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Editorial

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Smoking Marijuana. Is it Safe for the Heart?

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Different preparations of Cannabis sativa (commonly marijuana and hashish) are widely used mainly for their euphoric effects. Cannabis after alcohol consumption is by far the most commonly used recreational drug in Europe. About 20% of adults in the European Union (aged 15–64 years), over 62 million people, have tried cannabis at least once in their life [1]. Users and lay people believe that marijuana or hashish is safe. Many cases of cardiovascular events have, however, been related to a cannabis consumption [2-4], and cases of acute ischemia or thrombosis even on the ground of normal coronary arteries have been reported [5-10].

Several mechanisms have been proposed by which cannabis use might trigger cardiovascular events [11]. These mechanisms include a) proarrythmic effect mediated by catecholamines b) cardiac ischemia due to an increase in heart rate and cardiac workload in susceptible individuals c) postural hypertension d) delay in seeking medical care for acute coronary events due to analgesic properties of cannabis e) impaired oxygen supply to the heart secondary to increased blood carboxyhemoglobin levels d) production of oxidant gases by marijuana smoking resulting in cellular stress, which may highten cardiovascular risk through activation of platelets, increased oxidized LDL formation, enhanced factor VII activity and induction of an inflammatory response. Angina pectoris, myocardial infarction, ventricular tachyarrythmias, generalized vasoconstriction has been reported to cannabis users. Congenital heart disease after parental marijuana use has also been reported. All these have made cardiologists to consider cannabis smoking a cardiovascular risk factor [12]. During cannabis smoking the concentration of Δ^9-tetrahydrocannabinol in the bloodstream reaches peak levels even before the end of the smoking period and then it is rapidly distributed to the tissues [13]. Its use leads to dose-dependent tachycardia, raised blood pressure and cardiac output, for which tolerance rapidly develops [14,15]. Decreased peripheral vascular resistance and postural hypotension frequently occur [14]. These effects are mediated by the central autonomic nervous and cannabinoid receptor systems [15]. Electrocardiographic effects of cannabis are sinus tachycardia, sinus bradycardia, second degree heart block, atrial flutter and fibrillation [16]. Smoking cannabis is associated with an increase in carboxyhaemoglobin, resulting in decreased oxygen carrying capacity [17]. Furthermore, cannabis smoking produces oxidant gases that contribute to cellular stress [18] and may contribute to cardiovascular risk by activating platelets, promoting formation of oxidized LDL, and inducing an inflammatory response [15]. Finally, patients with stable angina may experience a lower threshold for angina-related pain for some hours after marijuana smoking which results in impaired judgment in seeking medical assistance [14,15].

The cardiovascular effects of marijuana in humans, thought, a few decades ago, to be predominantly mediated centrally by the sympathetic nervous system, may also be modulated by the cannabinoid (CB) receptor system [15]. Indeed, the endogenous cannabinoid system appears to play an important role in cardiovascular regulation. Possible mechanisms for endocannabinoid vascular effects include inhibition of transmitter release from sympathetic nerve terminals, direct effects on vascular smooth muscle cells, and effects on endothelial cell function [14].

More specifically, the cardiovascular reaction to cannabis appears to be biphasic. The initial increase in adrenergic tone is followed by a later increase in parasympathetic tone. So, the initially increased heart rate and blood pressure are followed by a decrease in both. These are mediated through two G-protein coupled CB receptors as the initial tachycardia is not accompanied by a raised plasma noradrenaline level which increases only 30 minutes after smoking and remain elevated for at least 2 hours [19,20].

In the recent years, a considerable number of cases of acute cardiovascular events, shortly after using cannabis, appear in the medical literature [2-7,13]. This is probably due to the increase of cannabis use during the last decades and even to the fact that cannabis users are growing older. The fact that older people in the past only rarely smoked cannabis in the United States and Europe may partially account for only rare case reports of adverse cardiovascular events in the former decades. Case reports are very useful in suggesting possible links between exposure and disease outcomes but their importance is limited by the fact that they cannot establish an etiologic role for an exposure and a quantitative assessment of disease risk cannot be made.

Only, few studies have systematically examined associations of cannabis use to cardiovascular disease outcomes using epidemiological methods that provide quantitative estimates of the risk of disease associated with marijuana use. Sidney et al. [15], reported on the relationship of marijuana use to mortality in a cohort of 65,171 men and women ages 15 through 49 years who completed self-administered research questionnaires on tobacco, cannabis, and alcohol use from mid-1979 through 1985 [21]. Follow-up for mortality was conducted through December 31, 1991 (mean=10 years of follow-up). The risk of circulatory disease death, myocardial infarction, all coronary heart disease, stroke, and all cardiovascular disease was neither increased nor decreased by cannabis use relative to nonuse of cannabis. A serious limitation of the above study is that the study group was relatively young (mean age=33 years at onset of follow-up), so that the cohort follow-up and cardiovascular deaths occurred in a relatively young age range that is not representative of the older age range in which the bulk of cardiovascular morbidity and mortality occurs. Rodondi et al. [22], used 15 years of longitudinal data from 3,617 black and white young adults participating in the Coronary Artery Risk Development in Young Adults (CARDIA) study, to assess whether marijuana use was associated with caloric intake, Body Mass Index (BMI), and cardiovascular risk factors. In multivariate analysis, the associations between marijuana use and systolic blood pressure and triglycerides disappeared, having been mainly confounded by greater alcohol use

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in marijuana users. The authors concluded that although marijuana use was not independently associated with cardiovascular risk factors, it was associated with other unhealthy behaviors, such as high caloric diet, tobacco smoking, and other illicit drug use, which all have long-term detrimental effects on health [22].

The above studies did not prove the role of chronic cannabis smoking as an independent risk factor for cardiovascular events. However, the possibility of cannabis use serving as a trigger for an acute cardiovascular event may exist. The strongest evidence implicating marijuana as a trigger of myocardial infarction was reported from a large epidemiologic study by Mittleman et al. [23]. They analyzed 3,882 patients with myocardial infarction and tried to determine causative factors. Of that number, 124 (3.2%) patients reported that they had smoked marijuana during the year preceding their myocardial infarction. Of the 124 patients who reported smoking marijuana, 37 reported smoking it within 24 h of myocardial infarction onset and nine reported use within 1 h of myocardial infarction symptom onset. In addition to these nine patients, three patients reported using marijuana between 60 and 120 min before the onset of symptoms. Mukamal et al. [24], conducted an inception cohort study of 1913 adults hospitalized with myocardial infarction at 45 US hospitals between 1989 and 1994, with a median follow-up of 3.8 years. The study found a statistically significant 4.8-fold increase in the risk of MI in the first hour following marijuana use, with a directly proportional decrease in risk as time increases. Cannabis smoking increased the risk of cardiovascular mortality, hazard ratio 1.9 and non-cardiovascular mortality, hazard ratio 4.9. The authors concluded that these preliminary results suggest possible hazards of marijuana for patients who survive acute myocardial infarction. In the Determinants of Myocardial Infarction Onset Study, in a series of 3,882 patients the risk of myocardial infarction onset was elevated 4.8 times over the baseline in the first hour after marijuana use (95% CI, 2.4-9.5). After 1hour the risk rapidly decreased [3]. Although marijuana use has not been associated with mortality in other populations, it may pose particular risk for susceptible individuals with coronary heart disease.

Despite the controversial data concerning the cannabis related problems in healthy young users, people with some degree of coronary artery or cardiovascular disease, may be susceptible to greater risks because of the above mentioned cannabis effects on the cardiovascular system, particularly when relatively non tolerant individuals are exposed. The perception of angina pectoris may be decreased after cannabis use, which may lead to delayed recognition of the cardiac event, and consequently to more serious and extended myocardial damage. The cardiologists should be aware of the potential risk of cannabis use and medical history should always include questions about it. The importance of abstinence from cannabis use should also be stressed to patients with cardiovascular disease.

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