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Synthetic Cannabinoid-Induced Psychosis

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SYNTHETIC CANNABINOID-INDUCED PSYCHOSIS

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Abstract

This paper explores the relationship between the intake of synthetic cannabinoids (SC) and the presentation of psychotic symptoms. The patient is a 37-year-old Caucasian male who presented with new-onset psychotic symptoms after reportedly smoking SC. His symptoms most notably included auditory and visual hallucinations, paranoia, disorganized thought process, delusions and specifically delusions of grandeur. The literature was reviewed, and it was found that the patient was exhibiting symptoms common of SC-induced psychosis. There is no antidote, nor are there specific treatments for SC intoxication; therefore, supportive treatment of symptoms is recommended. The main treatment recommendation in the literature for remission of symptoms of psychosis is antipsychotic medication. Olanzapine is noted to be used in many of the articles reviewed, which is the medication that was prescribed to the patient of interest in this paper. Benzodiazepines are frequently mentioned in the literature for symptoms of agitation, however, this patient did not present with agitation, and benzodiazepines were therefore not used in his treatment. SC-induced psychosis is an issue that has emerged in the United States over the past decade. Due to the continued availability of SC, this is an issue that is likely to be encountered by mental health care professionals. It is important for mental health care professionals to educate themselves on SC and be aware of the effects of use of SC, including symptoms of SC-induced psychosis, screening for SC use, and treatment of SC-induced psychosis.

Synthetic Cannabinoid-Induced Psychosis

Synthetic cannabinoid (SC) abuse has become a widespread problem. SCs have been available in the United States since 2008, and adverse effects from use, which range from changes in mental status to death, have been reported in all 50 states (Centers for Disease Control and Prevention [CDC], 2018). Though many SCs are illegal at the federal level, manufacturers continue to alter the chemical compositions, resulting in new compounds, which, in turn, are not technically illegal (CDC, 2018). Since they began collecting data, the number of calls to poison control centers each year reporting adverse health effects in individuals using SC has ranged from approximately 2,000 to a peak of nearly 8,000 in 2015 (American Association of Poison Control Centers, 2018). However, these are just the reported cases to poison control centers and do not account for the numerous cases that are not reported. There are a number of adverse effects caused by the use of SC that have been reported; these include various neurologic and other physical signs and symptoms and, most notable for this review, psychiatric signs and symptoms including hallucinations, delusions, psychosis, violent behavior, and suicidal thoughts (CDC, 2018).

The use of SC to get "high" is attractive to some because these chemical compounds are not detectable in the average urine drug screen. Some even believe SCs to be safe, as they can be purchased easily online and in some areas can be purchased at places like convenience stores and tobacco shops. SC are sold legally under many names, but two of the most well-known are "Spice" and "K2." Patterns of SC use are similar to those of other drugs of abuse with higher numbers of use for people in their twenties and thirties with men more likely to use than women. Users of SC are also more likely to abuse other drugs, including marijuana (CDC, 2018).

The likely user and psychiatric symptoms described here are fitting of the patient presented in this case report. The patient was a male in his thirties who admitted to smoking

marijuana on a regular basis. He presented with increasingly odd behavior, including paranoid thoughts, hallucinations, and psychosis following the use of SC.

Case Report

The patient is a 37-year-old Caucasian male who was brought to the inpatient behavioral health hospital on a 72-hour Minnesota Mental Health Hold. The patient's wife had called police due to his unusual behavior, and he was transported to the emergency department via law enforcement. In the emergency department, it was documented that the patient exhibited paranoid and delusional thought content, hyperreligiosity, and he expressed to his wife that he was Jesus. He reported auditory and visual hallucinations. Due to concerns for safety and the patient not wanting to be admitted voluntarily, the patient was placed on a mental health hold and referred to inpatient hospitalization for a full psychiatric evaluation. Though the patient's wife had accompanied him to his local emergency department, she did not accompany him to be admitted for inpatient hospitalization and was not available by phone when attempts to gather collateral information were made.

The patient displayed loosening of associations, flight of ideas, and an overall disorganized thought process. The exact time line of the history of present psychiatric illness was difficult to ascertain. However, through what the patient reported, it appeared that his odd behaviors had manifested over the previous two weeks. The patient attributed his behavior changes to smoking SCs given to him by a friend.

The patient lived with his wife of six years and their three children. He had recently been fired from his job at a cold storage warehouse facility due to odd behaviors and stated that his new job was to "spread the Word." The patient reported hearing "corporate" voices and described these as premonitions. He voiced paranoid thoughts and stated that he was afraid someone was trying to harm him and reported, "One guy took a picture of me and showed it to

another person." The patient also stated, "There was a murder that took place; whenever that happens they're trying to hide something." The patient reported he had only been sleeping approximately 40 minutes per night for years.

The patient had no known past psychiatric diagnosis, no prior psychiatric hospitalizations, and no history of outpatient psychiatric care. He denied any past trials of psychotropic medication. He did report a suicide attempt more than seven years ago via carbon monoxide poisoning but could not describe the circumstances leading to that event. The patient had a history of methamphetamine abuse, infrequent alcohol use, and current marijuana use on a nearly daily basis. He reported one occasion of inpatient substance abuse treatment, but it was difficult to determine whether it had been voluntary or mandated.

The patient's past medical history included two shoulder surgeries within the past three years, which resulted in chronic shoulder pain. He denied any other significant medical history or current medical conditions. Labs obtained in the emergency department included: complete blood count without differential, basic metabolic panel, hepatic function panel, thyroid-stimulating hormone, acetaminophen level, salicylate level, urine drug screen, and ethanol level. The patient's drugs screen was positive for tetrahydrocannabinol, and AST was elevated at 61 U/L, but all other labs were unremarkable.

The patient reported rectal pain, stating that he believed a "gold bug" crawled in his rectum. Because the patient's complaint focused more on the pain rather than the belief regarding the gold bug, there was concern that he had inserted foreign objects in his rectum; therefore, a consult for internal medicine was ordered. A certified nurse practitioner met with the patient and completed a visual exam and digital exam for the rectal pain with no significant findings. However, at that time the patient also reported left ear pain due to trying to "remove

the gold bug" from his left ear. The examination did reveal significant erythema and apparent self-inflicted trauma. Antibiotic eardrops were ordered.

The patient met all diagnostic criteria for the diagnosis of substance-induced psychotic disorder as described in the *Diagnostic and Statistical Manual of Mental Disorders,* Fifth Edition. The patient was experiencing delusions and hallucinations, as is noted in the previous description. His symptoms developed soon after the substance intoxication or withdrawal, and the substance is capable of producing the symptoms. The patient reported these symptoms as new and related it to the recent intake of SC, which has been documented as capable of producing these symptoms. The patient's disturbance was not better explained by a psychotic disorder, as there was no evidence that the symptoms preceded the substance use, and no previous psychiatric history was noted. The disturbance did not occur during the course of a delirium as there was no physiological evidence of delirium. The disturbance caused clinically significant distress, as evidenced by the patient's report of losing his job and his wife calling police due to his behavior (American Psychiatric Association, 2013). The patient also met criteria for a diagnosis of cannabis use disorder, severe, in a controlled environment. Differential diagnoses considered for this patient included brief psychotic disorder and bipolar 1 disorder with psychotic features.

Pharmacological treatment was the main focus for resolution of the patient's presenting symptoms. The patient had been admitted at 0400 and did go to sleep following admission. After being interviewed for his initial psychiatric evaluation later that morning, he was ordered a "now" dose of olanzapine 5mg due to his reported lack of sleep and presenting psychotic symptoms. The patient refused the olanzapine as he had been informed that it may help with his symptoms, including the auditory hallucinations, and he stated that he did not want to stop the voices. A daily scheduled dose of olanzapine 10mg PO HS was ordered, and the patient did take

it that night and every night as scheduled throughout his hospital stay. The patient was noted to sleep between six to seven hours per night the remaining nights of his admission.

Daily assessments noted obvious delusional thinking and disorganized behavior in the beginning of his stay; however, the noted symptoms dissipated over the course of his admission. On day five of his hospital stay, the patient requested discharge. At that time he denied auditory and visual hallucinations, paranoia, delusional thinking, and suicidal and homicidal ideation. No overt signs of psychosis or mania were noted, and the patient was not observed to be responding to internal stimuli. The patient was noted to have insight regarding his behavior changes and the departure from his usual thinking. It was believed that the patient had full capacity to make decisions and was deemed appropriate for discharge. The patient was discharged on olanzapine 10mg PO HS. He was set up for an outpatient medication management follow-up appointment one week from his discharge date and an appointment with a mental health therapist two weeks from his discharge date.

Literature Review

Pharmacodynamics

Delta-9-tetrahydrocannabinol (THC) is the primary psychoactive component in cannabis. SCs are analogs of THC and full agonists at the cannabinoid-1 and cannabinoid-2 receptors, while THC is only a partial agonist. When compared to THC, SCs have a higher affinity for these cannabinoid receptors and show increased efficacy, which some suspect is the reason why SCs can cause adverse effects that are often unpredictable (Deng, Verrico, Kosten, & Nielsen, 2018; Papanti et al., 2013). Natural cannabis plants also contain the compound cannabidiol (CBD). Though the use of natural cannabis has been associated with the occurrence of psychotic symptoms, it has been observed that cannabis with higher levels of THC and lower levels of CBD is more likely to be associated with psychotic symptoms while cannabis with higher levels

of CBD is less likely to be associated with the onset of psychotic symptoms. CBD has been shown to have antipsychotic and anxiolytic properties. SCs do not contain any CBD and, therefore, do not have the protective properties that may come along with it (van Amsterdam, Brunt, & van den Brink, 2015).

Effects of Use

Shortly after consuming SC, users experience the sought-after effects of euphoria, relaxation, and feelings of joy and laughter (Martinotti et al., 2017). However, a number of undesirable neuropsychiatric symptoms have also been noted; these include auditory hallucinations, visual hallucinations, paranoid delusions, flat or odd affect, depersonalization, dissociation, illusions, thought blocking, disorganized speech, bizarre or disorganized behavior, alogia, suicidal ideation/behavior, insomnia, psychomotor retardation, psychomotor agitation, catatonia, anxiety, agitation, and verbal or physical aggression (Bassir Nia, Medrano, Perkel, Galynker, & Hurd, 2016; Hurst, Loeffler, & McLay, 2011; Martinotti et al., 2017).

Psychotic disorders related to the use of SC have been observed in various types of patients including acute psychotic episodes in otherwise healthy people with no history of psychosis, a worsening of symptoms in patients already diagnosed with a psychotic disorder, and a relapse of symptoms in patients previously known to have a psychotic episode. For those who have never experienced psychotic symptoms, an acute psychotic reaction is possible after just one single use of SC (Martinotti et al., 2017).

Symptom Severity, Treatment, and Resolution of Symptoms

Studies have compared SC use with cannabis use in respect to psychotic symptoms. Hallucinations and delusions are more likely to occur with SC use, and psychotic episodes of SC users are more severe with higher rates of agitation and aggressive behavior, longer hospitalizations, and the patients are more likely to be hospitalized by court order (Martinotti et

al., 2017; Shalit et al., 2016). Bassir Nia et al. (2016) completed a retrospective chart review of patients admitted to a dual diagnosis psychiatric unit in which they compared SC users to cannabis users and patients who used neither SC nor cannabis. They found that, overall, SC users were more often diagnosed with a psychotic disorder, had longer hospital stays, and were prescribed higher doses of antipsychotics. In the review by Bassir Nia et al. (2016), they found that the mean length of hospital stay for those admitted with SC use without cannabis use had the longest mean length of stay in the hospital with a mean of nearly 17 days. In a study comparing patients admitted to the hospital for SC-induced psychosis versus those with schizophrenia, Altintas, Inanc, Oruc, Arpacioglu, and Gulec (2016) found that the mean length of hospital stay was just over 14 days for those with SC-induced psychosis, which was notably less than the mean 28 days for those hospitalized with schizophrenia.

There is no antidote available for SCs, such as naloxone is available for opioid overdose. Therefore, supportive care is offered for symptom management for acute SC intoxication (Cooper, 2016; Tait, Caldicott, Mountain, Hill, & Lenton, 2016). Symptoms of agitation can usually be controlled with benzodiazepines, though antipsychotics such as haloperidol are also used (Tait et al., 2016). A multicenter analysis conducted by Monte et al. (2017) looking at cases that were classified as SC toxicity found that the most common symptoms were agitation, delirium, and toxic psychosis. Benzodiazepines were the most common pharmacologic treatment provided, followed by antipsychotics, which both appeared to be safe as treatment options for these patients.

Oluwabusi, Lobach, Akhtar, Youngman, and Abmrosini (2012) presented two case studies of adolescent boys experiencing new-onset psychosis after smoking SC. One boy was trialed on quetiapine and then aripiprazole and was stabilized, but within months experienced a

relapse of symptoms so was treated with olanzapine. The second boy was started on olanzapine as a first choice medication. Both boys had successful treatment of symptoms with olanzapine.

Deng et al. (2018) reviewed 29 articles presenting case studies, with some articles presenting multiple case studies, reporting SC induced psychosis. Most case studies focused on first-onset psychosis in patients with no previous history of psychosis while a few discussed patients with a previous history of psychosis reporting psychosis relapse. For those case studies that named the medications used for treatment, olanzapine was the antipsychotic named most often, followed by haloperidol, risperidone, and aripiprazole, all with similar numbers, two cases with initiation of clozapine, as well as one mention of quetiapine. In this case study review, lorazepam was often used and was the only benzodiazepine specifically named.

Valeriani et al. (2015) conducted an analysis over the course of one year in which they monitored various websites focused on novel psychoactive substance (NPS) use, including synthetic cannabinoids. They found that the users of these NPSs had discussions via online forums regarding “bad trips” and how to best treat NPS-induced psychosis. Valeriani et al. (2015) found that olanzapine had been described as the “ideal molecule” by NPS-users to treat NPS-induced psychotic symptoms and end bad trips. Though this anecdotal data cannot considered as scientific proof, it is indicative of the benefits of olanzapine for SC-induced psychosis.

Psychotic symptoms resulting from SC use can vary in time to resolution. In a case report by Hurst et al. (2011) focusing on ten men with new-onset psychosis after smoking SC, they reported that the psychotic symptoms resolved within five to eight days for seven of the patients while three of the patients were reported to experience psychotic symptoms for more than five months.

One concern studied by Niemi-Pynttäri et al. (2013) is that substance-induced psychotic disorders can be a predictor of schizophrenia. They point out that an important feature of a substance-induced psychosis is that the symptoms often remit once the substance has been eliminated from the body. Following their 17-year investigation, they concluded that the substance-induced psychotic disorders may predict schizophrenia spectrum disorders to a higher degree than had been thought. Though this study took place before synthetic cannabinoids were a commonly used drug, it is noted that the eight-year cumulative risk of receiving a schizophrenia spectrum diagnosis for those initially admitted to the hospital with a cannabis-induced psychosis diagnosis was 46%. This was the highest of any substance investigated for this study. Therefore, Niemi-Pynttäri et al. (2013) suggest that a greater emphasis should be placed on clinical follow-up for those who are treated for substance-induced psychosis.

Testing and Detection

SCs cannot be detected by routine urine drug screens. To test for the presence of SC, samples often must be sent to a specialized lab costing additional time and money. Some SCs can be detected by laboratory tests designed for specific SC compounds, and some of the more common ones do have urine tests capable of detecting them. Unfortunately, the regular development of new SC compounds that are made available on the market make it difficult for laboratories to keep up with developing tests that are able to identify SC in patient samples. By the time testing is available for newly discovered SC compounds, SC developers have often already moved on to develop other new compounds (Castellanos & Thornton, 2012; Seely, Lapoint, Moran, & Fattore, 2012; Trecki, Gerona, & Schwartz, 2015).

Because testing is often not immediately available to detect SC use, clinicians may need to look for clues elsewhere. According to Castellanos and Thornton (2012), if a patient presents with signs and symptoms of natural cannabis use or an unexplained sudden onset of psychosis,

clinicians should suspect SC use if a routine urine drug screen is negative or the patient is in a situation where his or her urine is being monitored for drugs regularly. Also, even when cannabis use is known or detected, clinicians should still assess for SC use (Gunderson, Haughey, Ait-Daoud, Joshi, & Hart, 2012).

Implications

SCs are relatively new to the United States, so there is much to learn. The majority of the available literature includes case reports and retrospective chart reviews. Additional research, including research on long term effects, is needed. Many SC users see SC as a safe high due to its legal status and the fact that it can often be easily obtained in local stores. Education for clients and communities regarding the risks associated with SC is key. Though natural cannabis should not be presented as safe, it may be appropriate to provide education regarding the lack of protective CBD in SCs as well as the possibility that its higher affinity for cannabinoid receptors could cause unpredictable adverse effects. Such information could help educate and dispel the myth that SC can be considered a safe alternative to natural cannabis.

Nurse practitioners also need to educate themselves on SCs including patterns of use, signs and symptoms to watch for, and appropriate treatment options. Screening for SC use should become part of a nurse practitioner's usual substance use screening and should especially be screened for in patients presenting with agitation or psychosis of an unknown cause. The use of antipsychotics and benzodiazepines is appropriate in patients presenting with SC-induced psychosis and should be considered for treatment of symptoms of psychosis.

The United States, as well as other countries, has taken some measures to try to make SCs illegal. According to Fattore (2016), in 2011 the Drug Enforcement Administration placed a ban on SCs. In 2013 the Synthetic Drug Abuse Prevention Act was enacted to place SCs in the Schedule I category for controlled drugs. A number of SC compounds have also been banned

legislatively at the state level (Brents & Prather, 2014). Placing specific SC compounds on the list of banned substances became problematic as manufactures worked around these bans by synthesizing new compounds with minor changes. Some European countries have legislation that provides for a broader definition of prohibited drugs to target entire classes of substances instead of specific molecules (Fattore, 2016). Members of the community, including nurse practitioners, need to be active and involved in legislative pushes to get SCs banned completely to ensure that they are not readily available, which would help to reduce the number of people being seen with SC-induced psychosis immensely.

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