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Cardiovascular events post cannabis abuse during the COVID-19 pandemic

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ABSTRACT

Objective: The pandemic caused by Sars-CoV-2 (COVID-19) has changed dramatically individuals' life worldwide. The implication of measures of public health protection, the social distance and isolation, the lockdown and the decrease of social life activities caused escalated anxiety, depression, physical inactivity on the one hand and widespread unemployment and financial crisis on the other hand. Preliminary studies during COVID-19 pandemic reported an increase in the use of psychoactive substances, including alcohol and cannabis (CB). The latter has been linked with harmful cardiovascular and respiratory effects (eg. lung cancer, bronchitis and pulmonary emphysema). Especially people with substance use disorders were further stressed by the current circumstances and were found to intensify consumption of cannabinoids (**1-4**). This short review focuses on the possible cardiovascular impact of CB abuse in the era of Covid-19 pandemic. It aims to stress the worldwide clinical attention and the clinicians' awareness on the development of specific prevention and intervention strategies against CB addiction during pandemics.

Keywords: pandemic, psychoactive substances, marijuana, cannabis, cardiovascular, coronary syndrome, myocardial infarct, Sars-CoV-2, COVID-19

INTRODUCTION

The last decades many countries and states have legalized marijuana's (MJ) use and other cannabinoids for medical and recreational purposes. MJ derived from the hemp plant Cannabis sativa is the most commonly abused psychoactive drug around the privileged world and about 11.8 million young individuals in the United States report MJ use with a dramatic increase of consumption rates among all age groups (**5, 6**). Furthermore, nowadays these drugs are even more available and accessible to people stressed by the COVID-19 crisis which results on few systemic acute and long term side effects. Literature data report that serious adverse events of cannabinoids include myocardial infarction (MI), sudden cardiac death, cardiomyopathy, stroke, transient ischemic attack, and CB arteritis, vascular diseases (coronary, cerebral and peripheral), arrhythmias and stress cardiomyopathy to be the less investigated. Many of the victims of these disorders are young men with almost none cardiovascular risk factor. As MJ has become extremely prevalent in our society, the prevention of acute cardiovascular events post MJ use requires collaboration among cardiologists, drug users and addiction experts (**7, 8**).

Cardiovascular effects of cannabinoids (CB)

Physiology

The current available literature associates MJ with several serious adverse cardiovascular disease (CVD) events, due the interaction of cannabinoids with the endogenous endocannabinoid system with different mechanisms like "CB arteritis," CB- induced vasospasms and platelet aggregation (**9, 10**). The French Addictovigilance Network (during 2006-2010) reported that only 2% of all CB related events were proved to be CVD side effects, including mainly acute coronary syndromes and peripheral arteriopathies (**11**).

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Nevertheless, reports associate the increased frequency of MJ use with the risk of cardiac arrhythmias and MI, whereas the chronic cannabinoids use has been directly linked with increased angina frequency, due to a decrease in the angina threshold, diminished sympathetic and parasympathetic nervous system (NS) signal transduction, serum aldosterone increase, central and peripheral vasoconstriction, and hypertension (7). Most of the CVD effects of cannabinoids are mediated through the subsequent activation of the sympathetic NS and the inhibition of the parasympathetic autonomic NS (12). Thus, CB smoking increases the heart rate, the serum norepinephrine level and myocardial oxygen demand immediately, it reduces oxygen supply and leads to pro-coagulant or pro-thrombotic state, while the increased atropine inhibits the parasympathetic activity (12-17). According to recent reports, the CB use might also cause dose-dependent elevation of the systolic blood pressure and heart rate (18, 19) and induce atrial fibrillation shortly after smoking MJ (20). While smoking CB, the oxygen delivery to the heart and other vital organs is diminished and the carboxyhemoglobin levels are elevated, resulting in reduce of the time to onset of symptoms during exercise in patients with stable angina (12).

Complications of MJ abuse

1. **Acute Coronary Syndrome (ACS):** The CB use is found to increase fivefold the risk for ACS within a 5 hours window post abuse, whereas the reintroduction of MJ abuse is directly correlated with recurrence of the syndrome (12, 21), and this risk dramatically declines after the first hour of exposure to MJ (22, 23). Moreover, these acute MI events are associated with higher short-term mortality in CB users, perhaps due to the analgesic effect of MJ on anginal symptoms (14).

   Several case reports indicate the coronary vasospasm-induced cardiomyopathy as the principal effect of CB abuse (24-29), whereas most of them are patients without CVD history or related risk factors. The majority of these individuals presented at the Emergency Departments with ACS after MJ use, with ST-segment elevation in their Electrocardiogram (ECG) and increased cardiac enzymes and were subjected to cardiac magnetic resonance imaging or coronary angiography which were finally negative for occlusive atherosclerotic disease (12, 21), indicating the coronary vasospasm as the most possible cause of these CVD events (24). Retrospective systematic review of published articles showed ST segment elevation in 60% of EKGs, 36,8% of patients had normal coronary arteries, 35% had LAD coronary artery occlusion and 34% of cases had concomitant cardiomyopathy compared to non-users (30-32).

   In other cases, coronary angiogram revealed occlusive thrombus inside the coronary artery which was attributed to non-reversible platelet aggregation due to CB use (10, 33). The possible mechanism is that the CB use inhibits the parasympathetic system, induces an inflammatory effect in the arterial wall, which leads in endothelial erosion due to oxidative stress, plaque rupture, factor VII activation and finally to thrombus formation (23, 34, 35).

   Also, MJ smoking is proven to decrease the maximum exercise capacity in healthy individuals, while the cutoff of angina threshold is lowered when comparing individuals with MJ smoking and nicotine smoking. The exercise time to angina post MJ smoking is reduced by an average of 48% as compared to 23% after tobacco cigarette smoking, indicating that the increase in cardiac events was independent of tobacco use (22).

   On the contrary, cardiovascular mortality in patients with known CAD is increased by 3-fold especially after MI in MJ users compared to non MJ users (22). A meta-analysis on non-fatal MI related to the CB smoking indicated the MJ abuse as the third-highest-ranking associated variable (Hata! Başvuru kaynağı bulunamadı.).

2. **Left Ventricular Systolic Dysfunction:** Besides, cannabinoids were found to reduce myocardial contractility, whereas this systolic dysfunction might result from persistent tachycardia, atrial fibrillation or ischemia in the case with pre-existing CAD (12).

3. **Rhythm Disturbances and Sudden Cardiac Death:** The most commonly reported arrhythmia post cannabinoids smoking in individuals without cardiovascular history is atrial fibrillation (26%), followed by ventricular fibrillation (22%) and Brugada pattern (19%) (39). Retrospective studies report that the common mortality causes for CB users are different rhythm disturbances (sinus tachycardia, ectopic atrial or ventricular rhythm, and atrial or ventricular fibrillation). Most articles attribute these tachyarrhythmias to a hyperadrenergic state after MJ use (38).

   Adrenergic stimulation causes a reduction in action potential duration and results in a microreentrant tachycardia (17). Serious ventricular arrhythmias shortly after CB smoking may cause dizziness, syncope, cardiac arrest or even sudden cardiac death, due to acute myocardial microvascular spasm, acute MI, or pre-existing CAD (12, Hata! Başvuru kaynağı bulunamadı.).

   Thus, research studies found that MJ use is associated with a three-fold higher mortality rate after MI, with higher mortality rate among CB users with MI compared to non-users (39).

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