COMPLEMENTARY AND ALTERNATIVE MEDICINE (CAM) IN PSYCHIATRY AND NEUROLOGY

mhc MENTAL HEALTH CLINICIAN

CASE REPORT Open Access

Psychiatric symptoms and synthetic cannabinoid use: Information for clinicians

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How to cite: Sweet G, Kim S, Martin S, Washington NB, Brahm N. Psychiatric symptoms and synthetic cannabinoid use: Information for clinicians. Ment Health Clin [Internet]. 2017;7(4):156-9. DOI: 10.9740/mhc.2017.07.156.

Abstract

Background: Limited treatment information is available when patients present with psychotic symptoms secondary to synthetic cannabinoid (SC) use. Symptoms associated with use are often indistinguishable from those encountered with a primary mental illness and also include aggression, confusion, and anxiety. For these patients, clinicians rely on physical presentation, symptom(s) onset, and episode duration when evaluating patients.

Patient History: An adult man was involuntarily admitted to inpatient status secondary to reports of bizarre behaviors that included paranoia and psychomotor agitation. Because of the severity of the symptoms, he was unable to participate in the admission assessment. On day 2, he reported having smoked a substance provided by a friend. In addition, he admitted to previous SC use on 3 occasions, with each occasion resulting in an involuntary admission to inpatient status. The course of this admission was unremarkable.

Conclusions: A brief overview of psychiatric signs and symptoms of SC use and information to help clinicians are included. The presentation of psychotic symptoms secondary to SC may be consistent with those of psychosis or other substances of abuse. Because of the variability in the symptoms produced by SC use, clinicians are encouraged to consider SC use in the diagnostic evaluation.

Keywords: cannabinoid, cannabis, herbal incense, intoxication, K2, legal high, marijuana alternative, psychosis

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Disclosures: No funding was requested or received in conjunction with this project. The authors report no known or suspected conflicts of interest related, but not limited, to consulting fees, paid expert testimony, employment, grants, honoraria, patents, royalties, stocks, or other financial or material gain involved with or pertaining to the subject matter of this work.

Introduction

Cannabis has been used both medicinally and recreationally for thousands of years.[1] In 2004, a synthetic class of cannabinoids became available through unregulated channels.[2] These products were purported to be a mixture of herbs or other plant-based blends of various ingredients marketed and sold under a variety of brand names, such as *Spice*, *K2*, *Space*, *Dream*, or *Genie*, and were designed to

produce a marijuana-like sensation when smoked.[3] This category may be referred to as synthetic cannabinoids (SC) and marketed as one of two forms of incense: herbal or liquid. Herbal incenses are products composed of dried, shredded plant material and sprayed with a variety of chemicals with psychoactive properties; these are designed to be smoked. The products known as liquid incense are liquid formulations designed to be heated, vaporized, and inhaled via handheld electronic devices.[4] Because both the herbal and liquid forms are referred to as *cannabinoids* or *Fake Weed*, the perceived potential for adverse consequences may be hard to evaulate.[5] This is supported by recent data that indicate these synthetic products appear to be associated with potentially dangerous physical and psychiatric health effects more severe than reported with marijuana. Negative physical health effects reported include seizures, cardiac damage (including myocardial infarction), and renal impairment. Adverse psychiatric consequences included aggression, confusion, anxiety, and psychosis.[6]

Since 2004, a number of different products have been developed, and overall potency has increased.[6] Providing specific treatment options for intoxication may be limited to clinical presentation because of the lack of commercially available products for routine screening or detection.[7] To help clinicians and other health care providers identify potential SC users experiencing adverse psychiatric effects, a brief history describing a patient admitted to inpatient status secondary to prominent psychiatric symptoms is presented. Literature was reviewed to identify commonly reported psychiatric signs and symptoms of SC use to help facilitate clinician awareness.

Case Presentation

A 47-year-old African American man was presented for involuntary inpatient admission after being brought in by police secondary to bizarre behavior. No lab work was obtained in the emergency department prior to admission to inpatient status because of the patient's level of psychosis and inability to willingly provide blood or urine. Vital signs upon admission were temperature 98.9°F, heart rate 104 beats per minute, respiratory rate 20 breaths per minute, and blood pressure 153/103 mm Hg. The patient was subsequently able to report a history of hypertension and medication nonadherence. On presentation he exhibited delusions, hallucinations, and agitation. He was unable to participate in a full assessment. One olanzapine oral disintegrating 10-mg tablet was given. Use for agitation was unsuccessful; after several hours, the patient tried to leap over the nurses' station in efforts to escape and continued with aggression toward peers and staff. At that time he received a single intramuscular dose of haloperidol 10 mg in combination with lorazepam 2 mg and diphenhydramine 50 mg. He then spent the rest of the evening in a designated quiet room to decrease stimuli, where he slept all night and woke the next day, clear and coherent. At that time he was able to participate in the milieu and evaluation process. He continued to decline to provide either a blood or urine sample. He reported that he had smoked a substance called *King Kong* that a friend had given to him. He also stated that he had only smoked this substance on 3 occasions but admitted that on each occasion, he wound up involuntarily hospitalized. The remaining course of admission was unremarkable. He was discharged to continue his home regimen, which he refused to disclose and also refused to disclose his outpatient psychiatrist.

The patient profiled in the example was able to participate and provide additional information by the following day. The presence of polysubstance use could not be ruled out; during the course of this admission, evidence for the presence and diagnosis of a severe mental illness was not substantiated.

Discussion

Psychiatric symptom presentation related to the use of SCs has been reported in case reports/series and review articles. Aggregate information on psychiatric symptom presentation has been available through databases collecting and reporting toxicology findings. A 2010 state database of SC exposures (n = 464 343 males, 118 females, 3 unknown) identified common presentations of psychiatric symptoms, including agitation, anxiety, and auditory and visual hallucinations.[8] During the same year, a National Poison Data System 9-month survey of single-exposure data reported the following symptoms: delusional thinking, auditory and visual hallucinations, agitation, anxiety, and confusion.[9] More recently the Drug Abuse Warning Network released information on emergency department visits due to SC, specifically citing the statistically significant increase in use (estimated 8830 visits in 2010 compared with 19 923 in 2011). The report specifically identified the following psychiatric features: severe agitation, anxiety, hallucinations, and paranoid behavior. Physical health symptoms included gastrointestinal disturbances (nausea, vomiting), tachycardia, hypertension, and seizures.[10]

In 2016, Fattore[11] conducted a literature review to evaluate the relationship between SC use and psychotic symptoms between 2010 and 2015. The author focused on acute effects and psychosis, separating the latter into reemergence and new-onset cases. Acute effects included seizures, agitation, hallucinations, irritability, and chest pain. Psychosis was reported in SC-naïve and SC-experienced patients. There were 26 new-onset or SC-

naïve patient cases and 21 reemergent cases for the SC-experienced cohort. These data were based on information from poison control databases, case reports, and surveys.[11]

Health Care Provider Strategies

Standardized treatment protocols have not been developed because of patient population heterogeneity, a wide range of presenting symptoms, and the lack of controlled studies.

Consistent with treatment strategies for other psychiatric diagnoses, collecting the following information and resolving any findings that might be contributing factors are recommended: obtain lab results (basic metabolic panel, complete blood count, urine drug screen),[12] correct electrolyte imbalance(s), provide adequate hydration, identify and discontinue any suspected agent(s),[13] and evaluate for delirium.[14] Currently there are no established algorithms addressing SC-induced symptoms; pharmacotherapy options that have been used to treat a patient presenting with symptoms of SC intoxication include antipsychotics, benzodiazepines, and anticholinergics.[14]

Brown and colleagues[12] outlined a triage plan to provide a treatment algorithm for stabilization of these patients. Their evaluation and treatment strategies included the use of antipsychotic medication for patients with no preexisting history of or known cause for the psychosis, and patients with a known or suspected cause. Both treatment arms included the use of intramuscular ziprasidone and olanzapine. Given the rapid onset of action, the authors[12] opined these 2 agents may represent emerging first-line therapy options.

Adverse medication-related effects may be more problematic in patients with anxiety, psychosis, or agitation. Akathisia may exacerbate anxiety already present and may be mistaken for agitation, leading to the inappropriate use of an antipsychotic. This could further exacerbate akathisia. Ziprasidone[15] and olanzapine[16] studies reported rates for akathisia of 8% to 10% and 5% to 27%, respectively. Oral doses of quetiapine and risperidone have been helpful in managing patients with mild-to-moderate symptoms, provided they are able to take oral medication.[17] Considerations for the benefits of using second-generation antipsychotics compared with first-generation antipsychotics include the rates of drug-induced adverse effects, targeted behaviors (such as aggression and/or agitation), and the impact of long-term use if a primary mental illness is diagnosed.[14,17]

Currently, there is little definitive evidence to support the superiority of one antipsychotic over another in treating acute psychotic symptoms. However, studies have shown that first-generation antipsychotics, with or without anticholinergics or benzodiazepines, are superior to benzodiazepine monotherapy in patients experiencing acute psychotic symptoms, such as delusional thinking, hallucinations, and agitation.[14] Regardless of the agent selected, the need for rapid tranquilization to prevent injuries to the patient, peers, and caregivers should be considered in the context of risk/benefit. In addition, individual patient variables influencing product selection include the potential of prolongation of the QT interval and lowering the seizure threshold.[18] The need for additional monitoring, and the anticipated duration of therapy will help guide the clinical decision-making process.[18]

Individual facilities may develop a treatment algorithm to triage this patient population. Consideration should be given to a number of strategies in the establishment of these guidelines. These include considering SC use when evaluating patients presenting with signs and symptoms that may be consistent with substance use/abuse, regardless of urine drug screen results. If SC use is suspected, anticipate the duration of effects, which may range from 1 to 7 hours, prior to initiating pharmacotherapy. Provide contact information for the Poison Control Center toll-free number (1-800-222-1222) for assistance, management, and adverse effect(s) reporting.

Identifying SC use is challenging. Problems include the inability of standard urine drug screening products to detect these compounds and the variability of product formulation and potency. Detection assays based on enzyme-linked immunosorbent properties have been developed for some of the metabolites.[19] The extent to which these products are available and the cost of the screening are not known. Because of these limitations, patient evaluation may be limited to evaluation of a metabolic panel, complete blood count, urine drug screening available in the individual facility, and clinical presentation. Cases of suspected overdose, underreported presentations, or new, previously unreported side effects or interactions may not be obvious.

Conclusions

Synthetic cannabinoids encompass a group of compounds that may present with various psychiatric symptoms and effect durations, as shown by case reports/series, symptom surveys, and toxicologic reviews. Suggested treatment options were briefly reviewed. Clinicians are encouraged to use their professional judgment; base therapy choices on patient characteristics, symptom presentation, and anticipated duration of effects; and give special consideration to the potential adverse effect

profiles of pharmacotherapy options. In addition, clinicians are encouraged to report SC use to increase awareness and advance the body of literature around this subject.

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