

Cannabis use and cardiovascular complications: are we aware enough?

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ABSTRACT: Cannabis is the most widely used illegal drug. Over the last years more scientific studies focus on the cardiovascular complications of cannabis. This brief review cites the effects of cannabis in human myocardial tissue with emphasis on the risk of development of cardiovascular disease after the use of the drug.

Key Words: Cannabis, Cardiovascular disease, Δ^9 - tetrahydrocannabinol.

INTRODUCTION

Cannabis (also known as marijuana, hashish, grass or hemp) is a natural product prepared from *Cannabis plant*, which is known to humankind since ancient times¹, when it had been used as a medicine and a source of fibre². In Europe, it was brought by Napoleonic soldiers returning from the Middle East, in the 19th century.

The resin of the plant contains more than 480 chemical compounds, including at least 84 psychoactive substances known as cannabinoids³. The main psychoactive cannabinoid is Δ^9 - tetrahydrocannabinol (Δ^9 -THC or THC).

Due to the effects of Δ^9 -THC and the other cannabinoids, cannabis is used nowadays mainly as a recreational drug. The low price and easy accessibility of cannabis makes it one of the most widely abused recreational substances, together with tobacco, caffeine and alcohol⁴. Its huge popularity is also related to the fact that people believe that cannabis is harmless. It is estimated that so far almost 77 million people in the European Union have used the drug at least once in

their lifetime⁴. Most of them are young, aged between 18-25 years^{1,5}.

Despite the common perception about the drug's safety more and more scientific studies focus on the cardiovascular complications of cannabis use. The extensive interest emerged as many case reports have been published over the last four decades associating the use of cannabis by young people with, potentially lethal, cardiovascular disease^{2,6,7}. The trigger of writing this short review was the results of toxicological analyses of some fatal cases. The cause of death of these cases was cardiac arrest and the only toxicological finding was the detection of THC in blood and the THC metabolites in urine of the deceased.

In this short review we discuss the physiological and pathological effects of cannabis in human myocardium with emphasis on the risk of developing a cardiovascular disease after cannabis use.

Physiological effects of cannabis use

The physiological effects of cannabis can either be acute or chronic⁷. Acute effects include a rapid and

dose-dependent increase in heart rate and blood pressure that occurs as a result of beta-sympathetic stimulation⁸. Chronic use of cannabis leads into tolerance to the previous effects due to a decrease in sympathetic activity and a dose-dependent increase to parasympathetic activity⁷. Parasympathetic stimulation has the opposite effects to the cardiac function, causing bradycardia and hypotension⁸. As it is already mentioned, the time-dependent effects of cannabis are strongly related to the dose that has been used in each case. Low to moderate doses tend to cause tachycardia and increased blood pressure through the stimulation of the sympathetic nervous system whereas high doses lead to parasympathetic activation⁷.

Pathological effects of cannabis use

Several mechanisms have been proposed so far associating cannabis use with chronic cardiovascular conditions or acute cardiovascular events^{7,9,10}. Most of the experimental and clinical outcomes support that:

1) THC stimulates the production of catecholamines leading to proarrhythmic effects. Several studies support that cannabis use can lead to profound sinus tachycardia and frequent premature ventricular beats⁵ and can also produce significant cardiac arrhythmias. Rezkalla et al.¹¹ also postulated that THC may be linked to genesis of ventricular tachyarrhythmias by triggering activity in the Purkinje fibers.

2) Cannabis use by susceptible individuals can result in cardiac ischemia due to an increase in heart rate and cardiac workload that occurs via sympathetic stimulation. Additionally, increased sympathetic stimulation can lead to myocardial infarction in otherwise healthy individuals that use cannabis (or those with low cardiovascular risk). Several case reports associating cannabis with myocardial infarction have been reported⁵.

3) Orthostatic hypotension and consequently syncope can occur due to THC-mediated conduction of atrioventricular node, reduction of the left ventricular ejection time and decrease of peripheral vascular resistance mainly in the skeletal muscle⁷.

4) The analgesic properties of THC may lead to a delay in seeking medical care for acute coronary events. Coronary heart disease mortality and coronary artery calcification, which is an early indicator of

coronary atherosclerosis have been reported through cannabis users⁷.

5) THC can increase blood carboxyhemoglobin levels resulting in impaired oxygen supply to the heart, which results in a heart rate increase⁷.

6) Cannabis smoking leads to the production of oxidant gases causing cellular stress which may increase cardiovascular risk through the activation of platelets, the promotion of oxidized LDL formation, and induction of an inflammatory response¹⁰. On the other side, there are *in vitro* studies that support that Δ^9 -THC has a beneficial effect on cardiomyocytes, when used at low concentrations, protecting them from hypoxia during stress conditions¹².

However, parallel use of tobacco should always be considered when the the cannabis-associated risk of cardiovascular disease is studied, as there is a strong relation between tobacco cigarette smoking and cannabis use⁵.

CONCLUSIONS

As it was previously reported, cannabis use can lead to a number of acute or chronic cardiovascular effects that in some cases can possibly result in users' death. It is obvious that there is a need for better informing and understanding of the possible effects of cannabis in human cardiovascular system. Future studies should focus on cardiovascular outcomes and effects of THC on arrhythmic, vascular, and atherosclerotic events.

Χρήση κάνναβης και καρδιαγγειακές επιπλοκές: Είμαστε αρκετά ενήμεροι;

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ΠΕΡΙΛΗΨΗ: Η κάνναβη αποτελεί μία από τις ευρύτερα διαδεδομένες σε χρήση ψυχοτρόπες ουσίες. Τα τελευταία χρόνια όλο και περισσότερες επιστημονικές μελέτες επικεντρώνονται στις καρδιαγγειακές επιπλοκές που σχετίζονται με τη χρήση της. Στην παρούσα σύντομη ανασκόπηση, παραθέτουμε τις φυσιολογικές και παθολογικές επιδράσεις της κάνναβης στο καρδιαγγειακό σύστημα, επικεντρώνοντας στον κίνδυνο ανάπτυξης καρδιαγγειακών παθήσεων μετά από χρήση της ουσίας.

Λέξεις Κλειδιά: Κάνναβη, Καρδιαγγειακές παθήσεις, Δ⁹- τετραϋδροκανναβινόλη.

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