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CASE REPORT

Prolonged cardiac arrest complicating a massive ST-segment elevation myocardial infarction associated with marijuana consumption

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Recreational substance use and misuse constitute a major public health issue. The annual rate of recreational drug overdose-related deaths is increasing exponentially, making unintentional overdose as the leading cause of injury-related deaths in the United States. Marijuana is the most widely used recreational illicit drug, with approximately 200 million users worldwide. Although it is generally regarded as having low acute toxicity, heavy marijuana usage has been associated with life-threatening consequences. Marijuana is increasingly becoming legal in the United States for both medical and recreational use. Although the most commonly seen adverse effects resulting from its consumption are typically associated with neurobehavioral and gastrointestinal symptoms, cases of severe toxicity involving the cardiovascular system have been reported. In this report, the authors describe a case of cannabis-associated ST-segment elevation myocardial infarction leading to a prolonged cardiac arrest.

Keywords: *marijuana*; *myocardial infarction*; *cardiac arrest*; *ventricular fibrillation*

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Knowledge of evolving trends in recreational drug use, in particular the acute toxicity related to their consumption, is essential in informing clinicians of the risks associated with the utilization of these substances. Cannabis use and abuse are a part of the global burden of disease caused by illicit drug misuse that includes increased consumption because of its presumptive safe profile. The current wave of legitimization is expected to produce a large, widespread recreational consumption of marijuana. Cannabis overdose accounts for the third highest illicit drug-related hospitalization rate after heroin and amphetamines (1). Large studies conducted in Europe have shown that 18–37% of all acute recreational drug-related toxicity visits to emergency department (ED) are associated with the consumption of cannabis (2, 3). The most frequently observed signs and symptoms of acute toxicity resulting from the consumption of tetrahydrocannabinol (THC), the major psychoactive component of marijuana, are related to impairment of the neuropsychiatry system and include anxiety, psychosis, and depression (2, 4).

Although cardiovascular complications as a consequence of marijuana use have been reported during the past three decades, the use of cannabis is not considered an established risk factor for acute coronary syndromes. Cardiovascular manifestations associated with the use of cannabis develop from a biphasic dose-dependent physiological effect on the autonomic nervous system. There have been previous communications of dysrhythmias describing patients with type-I Brugada pattern, ventricular tachycardia, atrial fibrillation, and ventricular fibrillation (5–8). Although likely underreported, myocardial ischemia leading to myocardial infarction (MI) has also been described in several reports (9–15). More dramatic features of toxicity have illustrated patients with sudden cardiac death (16–19). Potential mechanisms for sudden cardiac death after marijuana use may be related to the development of acute MI and/or dysrhythmias. The consumption of marijuana with other recreational drugs creates a more pronounced synergistic effect on the myocardium, triggering significant tachycardia that may lead to ischemia. In 40–60% of acute recreational drug-related

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intoxication events involving marijuana, alcohol is also detected in the toxicology screen of these patients (2, 3, 20). In a large study, Elmer et al. reported that 14% of out-of-hospital cardiac arrests were deemed to be recreational drugs overdose-related with opiates and benzodiazepines followed by cocaine, methadone, and marijuana being the most common drugs isolated from these patients' toxicology screens (21). This report describes a patient who developed a prolonged cardiac arrest as a consequence of an ST-segment elevation MI associated with marijuana consumption, ultimately leading to brain death.

Case presentation

A notification was given by the Emergency Medical Service (EMS) to the ED in our hospital regarding a 40-year-old male who developed tonic–clonic seizures followed by cardiac arrest while at a party. When EMS arrived at the scene, a ventricular fibrillation rhythm was recorded and electrical cardioversion was delivered seven times followed by the administration of intravenous amiodarone. Advanced Cardiac Life Support (ACLS) was initiated, which lasted about 40 min. His past medical history was unremarkable, except for recreational drugs use. There was no documented family history of premature ischemic heart disease. On arrival to ED, blood pressure was not able to be registered, but his heart rate was 104 beats/min with regular rhythm. His oxygen saturation by pulse oximetry was 87% despite receiving a fraction of inspired oxygen (FIO_2) of 100%. Aggressive resuscitation with vasoactive drugs including norepinephrine, epinephrine, and dobutamine was initiated. Remarkable laboratory findings included a white blood cell count of 18,800/mm^3 (4.8–10.8), a lactic acid level of 15.3 mmol/L (0.5–2.2), a blood glucose level of 433 mg/dl (65–115), and a bicarbonate level of 14 mmol/L (24–31). Arterial blood gas (ABG), while on mechanical ventilation and receiving an FIO_2 of 100%, showed a pH of 7.02 (7.35–7.45), a pCO_2 level of 66 mmHg (35–45), and a paO_2 level of 100 (80–100). Troponin I and creatine kinase levels were elevated at 8.32 ng/ml (<0.1) and 2,799 U/L (25–215), respectively. Urine toxicology screen was positive for THC but negative for cocaine, amphetamines, barbiturates, benzodiazepines, methadone, or opioids. A qualitative urine toxicology assay using liquid chromatography–tandem mass spectrometry (Quest Diagnostics Nichols Institute Chantilly®) was negative for synthetic cannabinoids. Serum ethyl alcohol level was 119 mg/dl (<10). Liver function, creatinine, lipid panel, and coagulation profiles were within normal limits. Initial chest radiography showed bilateral infiltrates consistent with pulmonary edema (Fig. 1). A 12-lead electrocardiogram (ECG) demonstrated sinus tachycardia, with ST-segment elevation in leads II–III and aVF as well as V1–V5 (Fig. 2). Transthoracic echocardiogram displayed severely depressed left ventricular ejection fraction of 20% (55–65),

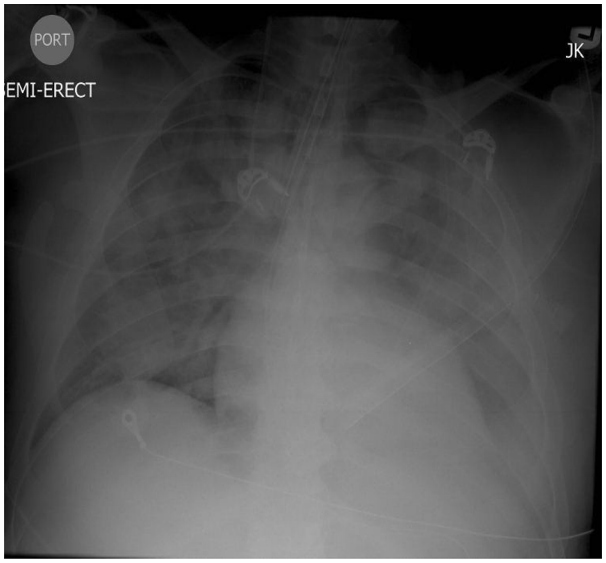

Fig. 1. Chest radiography showing bilateral pulmonary infiltrates.

global hypokinesis with apical septal akinesia, and a 3.14 cm^2 non-mobile, calcified apical thrombus (Fig. 3). Therapy with aspirin, clopidogrel, and intravenous heparin was initiated. Thrombolytic therapy was not considered because of the prolonged cardiopulmonary resuscitation (CPR) time. He was admitted to the intensive care unit (ICU) with the presumptive diagnosis of cardiogenic shock secondary to ST-segment elevation MI. According to the hospital policy, the presence of severe persistent hypoxemia and refractory hypotension despite the use of two vasopressors was considered as the exclusion criterion to initiate therapeutic hypothermia protocol. Within 48 h, hospital course was complicated by worsening kidney function, and severely depressed Glasgow Coma Scale despite being off sedation. Neurological examination disclosed findings compatible with possible diagnosis of brain death: dilated and fixed pupils, absence of corneal and gag reflexes, negative response to deep painful stimuli, no spontaneous breathing, and negative eye-caloric test. Head computed tomography showed diffuse loss of gray-white matter differentiation and ventricular effacement, compatible with global anoxic encephalopathy. No ischemic infarcts or hemorrhage was identified. Given the possibility that the initial neurological examination may had been confounded by the presence of central nervous system depressant drugs, a second neurological assessment was performed in the setting of a negative urine toxicology screen. The results were unchanged. On day 3 of ICU admission, a positive apnea test confirmed the diagnosis of brain death. Autopsy report revealed an *acute* anterior–lateral, septal, and posterior wall MI with a mural thrombus in the left ventricle as well as hypertensive and atherosclerotic heart disease as the main causes of death.

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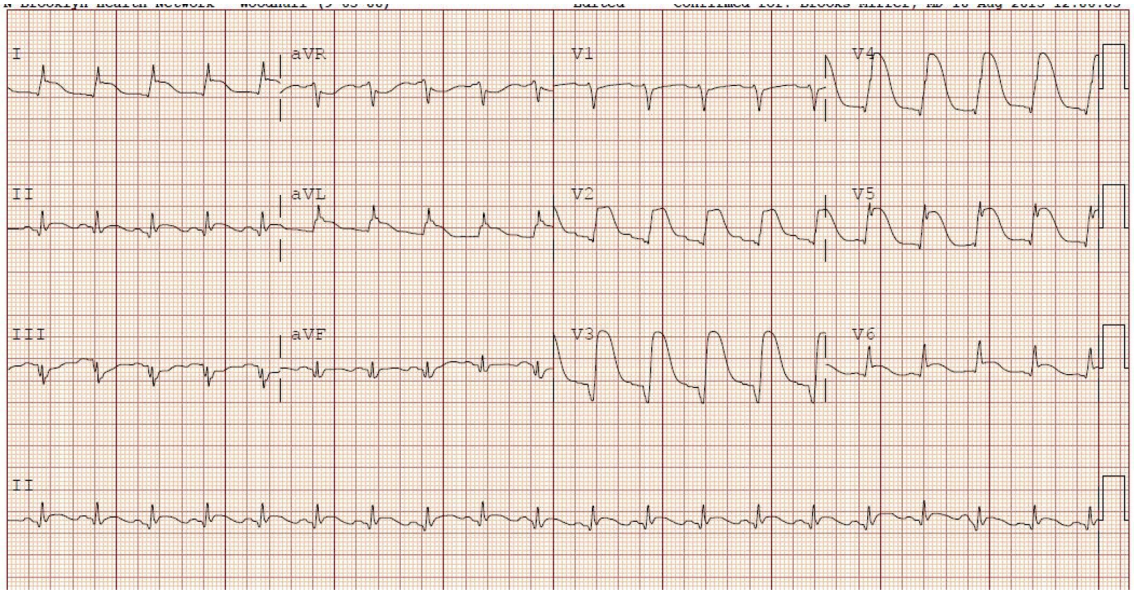

Fig. 2. Initial ECG demonstrating ST-segment elevation in multiple leads.

Discussion

It is difficult to establish the cause–effect relationship between marijuana use and cardiovascular disease. A review of the literature was undertaken to compare our case with other reported occurrences of cannabis-related MI. A MEDLINE search using the words "marijuana" AND "myocardial infarction" yielded 36 cases of acute coronary events likely triggered by the consumption of marijuana. The majority of these patients were male (33, 92%) with a mean age of 30.9 years (median 30, range 17–51), and eight patients (22%) died. A similar search using the words "cardiac arrest" AND "sudden cardiac death" AND "marijuana" resulted in 30 reported episodes. Similarly, most of these patients were male (28, 93%) with a mean age of 34.6 years (median 31, range 15–61). In eight patients (27%), other recreational drugs were also found in toxicology screen (in five of these patients (63%), serum alcohol levels were positive). Twenty-five patients (83%) died. An acute cardiovascular event was the probable cause of death in all these subjects. Summary of cases of cardiac arrest and sudden cardiac death related to marijuana consumption is shown in Table 1. The patient described in this report paired the characteristics of those previously reported events: male gender, young adult, positive serum alcohol levels, and had an unfavorable outcome. Unfortunately, our patient was not able to be transferred to another institution for coronary angiography and possible percutaneous angioplasty because of his hemodynamic instability and elevated FIO_2 requirements. As previously outlined by Elmer et al., patients with recreational drug-related out-of-hospital cardiac arrests are less likely to undergo cardiac catheterization (21). It is possible that our patient might have had a non-diagnosed underlying coronary artery disease that may have been aggravated by the consumption of marijuana. This may be supported by the presence of a calcified apical thrombus, which suggests chronicity. It has been suggested that consumption of THC may worsen coronary ischemia in patients with baseline coronary artery disease, potentially triggering an MI (8).

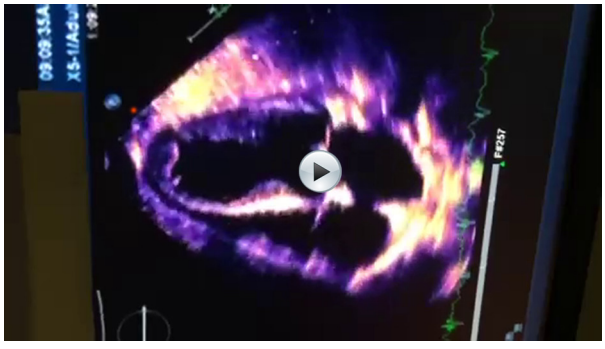

Fig. 3. Transthoracic echocardiogram showing a calcified apical thrombus and global hypokinesis.

The pathophysiological effects of marijuana in the cardiovascular system are well described, and they seem to be mediated by stimulation of the sympathetic nervous system through release of norepinephrine as well as by parasympathetic nervous system blockade (26). However, the mechanism underlying the association between marijuana use and MI has not been well established. It has been demonstrated that consumption of marijuana increases oxygen demands on the myocardium, leading to an increase in carboxyhemoglobin levels resulting in decreased oxygen-carrying capacity (27, 28). The rise in norepinephrine levels resulting from sympathetic stimulation reduces the left ventricular ejection time, thereby

Table 1. Summary of cases of cardiac arrest and sudden cardiac death associated with consumption of marijuana

Reference	Age, gender	Outcome
Lindsay et al. (8)	48, M	Survived
Casier et al. (16)	52, M	Dead
	23, M	Survived
	28, M	Dead
Hartung et al. (17)	23, M	Dead
	28, M	Dead
Menahem (18)	21, M	Survived
Bachs et al. (19)	39, M	Dead
	40, M	Dead
	43, M	Dead
	37, M	Dead
	17, M	Dead
	42, M	Dead
Tormey (20)[a]	17, F	Dead
	50, M	Dead
	19, M	Dead
	47, M	Dead
	28, M	Dead
	54, M	Dead
	47, M	Dead
	31, M	Dead
	61, M	Dead
	36, M	Dead
	20, F	Dead
	50, M	Dead
	59, M	Dead
Diffley et al. (22)	15, M	Survived
Daisley et al. (23)	18, M	Dead
Montisci et al. (24)	31, M	Dead
Sattout et al. (25)	15, M	Survived

F, Female; M, male.
[a]Autopsy cases.

lowering the threshold for angina. Interference with the integrity of peripheral vascular reflex responses and vascular inflammation with the subsequent increase in platelet activation have been also proposed as mechanisms responsible for cardiac events among cannabis users (29, 30). Reversible vasospasm seems to be the most commonly suggested etiology for cannabis-associated acute coronary syndromes. One study showed that cardiovascular complications resulting from the consumption of marijuana have a mortality rate of about 25% (31). In a large epidemiological study, THC and its derivatives were reported to increase the risk of MI by 4.8 times in the first hour after use (32). Another cohort showed that in marijuana consumers, the population attributable fraction for MI was 0.8% (33).

It is unclear why our patient developed seizures before going into cardiac arrest. The relation between marijuana use and epileptic seizures is still controversial. Although cannabis is not commonly associated with seizures and may actually have medical use benefits for the treatment of epilepsy (34), there have been reports of seizures resulting from acute THC intoxication (2, 3). Even though prolonged cardiac arrest leads to hypoxia, which may result in seizures, we do not consider hypoxemia to be the leading cause of seizures in this case given the initial cascade of events, since our patient was initially presented with tonic–clonic seizures that were followed by a cardiac arrest. It is possible that our subject developed seizures because of the synergistic effect of marijuana and alcohol consumption (35). It is also feasible that the patient described in this report might have been under the effects of other recreational drugs unable to be identified by using conventional toxicology screens. Seizures have been reported to be a frequent feature of synthetic cannabinoids intoxication (36, 37). Unfortunately, we were not able to collect any analytical data on synthetic cannabinoids from our patients' serum except from a negative urine toxicology assay. Our subject's urine toxicology screen failed to detect the presence of synthetic cannabinoids, making the role of these substances unlikely in our patient's clinical presentation. We hypothesized that the development of cardiac arrest in our patient was the result of an extensive ST-segment elevation MI, in conjunction with the ventricular fibrillation likely triggered by myocardial ischemia. It is possible that the onset of ventricular fibrillation may have been provoked by tonic–clonic seizures, as previously reported in few other cases (38, 39). As a consequence of the prolonged CPR time and hypoxemia, severe global anoxic brain injury was developed that led to brain death. There have been previous similar reports of sudden cardiac deaths related to marijuana consumption. Dines et al. reported an 18-year-old male who succumbed to an asystole cardiac arrest while smoking marijuana and suffered hypoxic brain injury related to prolonged cardiac arrest (2). Similarly, Hartung et al. described a 23-year-old male who collapsed with ventricular fibrillation and died after 40 min of unsuccessful CPR (17). In a large cohort of patients with recreational drug overdose-related out-of-hospital cardiac arrests, brain death accounted for more than 30% of fatalities (21). Ventricular fibrillation has been sporadically reported as a result of marijuana consumption (2, 16). A possible explanation for the onset of ventricular dysrhythmias is that cannabis may increase the activity of the Purkinje fibers system (6, 40). The combination of alcohol with marijuana could potentially increase the cardiac toxicity and arrhythmogenic effects of THC by alteration of atrial refractoriness and conduction velocity.

Our report has two potential limitations: first, the initial ECG strip recorded by EMS showing ventricular fibrillation was not able to be recovered, so it is difficult to comment on the rhythm obtained after electrical cardioversion was delivered; second, no blood levels of

THC were obtained on admission and, therefore, it may be difficult to attribute the etiology of this acute coronary event directly to the consumption of marijuana. Postmortem toxicological tests were not performed. A positive urine toxicology screen for THC may be insufficient evidence in the linkage of cardiac arrest and marijuana. THC analysis in blood samples must be considered an essential requirement to estimate and correlate the time of last intake with the occurrence of acute cardiovascular events. Unfortunately, the association of marijuana consumption and the occurrence of cardiovascular events is rarely supported by an exhaustive toxicological examination and, when such investigation is performed, it is usually limited to a positive urine toxicological examination that is not reliable for the estimation of the time of last marijuana intake. In this case, as in majority of the previously reported events, the cannabis causality was assumed based on the result of a positive urine toxicology screen for THC and the absence of other substances known to be linked to acute coronary syndrome.

Conclusion

Despite the widespread use of marijuana, public awareness of the risk for potential cardiovascular complications remains low. Although uncommon, severe cardiovascular toxicity and death may develop from its consumption. Further investigations of clinical, toxicological, and epidemiological aspects are needed to enlighten causality between consumption of THC and acute cardiovascular events. Clinicians should be aware of these potential life-threatening complications resulting from the consumption of cannabis.

Conflict of interest and funding

No conflicts of interest among authors regarding the publication of this report.

References

1. Roxburg A, Dogenhardt L. Hospital stays related to illicit drugs in Australia 1993–2004. NDARC Technical Report, No. 261. Sydney: National Drugs and Alcohol Research Center, University of New South Wales; 2006.
2. Dines AM, Wood DM, Galicia M, Yates CM, Heyerdahl F, Hovda KE, et al. Presentations to the emergency department following cannabis use – A multi-centre case series from ten European countries. J Med Toxicol 2015; 11(4): 415–21.
3. Liakoni E, Dolder PC, Rentsch K, Liechti ME. Acute health problems due to recreational drug use in patients presenting to an urban emergency department in Switzerland. Swiss Med Wkly 2015; 145: w14166.
4. Volkow ND, Compton WM, Weiss SR. Adverse health effects of marijuana use. N Engl J Med 2014; 371(9): 879.
5. Romero-Puche AJ, Trigueros-Ruiz N, Cerdan-Sanchez MC, Perez-Lorente F, Roldan D, Vicente-Vera T. Brugada electrocardiogram pattern induced by cannabis. Rev Esp Cardiol 2012; 65(9): 856–8.
6. Rezkalla SH, Sharma P, Kloner RA. Coronary no-flow and ventricular tachycardia associated with habitual marijuana use. Ann Emerg Med 2003; 42(3): 365–9.
7. Sing GK. Atrial fibrillation associated with marijuana use. Pediatr Cardiol 2000; 21(3): 284.
8. Lindsay AC, Foale RA, Warren O, Henry JA. Cannabis as a precipitant of cardiovascular emergencies. Int J Cardiol 2005; 104(2): 230–2.
9. Caldicott DG, Holmes J, Roberts-Thomson KC, Mahar L. Keep off the grass: Marijuana use and acute cardiovascular events. Eur J Emerg Med 2005; 12(5): 236–44.
10. Gunawardena MDVM, Rajapakse S, Herath J, Amarasena N. Myocardial infarction following cannabis induced coronary vasospasm. BMJ Case Rep 2014; 2014: 207020.
11. Hodcroft CJ, Rossifer MC, Buch AN. Cannabis-associated myocardial infarction in a young man with normal coronary arteries. J Emerg Med 2014; 47(3): 277–81.
12. Safaa AM, Markham R, Jayasinghe R. Marijuana-induced recurrent acute coronary syndrome with normal coronary angiograms. Drug Alcohol Rev 2012; 31(1): 91–4.
13. Tatli E, Yilmaztepe M, Altun G, Altun A. Cannabis-induced coronary artery thrombosis and acute anterior myocardial infarction in a young man. Int J Cardiol 2007; 120(3): 420–2.
14. Renard D, Taieb G, Gras-Combe G, Labauge P. Cannabis-related myocardial infarction and cardioembolic stroke. J Stroke Cerebrovasc Dis 2012; 21(1): 82–3.
15. Kocabay G, Yildiz M, Duran NE, Ozkan M. Acute inferior myocardial infarction due to cannabis smoking in a young man. J Cardiovasc Med 2009; 10(9): 669–70.
16. Casier I, Vanduynhoven P, Haine S, Vrints C, Jorens PG. Is recent cannabis use associated with acute coronary syndromes? An illustrative case series. Acta Cardiol 2014; 69(2): 131–6.
17. Hartung B, Kauferstein S, Ritz-Timme S, Daldrup T. Sudden unexpected death under acute influence of cannabis. Forensic Sci Int 2014; 237: e11–13.
18. Menahem S. Cardiac asystole following cannabis (marijuana) usage-additional mechanism for sudden death? Forensic Sci Int 2013; 233(1–3): 3–5.
19. Bachs L, Moreland H. Acute cardiovascular fatalities following cannabis use. Forensic Sci Int 2001; 124(2–3): 200–3.
20. Tormey WP. Cannabis, possible cardiac deaths and the coroner in Ireland. Ir J Med Sci 2012; 181(4): 479–82.
21. Elmer J, Lynch MJ, Kristan J, Morgan P, Gerstel SJ, Callaway CW, et al. Recreational drug overdose-related cardiac arrests: Break on through to the other side. Resuscitation 2015; 89: 177–81.
22. Diffley M, Armenian P, Gerona R, Reinhartz O, Avasarala K. Catecholaminergic polymorphic ventricular tachycardia found in an adolescent after a methylenedioxymethamphetamine and marijuana-induced cardiac arrest. Crit Care Med 2012; 40(7): 2223–6.
23. Daisley H, Jones-Le Cointe A, Hutchinson G, Simmons V. Fatal cardiac toxicity temporally related to poly-drug abuse. Vet Hum Toxicol 1998; 40(1): 21–2.
24. Montisci M, Thiene G, Ferrara SD, Basso C. Cannabis and cocaine: A lethal cocktail triggering coronary sudden death. Cardiovasc Pathol 2008; 17(5): 344–6.
25. Sattout AH, Nicol MF. Cardiac arrest following cannabis use: A case report. Cases J 2009; 2: 208.
26. Gash A, Karliner JS, Janowski D, Lake CR. Effects of smoking marijuana on the left ventricular performance and plasma norepinephrine: Studies in normal men. Ann Intern Med 1978; 89(4): 448–52.
27. Weiss JL, Watanabe AM, Lemberger L, Tamarkin NR, Cardon PV. Cardiovascular effects of delta-9-tetrahydrocannabinol in man. Clin Pharmacol Ther 1972; 13(5): 671–84.

28. Renault PF, Schuster CR, Heinrich R, Freeman DX. Marihuana standardized smoke administration and dose effect curves on heart rate in humans. Science 1971; 174(4009): 589–91.
29. Trecki J, Gerona RR, Schwartz MD. Synthetic cannabinoid-related illnesses and deaths. N Engl J Med 2015; 373(2): 103–7.
30. Mittleman MA, Maclure M, Sherwood JB, Mulry RP, Tofler GH, Jacobs SC, et al. Triggering of acute myocardial infarction onset by episodes of anger. Determinants of myocardial infarction onset study investigators. Circulation 1995; 92(7): 1720–5.
31. Jouangus E, Lapeyre-Mestre M, Micallef J, French Association of the Regional Abuse and Dependence Monitoring Centres (CEIP-A) Working Group on Cannabis Complications. Cannabis use: Signal of increasing risk of serious cardiovascular disorders. J Am Heart Assoc 2014; 3(2): e000638.
32. Mittleman MA, Lewis RA, Maclure M, Sherwood JB, Muller JE. Triggering myocardial infarction by marijuana. Circulation 2001; 103(23): 2805–9.
33. Nawrot TS, Perez L, Kunzli N, Munters E, Nemery B. Public health importance of triggers of myocardial infarction: A comparative risk assessment. Lancet 2011; 377(9767): 732–40.
34. Zagnoni PG, Albano C. Psychostimulants and epilepsy. Epilepsia 2002; 43(Suppl 2): 28–31.
35. Lukas SE, Orozco S. Ethanol increases plasma delta(9)-tetrahydrocannabinol levels and subjective effects after marijuana smoking in human volunteers. Drug Alcohol Depend 2001; 64(2): 143–9.
36. Harris CR, Brown A. Synthetic cannabinoid intoxication: A case series and review. J Emerg Med 2013; 44(2): 360–6.
37. Hermanns-Clausen M, Kneisel S, Szabo B, Auwarter V. Acute toxicity due to the confirmed consumption of synthetic cannabinoids: Clinical and laboratory findings. Addiction 2013; 108(3): 534–44.
38. Ferlisi M, Tomei R, Carletti M, Moretto G, Zanoni T. Seizure induced ventricular fibrillation: A case of near-SUDEP. Seizure 2013; 22(3): 249–51.
39. Van der Lende M, Surges R, Sander JW, Thijs RD. Cardiac arrhythmias during or after epileptic seizures. J Neurol Neurosurg Psychiatry 2016; 87(1): 69–74.
40. Aryana A, Williams MA. Marijuana as a trigger of cardiovascular events: Speculation or scientific certainty? Int J Cardiol 2007; 118(2): 141–4.

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