CASE REPORT

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Dangers of synthetic cannabinoids (bonzai): A case report

Sentetik kannabinoid (bonzai) kullanımının tehlikeleri: Olgu sunumu

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ABSTRACT

Cannabis has become the most widely consumed illicit substance worldwide. Synthetic cannabinoids (SCs), known mostly as JWH agents, were found to have 2-100 times more potent than THC. These are obtained with very minor modifications on the original cannabinoid compound with varying chances to be detected in routine toxicological screens. Recently the use of SCs known as Bonzai has increased considerably and SC-related deaths have increased a lot. We present a male patient who was hospitalized with the history of SC (bonzai) abuse for 3 months and started to have convulsions after using SC and brought to emergency department with chest pain and loosing consciousness immediately after using SC 1 month ago. His toxicological analysis revealed no sign of illicit drugs. EEG showed paroxysmal slow waves with sharp characteristics in both hemispheres. Mortality due to SCs may be related to sudden cardiac death in the acute phase which may result from the stimulation of sympathetic nervous system and epileptic abnormalities may be due to inhibition of γ-aminobutyric acid (GABA) neurotransmission. Novel generalized seizures and chest pain especially in young people should be warning for neurologists and cardiologists in terms of potential SC abuse.

Keywords: *Synthetic cannabinoids, bonzai, generalized epileptic seizure*

ÖZ

Kannabis dünya çapında en yaygın olarak kullanılan uyuşturucu maddedir. Daha çok JWH maddeleri olarak bilinen sentetik kannabinoidler (SK). THC maddesinden 2-100 kat daha potent etki gösterebilmektedir. SK'ler orijinal kannabinoid maddesi üzerinde yapılan çok küçük değişikliklerle elde edilmektedir ve rutin toksikolojik taramalarda bu nedenle saptanamamaktadır. Yakın zamanda bonzai olarak bilinen SK'lerin kullanımı ve buna bağlı ölümlerde artış gözlenmektedir. Biz üç aydır SK (bonzai) kullanan, 1 ay önce SK kullanımı sonrasında bilinç kaybı ve göğüs ağrısı şikayeti ile acil servise götürülen, SK kullanımı sonrası epileptik nöbetleri gelişen bir hastayı sunduk. Hastanın toksikolojik taramasında uyuşturucu maddeye rastlanmamıştı. Elekroensefalografi sonucunda her iki hemisferde keskin karakterli yavaş dalgalar rapor edildi. SK kullanımına bağlı epileptik nöbetler γ-aminobütirik asit (GABA) nörotransmisyonunun inhibisyonuna bağlı ve mortalite artışı madde kullanımının akut döneminde gelişen sempatik sinir sistemi uyarımına bağlı ani kardiyak ölümler neticesinde olabilir. Genç hastalarda yeni ortaya çıkan jeneralize epileptik nöbetleri ve göğüs ağrısını değerlendirilmesinde nörologların ve kardiyologların olası SK kullanım riskini göz önünde bulundurmaları gerekmektedir.

Anahtar Kelimeler: *Sentetik kannabinoidler, bonzai, jeneralize epileptik nöbet*

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INTRODUCTION

Herbal cannabis contains more than 60 cannabinoids in which delta 9-tetrahydrocannabinol (THC) (marijuana) is the most effective substance among them (1). Cannabinoids became the most widely used illicit drugs worldwide. Action mechanism of cannabinoids have been demonstrated in the 1980s and 1990s with the detection of specific cannabinoid receptors, namely Cannabinoid Receptor 1 (CB1) in central nervous system and Cannabinoid Receptor 2 (CB2) in peripheral nervous system. The effects of cannabinoids have been started to be studied in diseases such as pain syndromes and neoplasms where their anti-neoplastic effects were claimed (2). Synthetic cannabinoids (naftoilindol the naftoilpirol, etc.) known mostly as JWH agents were first identified in 1990s and they were found to have 2-100 times more potent pharmacological effects than THC (3).

Variety of synthetic cannabinoids has increased rapidly in recent years and new synthetic derivatives of them are being produced in illegal laboratories. Especially "K2" in the United States, "spice" in Europe and "bonzai" or "jamaica" in Turkey hit the market due to lack of available toxicological screening methods. These psychoactive compounds are obtained with very minor modifications on the original cannabinoid compound and their amount and types tend to show regional differences with varying chances to be detected in routine toxicological screens which are mostly inavailable (4). In a study conducted in Turkey which investigated the ingredients of synthetic cannabinoids; 1-pentyl-3-(1-naphthoyl) indole (JWH-018) was found to be as 99,4%, 4-methoxynaphthalen-1-yl- (1-pentylindol- 3-yl) methanone (JWH-081) was found to be as 65,9% and other psychoactive substances were fount to be as 1.7% (5). Because of the constantly changing variety of synthetic cannabinoids, they are mostly not included among the controlled substances inside existing legislations. Therefore, the use of synthetic cannabinoids has become a common problem all over the world and the United Nations Office on Drugs and Crime published a declaration in order to draw attention to this problem in 2013 (6).

Relationships between the use of cannabinoids (marijuana) and myocardial infarction, sudden cardiac death, cardiomyopathy and other serious cardiac side effects, stroke, transient ischemic attack, and cannabis arthritis has previously been described (7). But side effects of synthetic cannabinoids have not been described thoroughly in the literature with detailed studies. Their side effects may include nausea and vomiting, shortness of breath or respiratory suppression, hypertension, tachycardia, chest pain, muscle twitches, acute renal failure, anxiety, agitation, psychosis, suicidal thoughts, cognitive impairment and generalized epileptic seizures (3). Long-term side effects are still unclear. We aimed to present this case report because SCs are increasingly becoming a social threat and our case report clinically demostrates the most important side effects of SCs.

CASE REPORT

Divorced, 37 years old male patient who had begun using THC and stimulating illicit drugs 6 years ago was hospitalized with the history of SC (bonzai) abuse for 3 months. Amount of SC abused rapidly increased up to 1.5 g per day and he reported to have irritability, self-mutilation, sweating and generalized pain whenever he did not used SC. He started to have convulsions after using SC and prescribed with carbamazepine 400 mg/day before hospitalisation. He was brought to emergency department immediately after using SC with chest pain and altered consciousness 1 month ago. He had psychomotor retardation when hospitalised. He had overvalued thoughts of reference but he had not clear psychosis including hallucinations. His toxicological analysis revealed no sign of illicit drugs. Bradycardia (52 beats/min) was detected in the ECG without arrythmia. His troponin levels were within normal values (000.4 ng/mL) and he had slightly elevated CK-MB levels (48 U/L). Echocardiogram examination was normal. Cranial MRI results were unremarkable. EEG showed paroxysmal slow waves with sharp characteristics in both hemispheres. Diazepam 40 mg/day and mirtazapine 30 mg/day treatment was started against withdrawal and epileptic symptoms. Carbamazepine was stopped after the consultation with neurology because his convulsions ceased after he stopped using SC. His withdrawal symptoms decreased gradually within 4 days and patient was discharged on his will at 15th day.

DISCUSSION

Ingredients of the SC our patient was using could not be determined because of the lack of resources at our biochemistry lab. But mostly identified compounds include HU-210, CP 47.497 and homologues, JWH-018, JWH-073, JWH-398, JWH-250 and oleamide in the literature (3). Some of the synthesized compounds in "fake marijuana" (SCs) bind much more strongly to THC receptors than regular marijuana, which can lead to a more powerful, unpredictable or dangerous effect.

In the literature, cannabinoids are usually related with psychotic like side effects in the long run, this should be the case for SCs too (8). But our patient had no clear psychotic symptoms, although he had some overvalued thought which may act as a delusional plot if he had used SCs for longer time. And psychomotor retardation is often

observed after cannabis use similar to our patient but SCs usually present with psychomotor agitation especially in the acute phase.

In the literature, the most common expressed side effect of SCs is tachycardia, although bradycardia was present in our case probably because he was not using SC for one day when hospitalized (9). So tachycardia may be considered as an acute phase side effect of SCs. Arrhythmias and myocardial infarction associated with the use of marijuana have been reported before but serious cardiac side effects of SCs including sudden cardiac death are just beginning to emerge with recent case reports. In a case report, myocardial infarction with troponin elevation and ST-elevation was presented after 60-90 minutes of "K2" use without any abnormalities in the coronary arteries (10). In our case, history of chest pain and loss of consciousness a month ago suggests a prior MI and he had slightly elevated CK-MB levels. Although his ECG findings were unremarkable, nonetheless, we made a full investigation of any cardiac pathology including echocardiography because mortality due to SCs may be related to sudden cardiac death. In the literature, cardiac side effects in the acute phase are thought to result from the stimulation of sympathetic nervous system which in turn causes release of norepinephrine (11).

Especially CB1 agonism due to JWH-018 can increase excitatory neurotransmitters presynaptically and decrease inhibitory neurotransmitters. In our case, epileptic abnormalities detected which had started after SC use. This may be due to the impact of SCs on CB1 receptors or inhibition of γ-aminobutyric acid (GABA) neurotransmission (12). Therefore, it is important to have an EEG control of such patients and use antiepileptics when necessary. Our patient had abnormal EEG which required to use carbamazepine and after succesful treatment of SCs use disorder, he no longer needed to use antiepileptics.

CONCLUSION

Action mechanism of better known cannabinoids has not clarified yet, therefore ever-changing effects and side effects of synthetic cannabinoids currently seems unlikely to predict. Epileptic and cardiovascular side effects of SCs are being reported increasingly in the literature. Novel generalized seizures and chest pain especially in young people should be warning for neurologists and cardiologists in terms of potential SC abuse.

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