicidal and homicidal ideations in addition to self-injurious behaviors have been reported in case studies. The implications of acute SC use on human health remains poorly understood and less is known about the long term effects of these drugs.

The history of synthetic cannabis dates back to 1979-1980 when Pfizer pharmaceutical first made the compounds CP 47 and 497 C8. Both of these compounds produce cannabis type effects when ingested. In 1988 HU-210 was first synthesized at Hebrew University in Israel, and it has anti-inflammatory and anesthetic properties. Dr. Huffman, a Harvard educated organic chemist, originally conducted research in Clemson University in South Carolina with intentions to find a cure or treatment for Muscular Sclerosis amongst other diseases. With the misleading labeling "not for human consumption" the brand "Spice" was released in 2004, and in 2006 the brand gained popularity, particularly throughout Europe. In 2006, SC was readily available in Europe and did not make its way to North America until 2009.

While working in our inner urban community hospital, we noticed a rise in patients admitted with psychosis and agitation whom had in fact reported SC use. As a treatment team we were aware that the patient would be difficult to manage and would potentially be violent, but what else? What do we really know about this drug? Our interest in SC and its clinical manifestations was the foundation for our project. We conducted a retrospective chart review where we evaluated patients admitted to the inpatient psychiatric service who self-reported SC use.

Methods

Data Collection

Our study received approval from the Institutional Review Board (IRB). For this study we obtained de-identified data from electronic health records (EHR) collected from 113 adult patients who were admitted to the adult inpatient psychiatric unit in an inner urban community hospital in New York City. Those patients that were evaluated required involuntary admission to the inpatient unit. As part of the initial evaluation, all patients received a comprehensive psychiatric assessment conducted by a psychiatrist. De-identified data derived from this comprehensive psychiatric evaluation from patients were extracted by the EHR specialist and used for our analyses. Extracted data included: self-reported K2 use, substance use history, assisted outpatient treatment (AOT), laboratory work-up on admission, quality of social support, medical history, previous substance use rehabilitation and detox admissions, demographic information; current and past psychiatric history including suicidal thoughts and behavior; legal and violence history; history of any type of abuse; and other relevant factors.

Instrument

We used a data extraction tool for information obtained for our research. The extraction tool was IRB approved and the study sample was limited to our own electronic medical records for inpatient psychiatric units.

Results

Baseline characteristics of all subjects

The study group included 113 patients who were admitted to Bronx Lebanon Hospital Center inpatient psychiatry service during a seven month period (January 01, 2015 to July 31, 2015). The study group included a total of 80 males (71%) and 33 females (29%). 57.7% of the subjects self-reported K2 use (K2 Group), while 42.3% denied any past or current K2 use (Control Group). Moreover, 94% of subjects from K2 Group had reported active comorbid substance use, while the number in the Control group was found to be 53%, with Marijuana use being the most common substance used by both groups. The most common psychiatric diagnoses amongst the study group as a whole was Schizophrenia (30%), followed by Substance Induced Mood/Psychotic Disorder (22.6%), Schizoaffective disorder (21%), Bipolar Disorder (18.9%), Major Depressive Disorder (4.5%) and other (3%).

Comorbid psychiatric diagnosis	Percentage (%)
Schizophrenia	30.0
Schizoaffective disorder	21.0
Bipolar disorder	18.9
Major depressive disorder	4.5
Substance induced mood/psychotic disorder	22.6
Others	3.0

Table 1: Comorbid psychiatric diagnosis prevalence.

Substance	K2 Group (%)	Control group (%)	p-value
Cannabis	81.3	38.3	<0.001
Nicotine	57.8	21.3	<0.001
Alcohol	48.4	19.1	<0.001
Cocaine	37.0	19.1	<0.001

Table 2: Self-reported comorbid substance use (Baseline).

Variable	K2 Group (%)	Control group (%)	P value
History of Arrest (s)	53	27.7	<0.01
Self-reported comorbid substance use	93.8	53.2	NS
Urine toxicology screen positive	71.9	76.6	NS

Table 3: Baseline data (comorbid psychiatric diagnoses, and legal history).

Subject Characteristics by Diagnostic Groups

The incidence of substance use was found to be significantly higher in the K2 group in comparison to the control group, including Marijuana (K2-81.3%; Control-38.3%; p <0.001), nicotine (K2-57.8%; Control-21.3%; p <0.001), alcohol (K2-48.4%; Control-19.1%; p <0.001) and cocaine (K2-37%; Control-19.1%; p <0.001). Although, the 2 groups were not found

to be significantly different when comparing the positive Urine toxicology screen on admission (K2-71.9%; Control-76.6%; p>0.05) and incidence of comorbid substance use (K2-93.8%; Control-53.2%; p>0.05). On further comparison, K2 group was found to have significant higher history of previous arrest(s) (K2-53%; Control-27.7%; p<0.01), need for emergent IM medication (K2-53%; Control-27.7%; p<0.01), need for seclusion/restraints for safety (K2-25.6%; Control-4.3%; p<0.01), being discharged to inpatient substance rehab (K2-7.8%; Control-0%; p<0.05) and treatment non-compliance evident from AOT services (K2-31.3%; Control-2.1%; p<0.001).

Variable	K2 Group (%)	Control Group (%)	p-value
Hospital stay (days)	31.2	20.0	0.05
Emergent IM* use	53	27.7	<0.01
Seclusion/Restraint	25.6	4.3	<0.01
Discharge to Rehab	7.8	0	<0.005
Readmission <30 days	3.1	4.3	NS
AOT*	31.3	2.1	<0.001
Anti-psychotic depot Inj.	65.6	51.1	NS

Table 4: Hospital stay parameters (Length of stay, IM, seclusion restraint, AOT, Rehab). *AOT: Assisted outpatient treatment; IM: Intra-muscular.

Discussion

There is scarce scientific literature published on the psychiatric presentation of the patients with history of synthetic cannabinoid use, with most being case reports about atypical side-effects of synthetic cannabinoid use warranting management for medical emergencies, including but not limited to seizures, intracranial hemorrhage, acute coronary syndrome, rhabdomyolysis, acute renal failure, hypertensive stated and coma/death. A total of 113 patients (71% men, 28% women) were assessed; 65 patients self-identified as SC users and 48 controls reported no use of SC. Demographic characteristics associated with higher SC (Synthetic Cannabinoids) use included male gender, younger age, and a comorbid substance use disorder. Moreover, the data analysis showed that subjects with SC use have significantly increased incidence of physical aggression, need for emergent medication, need for seclusion/restraint, treatment non compliance and being discharged to substance rehabilitation program. Furthermore, lack of specific treatment guidelines for managing the patient with synthetic cannabinoid associated/induced mood and/or psychotic symptoms on an inpatient psychiatric unit leave much to be desired for an appropriate treatment outcome, which was evident in the data analysis of our study sample. We want to emphasize the importance of studying the clinical characteristics of synthetic cannabinoid use, along with response to different treatment modalities (anti-psychotics versus mood stabilizers versus benzodiazepines) and the lack of socio-legal infrastructure to control this endemic from growing [3-5].

Conclusions

There are several limitations in our study including that it is a small sample size (n=113), is a retrospective design, lack of data from other hospitalizations and using self-reported SC use as inclusion criteria due to limited availability, high financial burden of synthetic cannabinoids screening test. On the contrary, this is one of the first studies trying to look at the psychiatric presentation of patient's with synthetic cannabinoid use, emphasizing the need for further efforts to improve our knowledge base to tailor the treatment strategies [6-8].

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