Cardiovascular Effects of Marijuana

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Introduction

Plants of the Cannabis species, commonly known as marijuana, contain numerous psychoactive components, including the primary psychoactive compound Δ-9-tetrahydrocannabinol (THC). The World Health Organization (WHO) describes cannabis as the most widely used, cultivated, and trafficked illicit drug in the world, with an estimated 147 million people using the drug annually. Consistent with worldwide reports, the Substance Abuse and Mental Health Services Administration estimated nearly 20 million active marijuana users in the United States in 2013, making it the most widely used illicit drug in the nation. Evidence of therapeutic potential for marijuana and its components has been suggested for a number of medical conditions, including cachexia, cancer, glaucoma, HIV/AIDS, muscle spasm, seizures, severe nausea, severe or chronic pain, and sleep disorders, though lack of scientific evidence regarding safety and efficacy has prohibited endorsement by the US Food and Drug Administration for any therapeutic use.

In a 1999 Institute of Medicine (IOM) publication, the IOM made a clear call to action regarding the need for trials examining safety and efficacy. Despite the IOM’s recommendation, few trials have been published. Nevertheless, the idea that marijuana use is safe is deep seated in the public and even among some health-care professionals. As such, use of marijuana for medical purposes has been approved in several states in the United States, and some physicians routinely prescribe cannabis to patients, particularly in instances of chronic pain or muscle spasms. In a recent publication related to the use of cannabinoids for the treatment of epilepsy in the New England Journal of Medicine, Friedman and Devinsky did an outstanding job of highlighting some of the major barriers to scientific investigation surrounding the therapeutic use of cannabis-related compounds. Despite these challenges, it is important that cannabis be evaluated like any other drug, weighing both the benefits and the side effects before universal acceptance of the scientific community. Furthermore, recent legalization of recreational use in a number of states presents substantial concerns about the potential for risk in the absence of any therapeutic benefit.

The potential for harmful cardiovascular effects of marijuana was first reported several decades ago, which, combined with known effects on behavior and cognitive function, prompted a surgeon general warning against marijuana use in August 1982. A recent review of reports over the past 2 decades describes ongoing evidence of adverse effects of marijuana use on rates of accidents and injuries, cognitive function, psychosocial consequences, and mental and physical health outcomes. In an era of ongoing illicit use of cannabis and increasing momentum toward legalization for recreational purposes, it is important that the medical community consider the physical health risks associated with recreational cannabis consumption, as such concerns are likely to present in the clinical setting. In this article, we discuss the potential cardiovascular effects of marijuana, with particular focus on its effects on the coronary, cerebral, and peripheral vasculature.

Marijuana and the Coronary Arteries

Endocannabinoids are endogenous mediators present in the coronary arteries with actions similar to THC. Endogenous cannabinoids play an important role in regulation of the cardiovascular system, particularly when the heart is challenged by pathological conditions, such as ischemia or cardiogenic shock. It is possible that exposure to exogenous cannabinoids may interfere with the delicate balance between endocannabinoids and various receptors in the coronary arteries, potentially modifying some aspects of the protective role of the endocannabinoid system. As such, several cardiovascular conditions, such as acute coronary syndrome, have been attributed to marijuana use.

In some of the earliest reports of the cardiovascular effects of marijuana exposure, even a single administration to healthy marijuana users led to an increase in both pulse rate and blood pressure, resulting in an increase in myocardial oxygen demand.

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demand.13 With nearly 200 published studies now present in the literature, these changes are well described as part of the consistent pharmacodynamic effects observed during marijua

1 Clinically, marijuana decreases exercise time to develop angina in volunteers with known angina pectoris1,4,15 and is implicated in numerous cases of acute coronary syndromes reported in the literature.16-21 Most cases of marijuana-associated acute coronary syndrome occur within 1 hour of exposure and are generally associated with coronary arteries that appear angiographically normal yet are prone to develop spasm, coronary thrombus, or coronary microcirculatory dysfunction. Acute coronary syndromes may also occur years after frequent use with no apparent precipitating factor other than marijuana use.22

In France, where all serious cases of drug abuse presenting to emergency departments must be reported to a national agency, evidence collected to date suggests that those who present with marijuana-associated cardiovascular complications have a mortality rate that is much higher than that in nonusers.23 In addition, the annual rate of marijuana users presenting to emergency departments with such complications in France appears to be on the rise. Importantly, many of the patients presenting to the emergency department with drug-related complications also had other significant cardiovascular risk factors, particularly tobacco use, and such reporting can only provide a rough estimate of the prevalence of drug abuse-related complications.

Acute coronary syndrome triggered by marijuana exposure may include angina pectoris, myocardial infarction, and sudden cardiac death. In a 2001 publication by Mittleman et al, 3882 patients with acute myocardial infarction were assessed for marijuana use, revealing a 4.8-fold increase in the risk of myocardial infarction in the first hour after marijuana use compared to nonusers.24 Further review of this cohort and other case reports suggest that marijuana-associated myocardial infarction occurs in a relatively young population, as young as 20 years old, and that while additional risk factors, such as tobacco use, are often present, marijuana may serve as a sole risk factor. Following marijuana-associated myocardial infarction, intravascular ultrasound provides no clear evidence of detectable atherosclerotic coronary artery disease, and findings most commonly noted during angiography were coronary spasm and intracoronary thrombus formation.25-31 We and others have also described myocardial infarction associated with marijuana use triggered by slow coronary flow.21,32 Prognosis is poor in marijuana users having myocardial infarction, with a 3-fold increase in mortality at a median follow-up of 3.8 years, compared to individuals with myocardial infarction who do not use marijuana.33 The mechanism behind this finding is not clear.

The coronary effects of marijuana exposure can also result in cardiac arrhythmias and/or sudden cardiac death. As early as 1973, Kochar and Hosko investigated the effect of THC on persons with normal electrocardiograms at baseline. Most volunteers had characteristic ST-segment elevation with decrease in amplitude of T waves.34 Occasionally, premature ventricular contractions were noted. Atrial fibrillation and asystole were also reported.35-37 Sudden cardiac death has been reported in marijuana users but appears to be a relatively rare event38-40 and less frequent than reports associated with the use of other illicit drugs.41

Marijuana and the Cerebral Arteries

Several series of ischemic strokes temporally related to marijuana use have also been reported. In most instances, patients were quite young and many had intracranial vascular etiology.42-45 This is in contrast to strokes in elderly individuals, which are usually thromboembolic or related to carotid artery disease. Occasionally, the neurologic symptoms were reversible.46 Many patients were also tobacco smokers, and further studies are needed to elucidate the role of marijuana, tobacco, or combination use as a risk factor for stroke in young people.47 Interestingly, association between marijuana use and development of stroke has also been reported following the use of synthetic marijuana products.48 In some reports, neurologic deficits were recurrent and related to further exposure to the drugs.49,50

Other Vascular Effects of Marijuana

Marijuana also impacts the peripheral arterial system. The effects of marijuana on peripheral blood vessels of the lower extremities have been described as a disease similar to thromboangiitis obliterans.51 However, the frequent use of both marijuana and tobacco makes the association somewhat weaker.52 Superficial thrombophlebitis and central retinal vein thrombosis temporally related to the recurrent use of marijuana have also been described.53,54 The frequent reports of the effect of marijuana smoking on various vascular beds, including in the heart, brain, and elsewhere, suggest a systemic vascular effect.

Conclusion

Despite the surgeon general warning about marijuana use several decades ago,10 and strong evidence for deleterious effects on the cardiovascular system, marijuana use remains common both for medical treatment and as a recreational substance.1,11 Evidence suggests that marijuana use can serve as a trigger for acute coronary syndromes and that marijuana-related vascular complications are associated with elevated mortality.22,23 As such, before more states legalize marijuana for recreational use, it would be prudent to fully evaluate the safety of the drug. We recommend a national reporting system for capture of data related to adverse drug effects seen in emergency departments. Such data would allow for interstate comparison regarding the frequency of such complications for states with and without recreational legalization and would help to inform public policy and scientific investigation moving forward.

Author Contributions

Rezkalla, S contributed to conception and design, acquisition, analysis, and interpretation; drafted the manuscript; critically the revised manuscript; gave final approval; and agrees to be accountable for all
aspects of work ensuring integrity and accuracy. Stankowski, R contributed to design, analysis, and interpretation; drafted the manuscript; critically revised the manuscript; gave final approval; and agreed to be accountable for all aspects of work ensuring integrity and accuracy. Klone, R contributed to conception and design, acquisition, analysis, and interpretation; drafted the manuscript; critically revised the manuscript; and gave final approval.

References
10. Centers for Disease Control. The Surgeon General’s warning on smoking and interpretation; drafted the manuscript; critically revised the manuscript; and gave final approval.


