

Research

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Cardiac Complaints Encountered After Use of Street Drugs: A Review of their Cardiac Toxicity Mechanism

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ABSTRACT

Objectives: The upward trend leading to versatility in street drug (SD) usage paves the way to numerous complications to organ systems, including cardiovascular events. But, findings on cardiac complications, as well as their prevalence and survey from SD abusers are not encountered in the literature.

Material and Methods: In this survey study, patients admitted to the emergency department (ED) with suspected substance abuse were collected prospectively and cardiac complications were observed. The relationship between variables and all types of SDs were analyzed. Prevalence of the cardiovascular events were calculated. Also, uncommon cardiovascular events after SD use were defined.

Results: In a total of 425 (424 male, 98.4%) participants, cardiac complaints after substance use were noted in 14.6% (n=62). High degree AV-node conduction block secondary to synthetic cannabis, and moreover occlusive ST segment elevated myocardial infarction (STEMI) after cannabis use was identified. In other 2 cases, ecstasy use was associated with both STEMI and tachycardia.

Conclusion: Emergency physicians and cardiologist must be competent in the management of patients with substance abuse and potential novel cardiac complications. Especially young males with substance use and suspicious presentations such as syncope, palpitation, and vomiting complaints may be at risk. Cardiac complications on rhythm disturbance, conduction delay or obstructive myocardial infarct can become other than in literature.

KEYWORDS: Street drug; Marijuana abuse; Atrioventricular block; Unstable angina.

ABBREVIATIONS: SD: Street drug; ECG: Electrocardiogram; ACS: Acute coronary syndrome; ED: Emergency Department; STEMI: Segment elevated myocardial infarction.

INTRODUCTION

Since street drug (SD) usage has become widespread, emergency department (ED) admissions of such cases and complications developing after substance use are observed with an increasing frequency.¹⁻³ Some of these are cases with severe cardiac complaints similar to the presentation of routine cardiac emergencies. However, some patients can hide the fact that they used a substance, which leads their underestimation as simple cardiac emergency cases without substance use. Moreover, development of cardiac problems associated with SD use is important since they may be of a type that is not commonly observed in literature. This research encountered cardiac complaints due to SD use for the 1st time or by addiction and in addition, important cases that were emerged different than in literature are defined.

MATERIALS AND METHODS

The study was reviewed and approved by local ethics committee. This prospective cross-sectional study was conducted in the ED of our tertiary-care hospital, between 1st January and 31st December, 2014. Written informed consent were obtained from the patient for publication of this study and accompanying images. Substance user patients over 18 years old diagnosed *via* self-reports or detected by the physician's queries were enrolled to the study. Cardiac complaints or accompanying other angina equivalent symptoms and their survey during the admission in the ED including electrocardiogram (ECG), blood gas analysis, blood biochemical parameters, Troponin I levels, consultations and cardiac intensive care unit admissions) were approached. Substance use characteristics are based on the personal statement of the patient, because of the tests for substance detection were not available. Patients were excluded from participation if they decline to give informed consent and disclaim using a SD. Statistical analysis was performed using SPSS for Windows, version 15.0 (SPSS Inc., Chicago, USA). Quantitative data are represented as ranges and mean±standard deviation. Types of SD consumed by the patients and their cardiac complaints, ECG findings, laboratory results were compared using Mann-Whitney U-test and Kruskal-Wallis significance tests were used for the comparison of dependent and independent variables. *p* values below 0.05 were considered statistically significant.

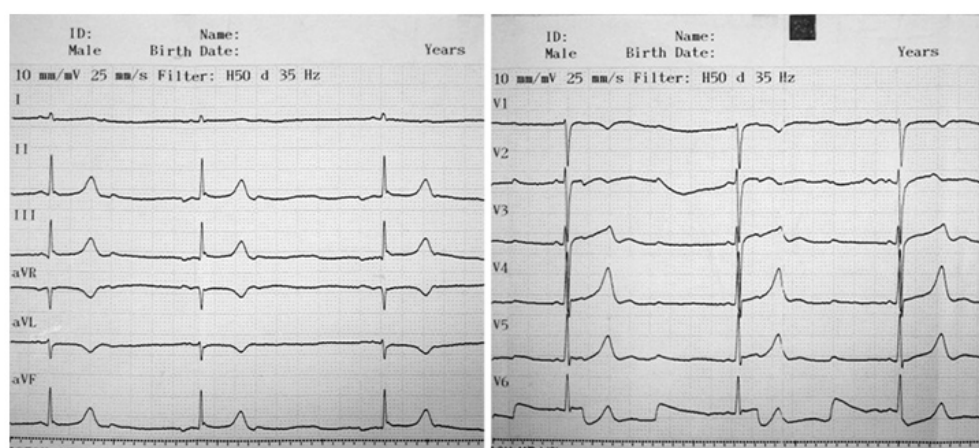
RESULTS

In a total of 425 cases, frequency of cardiac complaints observed after substance use was determined in 14.6% (n=62), and except for one, all of them were male. Distribution of these cardiac complaints were as follows: unconsciousness (more than a syncope attack) 10.4% (n=44), palpitation 1.9% (n=8, one case was first trimester pregnant), chest pain and accompanying other angina equivalent symptoms 1.9% (n=8, sweating, sense of fainting, vomiting, or abdominal pain), temporary syncope attack 0.2% (n=1), and stomach-ache with vomiting 0.2% (n=1) (Table 1). However, according to the complaint and ECG

evaluation, the rate of cases for which acute coronary syndrome (ACS) is considered and consulted with a cardiologist was found in 0.9% (n=4). Troponin I increase and/or cardiac arrest were not recorded in any of these cases. Statistical difference was not found between types of SD groups (marijuana, ecstasy, and amphetamine) consumed by patients cardiac complaints (unconsciousness, palpitation, chest pain, sweating, sense of fainting, vomiting, or abdominal pain), ECG findings (ST or T wave changes, tachycardia, bradycardia, non changes) and laboratory results (CK-MB and Troponin I) (*p*<0.05, *p*<0.05 and *p*<0.05 respectively). Here, in details of these important cases of SD users which were different than in literature.

Case 1

A 33-year-old 'bonsai' (a synthetic cannabinoid, including mostly JWH-018) abuser male patient was brought to the ED due to near syncope, sweating and vomiting after pure marijuana intake in the morning hours. He stated that he took only marijuana before arrival. High degree AV Block (Second degree AV/Mobitz type two Block) was observed on the electrocardiography trace (ECG; Figure 1). His initial vital signs were as follows; blood pressure 116/80 mmHg, heart rate 40 BPM, respiratory rate 12 BPM, oral temperature 98.6 °F, and a SpO₂ 100% on room air. Glasgow Coma Scale score was 15 and pupils were mildly dilated. His physical examination was unremarkable. No wall motion defect was found in transthoracic echocardiography and left ventricular ejection fraction was 60%. Normal sinus rhythm was restored following administration of atropine 0.5 mg intravenously. Cardiology consultation and admission to coronary intensive care unit was performed for monitoring the cardiac stability. Laboratory values of the patient were as creatine kinase (CK) 1792 U/I (normal range 0-171 U/I), CK-MB 9.01 ng/ml (normal range 0-5 ng/ml). No increase was observed in Troponin I level and in the repeated cardiac markers. Venous blood gas values were normal except for the lactate (2.1 mmol/L). Complete blood count revealed leukocytosis of 12.500 K/ μ L. It was learned that the patient left the hospital against medical advice during 1st day of admission in the coronary intensive care unit



ECG tracing demonstrates second degree type 2 (Mobitz type 2) block associated with cannabis use.

Figure 1: ECG trace from Case 1.

and had no complaints in the meantime.

Case 2

A 19-year-old male admitted to the ED with the complaints of palpitations, chest pain and blurry vision after ecstasy (MDMA; 3,4-methylenedioxy-methamphetamine; also called yellow star, Bugatti, superman) use for the first time. He was completely healthy previously except for using unknown bodybuilder drugs (unknown substance; may be anabolic steroid or either SD). Vital signs on admission were as follows; blood pressure 118/80 mmHg, heart rate 132 BPM, respiratory rate 12 BPM, oral temperature of 98.6 °F and SpO₂ 100% on room air. His first ECG was evaluated as sinus tachycardia and benign early Repolarization. ST elevation (STE) in lead D1 and avL ≤1 mm emerged in the following ECG (Figure 2). Cardiology consultation was administered and 10 mg Isosorbide dinitrate was administered orally to the patient. Although STE was improved later, sinus tachycardia remained. The initial troponin I level in the ED was reported as <0.01 ng/mL (normal range 0-0.03 ng/mL), and CK-MB was 6.93 ng/mL (normal 0 to 7 ng/mL). Repeated measures after 4 hours revealed no increase in troponin I level and CK-MB was lowered to 5.92 ng/ml. Creatine Kinase (CK) levels were 679 and 577 U/L respectively. Acute coronary syndrome treatment protocol was started (Advertising Standards Authority (ASA), clopidogrel, enoxaparin), and he was admitted to the cardiology department with the pre-diagnosis of STEMI. A coronary stress test was primarily performed on the patient. Although the STE ensued during cardiac stress test, his cardiac catheterization revealed normal coronary arteries, no wall motion abnormalities, and normal systolic function.

Case 3

A 31-year-old male patient admitted to the ED due to palpitations after use of ecstasy (MDMA) and alcoholic beverages in the previous evening. He had no chest pain. His vital signs were normal except rapid pulse rate (141 BPM) and venous blood

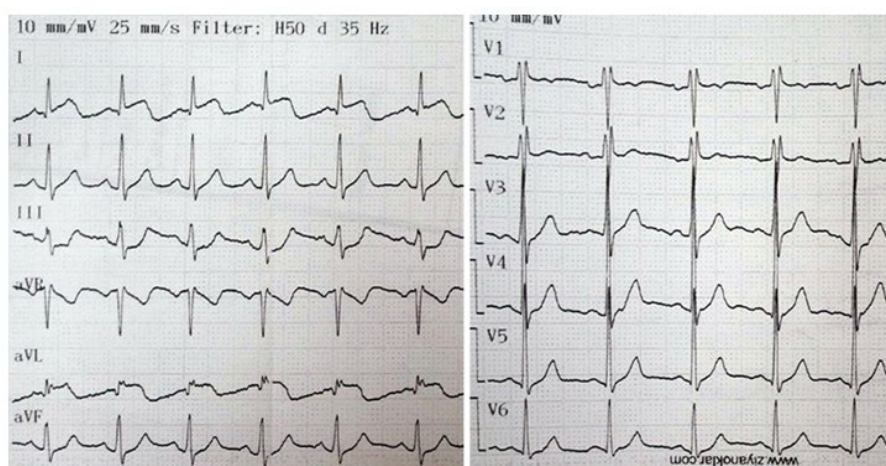
gas values were as follows; pH=7.6, pCO₂=22.5 mmHg, lactate 4.2 mmol/L. Cardiac follow-up was performed as he had sinus tachycardia and STE ≤1 mm in lead V1 detected on ECG. After cardiology consultation, he was discharged due to restoration of normal sinus rhythm without antiarrhythmic administration and lack of any abnormality in the laboratory results.

Case 4

A 44-year-old male admitted to the ED due to sudden-onset chest pain. Blood pressure was 155/112 mmHg, pulse rate 96 BPM and other vital signs were normal. The initial ECG revealed STE in the anterolateral leads. Coronary angiography was performed immediately. Endovascular stent was implanted after balloon dilatation to the patient whose left main coronary artery was observed as 100% occluded. No other complication was observed. It was learned that the patient confessed to cardiologists that he had been smoking for long years and he is a cannabinoid substance abuser. His pressure-like chest pain and cold sweating started two and a half hour after consumption of marijuana. His coronary angiography images are demonstrated in Figure 3.

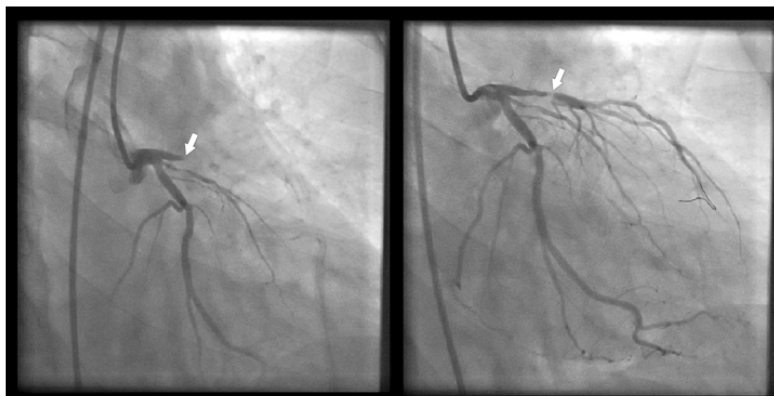
DISCUSSION

The prevalence of usage of illegal substances, called SDs is 4-5.8% in world population.¹ Cannabinoid, synthetic cannabinoid derivatives, amphetamine or synthetic amphetamine derivatives are among the most commonly used SDs.^{1,3} Marijuana is the most widely abused psychoactive SD that is obtained from jute plant *Cannabis sativa* (Δ^9 -tetrahydrocannabinol/ Δ^9 -THC).¹ The variety in the street name of the cannabinoid can be confusing. The most frequently used street names of the cannabinoid widely vary according to the specific geographical region or location of the production origin: (*Marijuana, Cigarette, Crazy bud, Spice, K2, Sky, Saddam, Holland, Henry, Mary Jane, Bonsai, Jamaica, Bombay blue*).^{1,3} Form of smoking the substance affects the onset and duration, and these characteristics are known



Leads D1 and aVL showed STE following use of ecstasy in the patient with chest discomfort

Figure 2: ECG trace from Case 2.



Coronary angiography shows an occluded left anterior descending coronary artery. The patient had used cannabinoids before the chest discomfort and ECG findings indicated STEMI.

Figure 3: Coronary angiography slides from Case 4.

well by the users. The marijuana plant is generally dried, cut into small pieces and smoked by wrapping into a cigarette for a rapid influence (*joint effect*: it starts in 15 minutes and lasts for 4 hours).³ Frequent side effects are dryness of the mouth, short-term loss of memory, hypo/hypertension, palpitation/tachycardia, nausea, vomiting and cardiac or cerebrovascular events.²⁻⁵ Subjective increase in the perception, depersonalization, psychomotor coordination disorder, tremor, concentration loss, paranoia, schizophrenic symptoms may develop in addicts.²⁻⁵ Prominent conjunctiva hyperemia appears in cannabis smokers.⁷ Cannabis and their synthetics may be detected for weeks once it is taken into the body and is stated that making accumulation especially in the neurons and lipid membranes plays a role in addiction.⁵ Cannabinoid receptors take place in the central neural and peripheral cells (CB1 and CB2 receptors, respectively).^{4,5} It affects the amount of aminergic transmitters such as CB1 receptors with gamma aminobutyric acid and Glutamate. *Synthetic Cannabis* derivatives are sold in the markets as being 30-800 times more potent.^{1,2,4} Synthetic derivatives that have a high central effect over CB2 receptors and that are commonly known include JWH-018 (*The most known street names are Jamaica, Bonsai, spice, K2, Holland e.g.*).¹ Users purchase the pure synthetic cannabinoid (i.e., JWH-018 powder) and extract and spray on any desired plant material.⁴ There is no specific treatment for cannabinoid addiction, but it is recommended to evaluate the findings objectively and take symptomatic approaches.

Vascular side effects of cannabis and their synthetics are cardiac and cerebral.^{2,5,9} Myocardial infarction has been previously reported in the setting of marijuana as well as synthetic cannabinoid use.^{4,10} The proposed mechanisms for cardiovascular events due to marijuana use include an increase in catecholamines (released with the CB post receptor effects), carboxyhemoglobin levels, postural hypotension, increased cardiac workload, and an increase in oxygen demands with a decrease in myocardial oxygen supply.¹⁰ In an article, that researched the effects from synthetic Cannabinoid, CB2 receptor knockout mice experiments suggested an association between CB2 receptor agonism and attenuation of post-myocardial infarction

ischemic-reperfusion injury.^{5,8} Mobitz type 2 Block is observed as a different case according to the literature in the 1st case.^{9,10} The rhythm responded to atropine. After marijuana use in the 4th case, angiography was performed by STEMI findings without troponin I increase and left anterior descending coronary artery was found to be 100% occluded: this is differently from vasospastic myocardial infarct that is expected in drug abusers. Cardiologist's reason for performing coronary angiography for a presumptive diagnosis of a STEMI, independent of the patient's marijuana use. Actually the cannabis user had a STEMI with completely occluded coronary artery (LAD). Literally, coronary vasospastic effect of the marijuana from the peripheral path and STEMI findings on ECG is called Type 2 myocardial infarction secondary to an ischemic imbalance.¹¹ Moreover, cannabis has a disturbing effect on coronary microcirculation and on coronary flow reduction.^{2,12} Because the effects of cannabis cause catecholamine increase, this will lead to increase in heartbeat, increase of myocardial oxygen demand, direct response in the left ventricular function and sudden death. Additionally, it is thought that there is increased platelet coagulability.² Although, case 4 above had real coronary obstruction and STEMI on ECG, troponin increase did not occur.¹²

Acute exposure to MDMA/ecstasy has profound cardiovascular effects on blood pressure and heart rate in humans and animals.¹³

Serotonergic (5HT) tone will decrease in the myocardial wall as inversely proportional with ecstasy dosage. It was reported that after consumption of MDMA, carnitine increases in myocytes which leads to energy balance changes in the direction of increase in the fatty acid metabolism.¹³ Likewise, it is observed that choline transmitter decreases and there are both parasympathetic desensitization and increased sympathetic effect in the tissue level. As in the 2nd and 3rd case presented, palpitations and accompanying STEMI on ECG can be encountered in ecstasy use. Coronary angiography was performed with coronary stress test positivity, but coronary blockage was not revealed. Similar case report is not frequent in the literature.

LIMITATIONS

The study was conducted as a single center study; hence, the results cannot necessarily be generalized to other EDs or other settings. Additionally, the same physicians performed all examinations within a year, also affecting the external validity. The advantage of this was, however, a consistent examination including cardiac procedures giving rise to collecting data about cardiac intensive care unit admissions of SD users. Blood or urine work-up was not performed to verify and characterize SD use, since resources were not available in the present hospital. Nonetheless, assessment of individuals using self-reports is cost-effective and is fairly accurate.

CONCLUSION

The frequency of cardiac complications by SD users is not high. However, emergency health care personnel must be on alert for young patients with substance abuse history, who present with altered mental status, chest pain and/or discomfort, syncope, palpitation and vomiting in terms of ACS. High-degree AV block and occlusive Type one STEMI may be observed after cannabinoid use.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

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