

Case Report

A case of Cardiac arrest following Synthetic Marijuana (K2) Use

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Abstract: Increasing use of synthetic cannabinoids has been noted in the recent years across the United States of America. The cardiovascular effects of synthetic cannabinoids are not well established. Bradycardia, tachycardia and postural hypotension following synthetic marijuana use have been reported. Various mechanisms are attributed in myocardial infarctions associated with the use of marijuana. Cases of acute myocardial infarction following synthetic marijuana use have been reported. We here present a case of cardiac arrest following synthetic marijuana use. To the best of our knowledge this is the second ever reported case of cardiac arrest associated with synthetic marijuana use.

Keywords: Cardiac arrest, synthetic cannabinoids, K2 use, marijuana

INTRODUCTION

Synthetic cannabinoids (SCs) are increasingly being reported as the drug of abuse in the United States of America and it is the second most common drug of abuse among teenagers [1]. Tachycardia, bradycardia, hypertension and postural hypotension are the most common cardiovascular manifestation of SC's [2]. We here present a case of cardiac arrest following K2 use in a patient with no previous history of coronary artery disease.

CASE REPORT

A 52 year old male patient with a past medical history of alcohol dependence, heroin abuse, opiate abuse and hepatitis C developed severe agitation following K2 use, for which he received midazolam en route to hospital. Upon arrival to hospital patient was agitated but subsequently became unresponsive, bradycardic, hypotensive and bradypnic. He was subsequently found to be pulse less, cardiac monitor revealed asystole; cardiopulmonary resuscitation (CPR) was initiated during which patient received epinephrine, sodium bicarbonate and calcium. Return of spontaneous circulation (ROSC) was noted after 15 minutes into CPR. Constrictive pericarditis was ruled out with echocardiography. Patient was intubated, normal saline and dopamine infusion were initiated through femoral central venous catheter. Electrocardiogram obtained after ROSC revealed atrial fibrillation with a rate of 81-

181 beats per min, antero-lateral infarct, repolarization abnormality in inferior leads and prolonged QT interval (Figure 1). Labs obtained following ROSC indicated acute kidney injury and severe metabolic acidosis with a pH of 6.82 and a serum bicarbonate level of 4 meq/dl. Urine toxicology was negative for barbiturates, benzodiazepines, cannabinoids, cocaine, methadone and opiates. JHW 0 18 N(4 OH-Pentyl) metabolites, JHW 0 18 N(5 OH-Pentyl) metabolites, JHW 0 73 N(3 OH-Butyl) metabolites, JHW 0 73 N(4 OH-Butyl) metabolites, AM 2201 M(4 OH-Pentyl) metabolites, JHW 019 N(5 OH-Hexyl) metabolites, and JHW 250 N(4 OH-Pentyl) metabolites were negative (reporting limit 0.5 ng/ml). Computer tomography of head without contrast revealed loss of grey-white differentiation indicating global anoxic injury to brain. A transthoracic echocardiogram revealed mild left ventricular dilation with a reduced ejection fraction of 40-45% and mild-diffuse hypo kinesis of with regional variability not corresponding to coronary artery distribution. He subsequently developed myoclonus secondary to ischemic hypoxic encephalopathy. Myoclonus was managed with levetiracetam and phenytoin. Hospital course was further complicated by sepsis which was medically managed. Goals of care were discussed with family; tracheostomy was performed for ventilation and percutaneous endoscopic gastrostomy (PEG) tube was placed to provide enteral nutrition. Patient's family consented for do not resuscitate orders. After medical

stabilization he was discharged for a long term care facility.

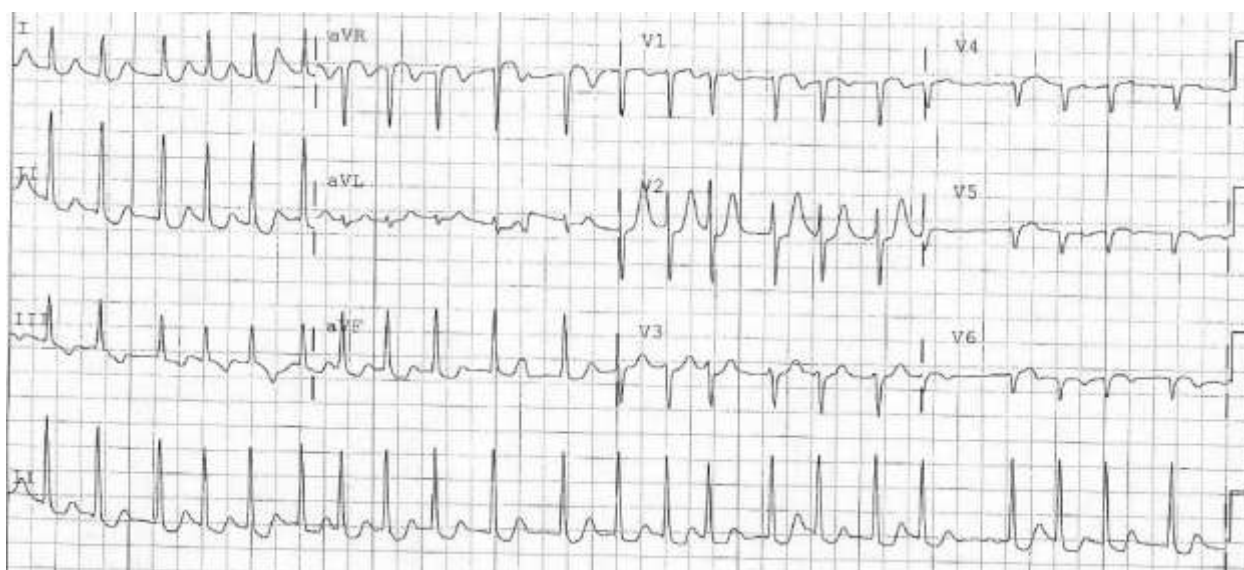


Fig-1: EKG obtained after ROSC showing atrial fibrillation with a rate of 81-181 beats per min, anterolateral infarct, repolarization abnormality in inferior leads and prolonged QT interval

DISCUSSION

Synthetic cannabinoids (SC's), commonly known as synthetic marijuana, spice, K2, black magic or crazy clown is increasingly being abused and is the second most abused drug among high school students [1, 3]. Since 1960 analogs of Δ^9 - tetra hydrocannabinol (Δ^9 - THC) were developed which include HU-210, JWH-018, JWH-073, JWH-398, JWH-250CP47, 497 and others. SC's are structurally unrelated to Δ^9 - THC and are mostly marketed through head shops and internet. Inter-brand and intrabrand variations in SC content are well documented. SC's are blended with plant ingredients such as Indian Warrior, Lion's Tail, Bay bean, Blue Lotus and Vanilla honey etc. The toxicology of these plants is yet to be understood [4]. SC's are cannabinoid receptor (CB1 and CB2) agonist, but their action is not entirely characterized. Some SC's have higher potency, affinity [5], longer half life [6], produces active metabolites [7] and may cause tachyphylaxis [8].

CB1 receptors are found on cardiomyocytes and mediate coronary vasodilation; CB2 receptors are expressed on cardiomyocytes, coronary endothelium and smooth muscles. CB2 receptors play a role against ischemic-reperfusion injury by decreasing endothelial cell activation and suppression of various inflammatory markers and cytokines, and decreases recruitment of inflammatory cells [9]. Jarai *et al.*; have reported an endothelial receptor distinct from CB1 and CB2 [10]. Cardiovascular effects of smoked marijuana are well characterized. Dose dependent increase in heart rate, blood pressure and postural hypotension has been reported. Increase carboxy hemoglobin levels, increased activity of factor VII and increased platelet activity

possibly contribute to dyssynchrony between myocardial oxygen demand and supply; this has been attributed as the cause of marijuana associated myocardial infarctions. Vulnerable plaque disruption may happen secondary to hemodynamic changes induced by marijuana smoking. Such unstable plaques may subsequently become thrombosed [2]. Marijuana induced reversible slow coronary flow in the absence of atheromatous lesion is recognized [11] and such slow coronary flow has been attributed to ventricular tachycardia [12]. Excessive sympathoadrenal discharges associated with marijuana smoking [13] could possibly increase risk for arrhythmogenesis. CB1 receptors have been shown to promote oxidative stress and cell death in human cardiomyocytes [14]. The risk of developing myocardial infarction is 4.8 times higher with marijuana use [15]. The risk of sudden cardiac death with marijuana use is rare [16, 17]. The long term effect of marijuana smoking in the pathogenesis of atherosclerosis is yet to be studied.

Cases of myocardial infarction associated with SC's are rare (table 1). SC's are stronger agonists of CB1 and CB2, hence above mechanisms may possibly contribute to myocardial ischemia [9-17]. Action and direct toxic effect of SC's and herbal contents on cardiomyocytes, autonomic nervous system, and intracardiac neurons warrants investigations. The clustering of SC induced myocardial infarction cases in the adolescent age group is indication of widespread use of SC's in this population across the United States of America [18-20]. Data on effect of marijuana and SCs on ionic channels are largely lacking. Al Kury *et al.*; in their rat cardiomyocytes documented the inhibitory effect of endogenous cannabinoid-an-

andamide on sodium channels and L-type calcium channels which was independent of CB1 and CB2 activation [21]. Foadi *et al.*; showed sodium channel inhibition by SC Ajulemic acid [22]. Krylatov *et al.*; demonstrated CB1 receptor mediated negative chronotropic effect of SC HU-210 [23].

Ibrahim et al reported the first case of cardiac arrest following SC use in a 56 year old patient with hypertension, dyslipidemia, coronary artery disease and myocardial infarction with previous four vessel bypass surgery [24]. The case we present here is a case of cardiac arrest following K2 use in a patient with no previous cardiovascular risk factor. Urine screen was

negative metabolites of few SC tested, however this is insufficient to rule out SC use as previously reported case of STEMI following SC use failed to reveal Sc in urine toxicology [1]. The SC screening failed to reveal the culprit compound. This is possibly because of the various SC's compounds available, intra-brand variation and inter-brand variation in SC's compositions. Beta-agonist contaminants in SC brands may further contribute clinical presentation in SC abuse [25]. Physicians across the U.S.A should keep their suspicion low and must enquire about SC abuse in patient who present to emergency room with symptoms suspicious of SC abuse.

Table 1: Reported cases of myocardial infarction associated with synthetic cannabinoid use

Serial number	Author and year of report	Case report from	Age of the patient	Electrocardiography (EKG)	Coronary vasculature
1	Mir <i>et al.</i> ; 2011 [18]	Texas, U.S.A	16 years	ST segment elevation in infero-lateral leads	Normal
2	Mir <i>et al.</i> ; 2011 [18]	Texas, U.S.A	16 years	ST segment elevation in infero-lateral leads	Normal
3	Mir <i>et al.</i> ; 2011 [18]	Texas, U.S.A	16 years	ST segment elevation in infero-lateral leads	
4	Ugan Atik <i>et al.</i> ; 2015 [19]	Istanbul, Turkey	16 years	ST segment elevation in inferior leads	Normal
5	Sherpa <i>et al.</i> ; 2015 [20]	Maryland, U.S.A	45 years	ST segment elevation in infero-lateral leads	
6	Clark <i>et al.</i> ; 2015 [21]	Washington, D.C, U.S.A	15 years	T wave inversion in inferior leads followed by ST-T wave elevation in precordial leads, T wave inversion in lead III	
7	Clark <i>et al.</i> ; 2015 [21]	Washington, D.C, U.S.A	16 years	ST elevation consider anterolateral injury or acute infarct, T wave inversion more evident in inferior leads	
8	Clark <i>et al.</i> ; 2015 [21]	Washington, D.C, U.S.A	17 years	ST elevation; consider anterolateral injury or infarct, ST more elevated in V2-V3	

CONCLUSION

Cardiac arrest and acute myocardial infarction are rare manifestations of SC use. For now, history remains the key in diagnosis of SC abuse. The toxicology tests for SC are not widely available and when available intra-brand and inter-brand variations may fail such tests which are designed to test only a few SC compounds. Research to understand effects of marijuana and SC on cardiac physiology demands attention from the scientific community.

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