Occurrence of Takotsubo Cardiomyopathy after Synthetic Cannabinoid Consumption

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Abstract

Background: Synthetic cannabinoid use such as “K2” and “Spice” is popular due to its inability to be detected in a urine drug screen. It is associated with a wide range of myocardial pathologies including obstructive and non-obstructive coronary disease such as Takotsubo cardiomyopathy.

Case Report: A case report of an emancipated 15-year-old male experiencing Takotsubo cardiomyopathy after using the synthetic cannabinoid “Spice” is presented here.

Conclusion: Synthetic cannabinoids act as full agonists and bind to cannabinoid receptors (CB receptors) with a much greater potency compared to natural forms of marijuana. In particular, “Spice” decreases the release of glutamate via the CB receptor type 1 (CB1 receptor) in higher concentrations, which causes mitogen-activated protein kinase (MAPK) activation with substances released in response to stressful environments being experienced in the body. These effects can cause the sympathetic system to become activated by synthetic cannabinoid use, leading to a surge in catecholamines and a change from normal positive inotropy to abnormally-mediated negative inotropy. Use of synthetic cannabinoids can therefore be associated with Takotsubo cardiomyopathy. This case has important implications for additional examination due to the sparse information describing co-occurrence of Takotsubo cardiomyopathy and synthetic cannabinoid use.

Keywords: Designer drugs; Takotsubo cardiomyopathy; Cannabinoids

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Introduction
Marijuana usage has become rampant in today’s society, especially with the legalization of recreational utilization in several states and countries. Subsequently, users may develop tolerance and crave a more potent product and subsequently turn to the consumption of synthetic cannabinoids. Synthetic cannabinoids come in many flamboyant names such as “K2”, “Spice”, and “Cloud 9”, to name a few.¹ The original synthetic version was created sometime around the 1960s to 1970s.¹ These types of cannabinoids have been thought to be natural by some consumers but are actually psychoactive plants such as Leonotis leonurus or Pedicularis densiflora among others, combined with a solvent that can be easily evaporated, leaving varying degrees of the synthetic cannabinoid.² This form is also more popular due to its inability to be detected in urine.³ As a result of the high affinity for cannabinoid receptors (CB receptors), several side effects such as psychiatric manifestations, seizures, anxiety, paranoia, and aggression as well as delusions and hallucinations have been documented.⁴ Acute kidney injury (AKI), pulmonary manifestations, and myocardial infarction (MI) have also been prevalent side effects.⁵ MI has occurred with synthetic cannabinoid consumption, but few cases of Takotsubo cardiomyopathy in a pediatric patient have been reported. It remains an important complication due to the type of therapeutic intervention required by this side effect and the effect on the patient’s quality of life. The objective of this case report is to describe the relationship between Takotsubo cardiomyopathy and synthetic cannabinoid use in a pediatric patient.

Case Report
A 15-year-old male presented to the emergency department with a 4-hour history of substernal chest pain and reported an episode of syncope lasting a few minutes. He also reported homicidal ideation and audiovisual hallucinations. The patient reported using “Spice”, a synthetic cannabinoid, repeatedly over the last few hours in order to maintain his euphoric mood. He used a vaporizer for consuming “Spice”. The patient was agitated and experienced audiovisual hallucinations instructing him to harm himself and others. He had no prior psychiatric or medical history. He denied drug allergies. Surgical and family history was unremarkable. Social history revealed that the patient was an emancipated minor, smoking a pack of cigarettes per day, drinking 3-5 beers per month, and a regular user of marijuana and synthetic cannabinoids. He also reported smoking crack cocaine once at age of 13. Physical examination revealed normal cranial nerve examination, tachycardia, hyperventilation, and an erythematous lesion resembling a canker sore in the lateral tongue with surrounding erythema. Blood pressure was 137/83 mmHg, temperature was 37.3 °C, pulse rate was 75 beats per minute, and respiratory rate was 12 breaths per minute. Laboratory testing revealed no electrolyte abnormalities. Electrocardiography (ECG) showed ST segment elevation in leads V1, V2, V3, and V4, non-specific ST, T-wave changes, and T-wave inversion. Erythrocyte sedimentation rate (ESR) was mildly elevated. Cardiac enzymes were 3.2 ng/ml. Echocardiography revealed hypokinetic systolic dysfunction of the left side of the heart. Liver function tests were within normal limits. Aspirin was immediately administered to the patient and he was admitted to the cardiac catheterization lab, where no blockages in the coronary vasculature were seen. He was given a diagnosis of Takotsubo cardiomyopathy, after that catecholamine levels were seen to be elevated and urine drug screen was negative.

Discussion
Takotsubo cardiomyopathy is also known as stress cardiomyopathy and is characterized by systolic dysfunction of the left ventricle with an absence of angiographic evidence of coronary disease of an obstructive nature.⁶ This type of cardiomyopathy is poorly understood though several mechanisms of actions have been postulated. Underlying non-obstructive coronary artery diseases (CADs) such as vasospasm, perfusion abnormalities, excessive vasoconstriction, and improper vasodilation are all purported mechanisms of action.⁷ The more popular mechanism of action of Takotsubo cardiomyopathy is a vascular spasm or direct toxicity caused by a surge of catecholamines usually in response to an emotional stimulus.⁸ Synthetic cannabinoids have a greater binding
ability to the CB receptors type 1 and type 2 (CB1 and CB2) in the brain compared to delta-9-tetrahydrocannabinol (THC) as the synthetic version has full agonist properties compared to the partially agonistic abilities of delta-9-THC. High levels of CB1 receptors are found in the basal ganglia and cerebellum. In addition, the cardiovascular system contains several CB receptors in the myocardium, vasculature, and other blood cells. The function of the cardiovascular system can also be regulated by some of these receptors at times. The cardiovascular effects of CBs, whether natural or synthetic, stem from the presence of THC, which tends to moderate the CB receptor adverse effects.

The pathological side effects of CB receptor activation are vast and expansive. Studies have indicated almost complete overlap of cardiac symptoms and pathologies with both natural and synthetic versions of marijuana. These adverse diseases include stroke, vasculitis, thrombosis of the coronary vasculature, an array of arrhythmias, and acute heart failure (AHP). As a result of synthetic cannabinoid use, cardiomyocytes, in particular, are additionally susceptible to reduced contractility, production of reactive oxygen species (ROS), and apoptosis via p38 and mitogen-activated protein kinase (MAPK) activation pathways when synthetic cannabinoids are used. Synthetic CB receptor agonists such as “Spice” and other similar pharmacological compounds are also proatherogenic and profibrotic in nature and can be an explanation for obstructive CAD. Inflammation of the cardiac vasculature and atherosclerosis can occur due to the CB receptor signalling system and also ROS signalling as well.

In addition, the activation of the CB receptor can induce the stimulation of sympathetic system that is dependent on the amount of synthetic cannabinoid consumed and even route of administration. One proposed mechanism of pathogenesis of Takotsubo cardiomyopathy is catecholamine-induced coronary vasospasm, leading to a reversible cardiomyopathy which may postulate the role that synthetic cannabinoids play in this scenario. Although catecholamine increase is not seen in all cases of stress cardiomyopathy, there is sufficient evidence to associate an increase in catecholamines and even sympathetic surge with Takotsubo cardiomyopathy, as evidenced by the appearance of this type of cardiomyopathy in those with pheochromocytoma. Furthermore, increased levels of epinephrine tend to induce a change from Gs protein signalling which is actually positively inotropic to Gi protein signalling which is negatively inotropic.

**Conclusion**

Synthetic cannabinoids bind with a much greater potency to CB receptors than natural forms of marijuana. A cascading effect of a multitude of coronary diseases including both obstructive coronary disease and catecholamine-induced Takotsubo cardiomyopathy can occur.

**Conflict of Interests**

The Author have no conflict of interest.

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**References**


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چکیده
مقدمه: استفاده از کانابینوئید سنتری مانند K و اسپایس به دلیل عدم توانایی تشخیص آن در آزمایش اعتیاد به مواد مخدر(ادرار) متنازل است. استفاده از این ماده، طیف وسیعی از اسپیشناستی میوکاردیت از جمله بیماری‌های انسدادی و غیر انسدادی عروق کرونر مانند کاردیومیوپاتی ناگوی باعث همراهی می‌شود.

گزارش مورد: در پژوهش حاضر، گزارش موردی از یک پسر 15 ساله رها شده با تجربه کاردیومیوپاتی تاکوتسوبو پس از مصرف کانابینوئید سنتری اسپایس ارائه گردید.

نتیجه‌گیری: کانابینوئیدهای سنتری به عنوان آگونیست‌های کامل عمل می‌کنند و با کاراکتر بیشتری نسبت به اشکال طبیعی ماریوا به کانابینوئید ممکن است به عنوان ایمن‌تر نظر گرفته شوند. از طرفی، این آژانس از طرفی به دلیل همبستگی با اندورفین و سباستین سیستم سمپاتیک، به دلیل استفاده از کانابینوئید سنتری ممکن است به عنوان یک مدل جدیدی از پاسخ‌ها به تنش‌های دیگر معرفی شود. این تأثیرات از دیدگاه جدید، دارای معنی مهمی برای بررسی کاراکتر و تنش‌های دیگر ممکن است.

واژگان کلیدی: داروهای ساختنی، کاراکتریبیا، کانابینوئیدها


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