Cannabis Smoking and Risk of Lung Cancer in Men

A Pooled Analysis of Three Studies in Maghreb

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Background: Cannabis is the most widely consumed illicit drug worldwide and the relation between cannabis smoking and lung cancer is suggestive, albeit inconclusive.

Method: We conducted three hospital based case-control studies in Tunisia, Morocco, and Algeria, three areas of high prevalence of cannabis consumption as well as production. This paper presents the pooled analysis of these three studies restricted to men with a total of 430 cases and 778 controls.

Results: Ninety-six percent of the cases and 67.8% of the controls were tobacco smokers and 15.3% of the cases and 5% of the controls were ever cannabis smokers. All cannabis smokers were tobacco users. Adjusting for country, age, tobacco smoking, and occupational exposure, the odds ratio (OR) for lung cancer was 2.4 (95% confidence interval [CI]: 1.6–3.8) for ever cannabis smoking. This association remained after adjustment for lifetime tobacco packyears as continuous variable, OR = 2.3 (95% CI: 1.5–3.6). The OR adjusted for intensity of tobacco smoking (cigarette/d) among current tobacco smokers and never cannabis smokers was 10.9 (95% CI: 6.0–19.7) and the OR among current tobacco users and ever cannabis smokers was 18.2 (95% CI: 8.0–41.0). The risk of lung cancer increased with increasing joint-years, but not with increasing dose or duration of cannabis smoking.

Conclusion: Our results suggest that cannabis smoking may be a risk factor for lung cancer. However, residual confounding by tobacco smoking or other potential confounders may explain part of the increased risk.

Key Words: Cannabis, Lung cancer, Maghreb, Tobacco, Pooled case-control study.

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With 1.18 million deaths in 2002, lung cancer is the leading cause of cancer deaths among men.[1] In 2002, more persons died of lung cancer in the developing countries than in the developed countries.[1] In Northern Africa, the lung cancer incidence rate was 12.0 per 100,000 men-years in 2002 after adjustment for the age structure of the world population, where particularly high rates were observed among men in the Maghreb (Algeria, Morocco, and Tunisia), with 16.9, 20.1 and 27.8/100,000 men-years, respectively.[1]

Tobacco smoking is the major cause of lung cancer[2] although other factors such as exposure to asbestos and radon have also been established as risk factors of lung cancer.[3] The role of other smoked products (such as pipe, cigar or narghile) is recognized[4] and some studies have suggested an association between cannabis smoking and lung cancer.[5–7] Two published studies conducted by our team suggested that consumption of hashish/kiff with snuff in Morocco[8] and cannabis smoking in Tunisia[9] are associated with lung cancer risk (kiff is a mixture of black tobacco and sieved resin of cannabis).

To further evaluate this association, particularly with more powerful means of control for potential confounding by tobacco smoking we pooled the data from the studies conducted in Morocco[8] and Tunisia[9] with the data from a third, yet unpublished study conducted in Algeria. The objective of this pooled analysis was to estimate the risk of lung cancer associated with cannabis smoking in Maghreb.

PATIENTS AND METHODS

Study Design

Three hospital-based case-control studies conducted in Morocco,[8] Tunisia,[9] and Algeria were pooled. The protocols of the three studies were similar and are briefly presented below. Except for the unpublished study from Algeria the detailed methodology is described in the published papers[8,9];

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and only briefly summarized here. All studies were approved by both the local and the International Agency for Research on Cancer ethical committees.

Morocco

A hospital based case-control study included 118 cases and 235 controls that were enrolled in the Ibn Rochd Hospital of Casablanca, Morocco, between January 1996 and January 1998. Cases were defined as subjects diagnosed with primary incident lung cancer. All cases were diagnosed radiologically and 77 cases (68%) were histologically confirmed. Two controls were matched to each case on age (±2 years for 62% and ±5 years for 99% of the study population), sex, and place of residence. Controls were selected in the same hospital and during the same period as cases and had a diagnosis not related to tobacco consumption. They were hospitalized with the following conditions: diabetes ($n = 54$), acute and chronic gastrointestinal illnesses ($n = 48$), acute or chronic urinary tract diseases ($n = 21$), liver and biliary tract diseases ($n = 33$), inguinal and abdominal hernias ($n = 13$), ocular symptoms and diseases ($n = 27$), prostatic disease ($n = 9$), endocrine diseases ($n = 6$), other infectious diseases ($n = 7$), circulatory diseases, such as hypertension ($n = 12$), anemia ($n = 2$), and osteoarticular diseases ($n = 3$). Women from this study were excluded from the pooled analysis because of the small number (four cases and eight controls).

Tunisia

A hospital based case-control study was conducted among men only, in Tunis, Tunisia between March 2000 and February 2003 and included 149 cases and 188 controls. Cases were enrolled in the Salah Azaiz Institute (the National Cancer Institute) and the Ariana hospital. Cases were defined as patients with primary incident lung cancer with histologic or cytologic confirmed diagnosis except for two cases with only a radiologic diagnosis. Controls were men recruited in the same period in the Salah Azaiz Institute, the Ariana hospital and the Charles Nicolle hospital. Hospitalization was for nonmalignant diseases of the genitourinary system ($n = 112$), endocrine, nutritional, or metabolic diseases ($n = 28$), blood or circulatory system disease ($n = 10$), muscular or osteoarticular disease ($n = 18$), pneumothorax, pleurisy or infectious pneumopathy ($n = 10$) or other infectious disease ($n = 9$). The diagnosis for one control is missing. Controls were matched to each case on age and place of residence.

Algeria

A hospital based case-control study was conducted in the Wilaya of Setif, Algeria between March 2003 and December 2004 and included 167 cases and 340 controls. Cases and controls were enrolled in the University Hospital of Setif. Cases were defined as men with primary incident lung cancer and diagnosis was confirmed by histologic or cytologic examination. Two controls were matched with each case on age and place of residence. Controls were men recruited in the same hospital and during the same period as cases, with the following conditions: cardiovascular disease ($n = 118$), diabetes ($n = 71$), chronic or acute disease of the genito-urinary track ($n = 49$), healthy controls (visitors from patient's family) ($n = 33$), chronic or acute gastrointestinal disease ($n = 31$), infectious disease ($n = 16$) osteoarticular disease, fracture or trauma ($n = 12$), dermatological disease ($n = 9$), and various other diseases ($n = 24$).

Instruments

For the three studies, a questionnaire was used to obtain information about demographic factors, tobacco and cannabis smoking and occupational exposures (asbestos, nickel, arsenic). The questionnaire was administrated by a trained physician in Arabic language after informed consent was obtained from each individual. The first questionnaire was initially designed for the study in Morocco. It was further improved and questions on quantitative information on cannabis smoking were added for the two studies conducted in Tunisia and Algeria.

Cannabis Smoking

In the study in Morocco the question on cannabis was an open question: "Have you ever used other smoked products?" The question was amended for the studies in Tunisia and Algeria and allowed the definition of three categories of cannabis smokers: non smoker, former smoker, and current smoker (see Appendix). Further information on intensity and duration of cannabis smoke was also collected. Due to the very low number of self-reports on current cannabis smoking (one control and three cases from the study in Algeria), cannabis smoking was defined as never or ever smoking cannabis in lifetime. For the pooled analyses the information on cannabis smoking was missing for 27 cases and 23 controls. Based on a conservative recoding strategy, these subjects were assigned to the never smokers of cannabis.

The cumulative consumption was assessed in the studies from Tunisia and Algeria using the variable 'joint-years.' It was defined as the number of joints per day multiplied by the duration of smoking cannabis in years.

Tobacco Smoking

Smoking status was defined using categories of never, former (stopped smoking at least 1 year before diagnosis for cases and equivalent period for controls) (see Appendix) and current smoker. In 3 cases and 6 controls among current smokers, and 26 cases and 14 controls among former smokers, the numbers of cigarettes per day were not available. The missing values were recoded using the median value of 20, estimated from the number of cigarettes smoked per day among former and current smokers in controls. For 7 cases and 21 controls, the duration of smoking exposure could not be calculated due to missing values for age at initiation and was replaced with a minimum value of 1 year. To estimate the odds ratio (OR) for different levels of tobacco smoking, we constructed a five-category variable with the never exposed individuals as the reference category. The other categories were former smokers, current smokers with the duration of use less than 25, 25 to ≤35 and more than 35 years. Pack-years of tobacco smoking were estimated for former and current smokers as the product of number of cigarettes per day divided by 20 and multiplied by the number of years exposed. When considering pack-years as a continuous variable, a value of zero pack-years was assigned to never smokers.

