

Psychotic Disorder Associated With Synthetic Cannabinoid Receptor Agonists: A Case Report



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SUMMARY

Recently, synthetic cannabinoid receptor agonists (SCRA) rank among the most frequently used abused substances. The most frequently used SCRA in the Turkish Republic of Northern Cyprus is JWH-018, which is also known as 'Bonsai' on the streets. For the cases reported on SCRA use, the most frequently observed symptoms are agitation, irritation, delusions of persecution and delusions of reference, disorientation, epileptic seizures, and nausea. Although the overall effects of SCRA are similar to cannabis, its stimulating effects are greater. The lack of cannabidiol agent in preparations containing SCRA, which is reported to decrease the psychosis triggering effects of cannabis, may explain the relation between SCRA and the psychotic disorder. In this report, a case of a rare psychotic disorder that developed following repeated use of SCRA and its treatment are presented.

Keywords: Synthetic Cannabinoid Receptor Agonist, psychotic disorder, cannabis

INTRODUCTION

Recently, synthetic cannabinoid receptor agonists (SCRA) rank among the most frequently abused substances. The first online sale of SCRA over the internet started in 2004 (Bozkurt 2014). Despite health issues and dependency risk, SCRA's have not been defined as illegal substances in many countries (Tung et al. 2012). Until now, more than 140 substances that contain SCRA have been defined (Levin et al. 2014). Although there are many substances containing SCRA, the most widely used SCRA's are K2 (United States), Spice (Europe), Chronic (Australia), and Bonsai and Jamaican (Turkey). The most frequently used SCRA, Bonsai, is also known as JWH-018. The use of this substance was prohibited after the year of 2011.

Cannabinoids are psychoactive substances that act upon cannabinoid type 1 (CB1) and cannabinoid type 2 (CB2) receptors (Kayaalp and Uzbay 2012). CB1 and CB2 are dependent on G proteins that suppress adenyl cyclase activity (Pertwee

1999). The most widely known natural cannabinoid is Δ^9 -tetrahydrocannabinol (THC) which is found in cannabis. The use of it was restricted due to its dependency potential risk in the beginning of twenty first century (Bozkurt 2014). On the other hand, SCRA was produced for medical use in the laboratory setting (Huffman et al. 1994). SCRA is known for its enhanced effectiveness and has greater psychoactivity than THC (Harris and Brown 2013). This is most likely due to the fact that THC has a partial agonistic effect on its receptors, while SCRA are full receptor agonists (Jerry et al. 2012).

Although the exact usage frequency of SCRA is not known, it is believed to be more frequently used among teenagers (Bozkurt 2014). In a study conducted with 852 university students (with a mean age of 20.6 ± 5.1 , 47 % female), the ratio of K2 use was reported to be 8.0% with a higher prevalence in men. In this study, it was observed that the use of K2 was more frequent at the ages of 18-19 compared to 20 and above and ones in their first two years compared to the ones in their third and fourth year in the university (Hu et

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al. 2011). In a study performed in Germany, SCRA use was reported to be 1.8-1.9 % for the ages of 18-24, and it was reported to be 0.1-0.3% between the ages of 30-49 (Pabst et al. 2010). In a study conducted investigating SCRA use in Australia, the reasons for the first use were determined as 'curious' (50%), 'legal' (39%), 'availability' (23%), 'entertainment' (20%), 'therapeutic' (9%), 'not determined in standard urine tests' (8%), and 'aimed to decrease or cease cannabis use' (5%) (Barratt et al. 2013).

There are a limited number of psychotic disorder cases following the use of repeated SCRA use (Muller et al. 2010, Hurst et al. 2011). This case reported here features a rare acute psychotic disorder that developed following repeated SCRA use. Its treatment regime will also be discussed.

CASE

A 31 year old unemployed male that was single with a secondary school graduate degree was living with his parents. The patient was admitted to a psychiatry clinic for the first time by his family due to complaints of anger, insomnia, and suspicion. He was smoking 2 grams of Bonsai three times a week for 6 months, followed by 6 grams almost daily in the last 6 months. In this period, there were no breaks from smoking Bonsai. Two months ago, insomnia and the thoughts of harming his family as well as himself started. He began thinking that he was being followed by his neighbor, and that drug was put into his meal when he went out for meals.

The patient had no previous history of substance or regular alcohol use or abuse. No specific characteristic was determined in the family history. He had used bonsai 10 hours prior to applying to our clinic. In the mental status examination, his psychomotor activity was increased. Nervous and distressed affect as observed, and nervous and distressed mood was reported. He was talking with a loud voice, and his associations were loose and were out of scope. In his thought content, delusions of persecution and reference were defined. No distortion of perception was found. The assessment of reality was distorted. The patient was assessed with a Brief Psychiatric Rating Scale (BPRS) during his clinical follow-up (Overall and Gorham 1962. Translated To Turkish By: İncila Kaplan, M.D, Mehmet Akif Sayılğan, Psy. D, Nilgün Tanrıverdi, M.D, Senar Yıldız, Psy.). His BPRS score at the admission was 51.

The results of Brain Computed Tomography (CT) Imaging, Full Blood Count, biochemistry, thyroid function tests, and B12 vitamin level tests (which were requested to exclude disorders related with a medical condition) were normal. The urine and blood tests results were negative, and exclusion of other substances was validated. The patient had no signs of withdrawal symptoms specific to a substance.

The patient was diagnosed with Substance Induced Psychotic Disorder (SIPD) according to DSM IV (American Psychiatric Association 2000), and was administered 20 mg/day olanzapine treatment with hospitalization. In the psychiatric examination performed five days later, psychomotor activity was normal, affect was distressed, and associations were regular and relevant. His delusions of persecution and reference were regressed. At the end of the tenth day, no psychotic symptom was observed in the psychiatric examination. His BPRS score was 10. The patient was discharged with 20 mg/day olanzapine and cognitive behavioral psychotherapy.

DISCUSSION

Although the effects of SCRA are similar to cannabis, acute intoxication has a much more similar quality to stimulating and sympathomimetic substance use in SCRA (Bozkurt 2014). The most common symptoms in acute intoxication that develops with SCRA use is reported as perceptual changes, impaired vision and visual hallucinations, anxiety, outburst, tachycardia, hypertension, nausea, hypocalcemia, mydriasis and hyperglycemia. Agitation, seizure, hypertension, nausea, and hypocalcemia which are seen in SCRA intoxication are not symptoms generally seen in high dose cannabis use. Most likely, these findings are related to the strong stimulation of KB1 receptors (Hermanns-Clausen et al. 2013). Barratt and colleagues (2013) reported that 68% of individuals who use SCRA experienced at least one side effect. The most commonly reported side effects in this study are the decrement in motor coordination (39%), dissociation (22%), dizziness (20%), paranoia (18%), and psychosis (4%). In the cases related with SCRA use, the most common symptoms are agitation, bursts of anger, disorientation, delusions of persecution and reference, seizures, and nausea (Schneir et al. 2010).

In our case, bursts of anger, agitation, and delusions of persecution and reference were prominent, while there were no seizure, hypertension, and hypocalcemia. We can explain this variety of symptoms observed as related with SCRA with the effects of SCRA on KB1 and KB2 receptors. KB1 receptors are intensely seen in the amygdala, ventral tegmental area, and the nucleus accumbens, which are related with sensory regulation of the brain in the hippocampus and neocortex (Glass et al. 1997). KB1 receptors are additionally found in the brain stem, and their stimulation may be responsible for cardiovascular, respiratory, and emetic effects of SCRA (Muccioli 2007). KB2 receptors are intensely found in spleen, timus, and tonsils; and therefore, are known as immune function regulators (Seely et al. 2011).

In the literature, one case reported didn't have psychotic symptoms, despite the use of high amounts of THC for long years. This patient was observed to have psychotic periods with agitation, visual hallucinations, and disorganized and

bizarre behaviors after using SCRA for 60 days (Peglow et al. 2012). Again in other cases, SCRA was demonstrated to result in acute psychosis (Muller et al. 2010, Every-Palmer 2010). In New Zealand, 17 patients were reported to be hospitalized 21 times after using SCRA and were found to have psychotic symptoms like paranoia, disorganized behavior and mood changes (depression and anxiety), and suicidal ideation and behavior (Glue et al. 2013). In the history of our case, the absence of alcohol and other substance abuse provides strong support for the use of SCRA leading to acute psychosis. In preparations containing SCRA, the lack of cannabinoid substance which is known to decrease the effects of cannabis may explain the relation between SCRA's and psychotic disorders (Spaderna et al. 2013).

In Germany, a case who had a use of SCRA also known as Spice for 8 months regularly and who had withdrawal symptoms including tremor, headache, nightmares, nasal discharge, the desire to use the substance, hypertension and tachycardia on the fourth day of hospitalization after quitting SCRA use was reported (Zimmermann et al. 2009). As for our case withdrawal symptoms were not observed. THC resulting in withdrawal symptoms is a controversial issue. According to DSM IV withdrawal symptoms related with cannabis use were not clinically significant. In a study which reports that after quitting THC use, withdrawal symptoms like anxiety, nervousness, stomach ache, and loss of appetite appeared and the long half-life of THC was reported to make the appearance of sudden withdrawal symptoms difficult (Alici and Uzbay 2006).

There is no antidote that can be used for SCRA intoxication. Symptomatic and supportive treatment is suggested (Spaderna et al. 2013). The vital signs of patients must be monitored, intravenous liquid support should be provided against dehydration, and cold application should be made in case of hyperthermia (Bozkurt 2014). Benzodiazepine for agitation, olanzapine and haloperidol for psychotic symptoms can be used (Spaderna et al. 2013, Bozkurt 2014). In seizures related with SCRA's intravenous benzodiazepines may be used (Simmons et al. 2011).

In conclusion, we describe a patient with a rare psychotic disorder, which developed following repeated use of SCRA. The introduction of SCRA to the market with different names poses a major problem, and has allowed this chemical to overcome legal restrictions. It is more powerful and dangerous than cannabis and may be related to some acute psychotic disorders, but further research must be performed.

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