Cannabis, Cigarette Smoking and Lung Function –not all downhill?

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Summary

The adverse effects of cigarette (tobacco) smoking are well established and well known. Cannabis (also called marijuana) is the most widely used illicit drug and the second most smoked substance. In its various forms it has been increasingly licensed for recreational as well as medical use. Cannabis contains many pharmacologically active substances and cannabinoid pharmacology is very complex. Much is known about its psychoactive properties but rather less about its pulmonary effects. Cannabinoids have well documented anti-inflammatory and immunomodulatory effects. This review explores the information available regarding its effects on the lungs.

In normal subjects acute exposure to inhaled and oral marijuana produces substantial bronchodilatation. This also occurs in asthmatic subjects and patients recovering from an asthma exacerbation. Less information is available in COPD.

Epidemiological information about chronic exposure to marijuana is compounded by the difficulties of studying an illicit substance, the problems of variability in composition and quantification of consumption and the fact that it is usually smoked in combination with tobacco. Available data suggest that cannabis smoking commonly leads to chronic bronchitis (cough and phlegm). However, surprisingly it does not generally cause progressive airflow obstruction and COPD. It produces an increase in vital capacity rather than a fall in FEV_1. It has been associated with the development of bullous lung disease but not definite emphysema in the limited studies. It does not seem to be associated with lung cancer nor with frequent respiratory infections.

Key Message

Cannabis smoking frequently causes bronchitis with symptoms of productive cough but unlike cigarette smoking does not generally lead to COPD. Long term exposure increases vital capacity rather than reducing FEV_1. Acutely, marijuana produces bronchodilatation in normal subjects and in asthmatics. The pharmacology of cannabinoids is complex but merits further investigation.

Introduction

Cannabis is the most widely used illicit drug in the world. Cannabis, commonly called marijuana, is the second most smoked substance, after tobacco. Cannabis comes from a flowering plant, native to central Asia and the Indian sub-continent. The genus includes 3 different species, *Cannabis sativa*, *Cannabis indica* and *Cannabis ruderalis.* They contain 2 major active compounds, delta-9-tetrahydrocannabinol (d-9-THC) and cannabidiol (CBD). Altogether about 90 cannabinoids and over 400 compounds are produced. The psychoactive compound is THC but this is modulated by CBD. Higher THC content occurs in *sativa*-dominant strains while the *indica*-dominant strains have more CBD. Recently, skunk-like cannabis containing very high THC concentrations has become prevalent.

The flower tops of the plant, are called ‘bud’, the resin ‘hash’ and other common names include ‘weed’, ‘dope’, ‘grass’, ‘hemp’, ‘ganga’, ‘reefer’, ‘spliff’, ‘toke’ and ‘blunt’. Cannabis can be smoked in a variety of ways, usually without a filter and burned at a higher temperature, and with users generally holding their breath for longer periods of time, compared to tobacco smokers. Joints can be made using just cannabis leaves or can be mixed with tobacco in ‘spliffs’. Many cannabis users also concurrently smoke tobacco cigarettes. Routes of administration vary by geographical region as well, with European countries mostly smoking spliffs while Americans largely smoke cannabis-only joints. Aside from joint smoking, users may also use water bongs, pipes and, more recently, vaporisers [1].

Recreational cannabis use, estimated at 240 million world-wide, has been legalized in Uruguay since 2013, in 5 US states and, very recently, in Canada. Medicinal use is legal in 31 US states, at least 30 countries and is imminent in the UK. However, we still know very little about the long term effects of smoking cannabis on the respiratory system and on health in general. This review focuses on effects on the lungs.

Tobacco smoking is well known to increase the risk of chronic bronchitis, emphysema, and small airways disease (all components of chronic obstructive pulmonary disease -COPD) as well as the development of various forms of lung cancer and other neoplasia. Chronic cannabis smoking might be expected to have similar effects, considering that the contents and properties of tobacco and cannabis smoke are similar [2].

Symptoms

Respiratory symptoms such as cough, sputum production, and wheeze are increased in current cannabis use [3,4,5,6]. However, surprisingly, associations with shortness of breath were not found in the larger studies [4,5,6]. This suggests that cannabis smoke causes chronic bronchitis in current smokers but not shortness of breath or irreversible airway damage. Studies examining the effect of quitting marijuana smoking support this showing a significant reduction in morning cough, sputum production, and wheeze compared to continuing smokers [4]. No increased risk of developing chronic bronchitis was found in quitters compared to non-smokers at 10 years follow up [4]. In young adults vaping cannabis is increasingly popular but long-term respiratory health effects are not known.

Acute airway effects of cannabis

Experimentally, the acute bronchodilator effect of inhaled cannabis, seen in normal and asthmatic subjects and asthmatics recovering from exacerbations is well described as an effect of THC [7,8]. However, since cannabinoids can have partial agonist, or even antagonist, effects little is known about differences in airway effects from different strains of cannabis containing varying concentrations of cannabinols.

Chronic effects on Lung function

COPD is conventionally diagnosed when a patient has an irreversible reduced forced expiratory volume in 1 sec (FEV_1) compared with forced vital capacity (FVC) on spirometry. Several large, recent, observational studies have reported an increase in FVC with little or no change in FEV_1 in long-term marijuana-only users, even after 20 joint years of smoking (1 joint-year is equivalent to 365 joints per year) [3,4,6,9]. A reduced FEV_1/FVC ratio due to the increased FVC, clearly differs from the classical spirometric changes seen in tobacco smoking. The mechanism(s) of this increase in FVC are not clear. Respiratory muscle training by the breath-holding techniques used during marijuana smoking has been proposed. However, there is little evidence that training can increase FVC.

Additional lung function measurements have only been examined in smaller studies. Several studies have reported very small, not always consistent, changes in total lung capacity, functional reserve capacity, residual volume and specific airways conductance and resistance. Small reductions in carbon monoxide transfer factor have been reported only in smokers of cannabis and tobacco. Interestingly, a 13% reduction in exhaled nitric oxide, was recorded after marijuana use within 0 to 4 days [10]. Rather conflicting results on airway responsiveness have been reported in 3 studies with significant methodological differences.

We do not know why cannabis smoking does not produce COPD. Possible explanations include a persistent bronchodilator effect (offsetting airway narrowing) or anti-inflammatory or immunomodulatory effects of THC [11].

Bullous Lung Disease

Bullous lung disease, predominantly upper lobe involvement with added peripheral emphysema usually presenting with pneumothorax, is widely recognised in heavy marijuana smokers. However, there are actually few relevant data with only 57 cases in 7 case series and 11 case reports up to 2018 [1]. They are not representative of the general marijuana smoking population. A single cross-sectional study examined radiological changes among New Zealand marijuana smokers reporting an increase in macroscopic emphysema in tobacco smokers compared with non-smokers but not in cannabis-only smokers. Low density lung regions on HRCT in cannabis smokers were interpreted as hyperinflation rather than microscopic emphysema [6]. A study in spontaneous pneumothorax recording smoking status and emphysema on CT found no difference in emphysema prevalence among tobacco smokers and tobacco + cannabis smokers (there were no cannabis only smokers) [12]. No definite association of cannabis smoking and early emphysema has been established.

Cannabis and Lung Cancer

Although some studies have suggested precancerous histological changes in the bronchi of marijuana smokers no definite association of cannabis smoking and lung cancer has been established. Pooled analysis of 6 case-control studies including 2,159 lung cancer cases and 2,958 controls found little or no association between cannabis smoking and lung cancer. A large retrospective cohort study of 64,855 subjects found no increased risk of cancer after 8.6 years, although mean age was relatively young [13]. One 40-year longitudinal cohort study of 49,321 Swedish conscripts reported a doubling of lung cancers in those who had smoked cannabis more than 50 times [14].

Conclusions

Acutely marijuana is a bronchodilator. Chronic cannabis smoking is associated with chronic bronchitis but not progressive airflow obstruction and COPD. A small unexplained increase in VC occurs. Heavy marijuana smoking is associated with bullous disease but there is no definite association with emphysema, lung cancer or recurrent infections. The general paucity of data, the evolving nature of available marijuana (newer, stronger forms, different modes of inhalation etc) and the important confounding factor of tobacco use have led to difficulties interpreting the health impact of marijuana on the lungs. More research, particularly prospective studies disentangling the effects of concurrent tobacco smoking are required.

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