



Short communication

Marijuana use is associated with hypersensitivity to multiple allergens in US adults

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ABSTRACT

Background: The recent legalization of marijuana use for both medical and recreational purposes in several states of the United States is expected to further increase the already high prevalence of marijuana use. Although allergic reactions are uncommon, the potential of marijuana use and cultivation to cause allergy should be considered. We aimed to investigate whether marijuana use is associated with the prevalence of sensitization to specific allergens.

Methods: A total of 2671 adults (aged 20–59 years) who participated in the 2005–2006 National Health and Nutrition Examination Survey were included. Participants completed a questionnaire on marijuana use and underwent sensitization tests to 19 specific allergens. Those who reported marijuana use for at least 1 day in the past 30 days were considered marijuana users.

Results: No difference was found in the history of allergy between marijuana users and non-users. Compared with marijuana non-users as a reference group, the adjusted odds ratio (AOR) of sensitization to a specific allergen among marijuana users was significantly greater for antibodies against the following: *Alternaria alternata* (AOR = 1.67; 95% confidence interval (CI), 1.04 – 2.70), *D. farinae* (AOR = 1.68; 95% CI, 1.27 – 2.22), *D. pteronyssin* (AOR = 1.65; 95% CI, 1.32–2.06), ragweed (AOR = 1.84; 95% CI, 1.30–2.59), rye grass (AOR = 1.49; 95% CI, 1.12 – 1.97), Bermuda grass (AOR = 1.55; 95% CI, 1.03 – 2.33), oak (AOR = 1.76; 95% CI, 1.14 – 2.70), birch (AOR = 2.09; 95% CI, 1.23 – 3.55), peanut (AOR = 1.91; 95% CI, 1.25 – 2.92), and cat dander (AOR = 1.51; 95% CI = 1.13 – 2.03).

Conclusions: We provide preliminary findings to suggest that marijuana use is associated with sensitization to specific allergens, including molds, dust mites, plants, and cat dander.

1. Introduction

Cannabis, also known as marijuana, is the most frequently used illicit drug worldwide. The overall global prevalence of marijuana use is considered to be stable, whereas it is relatively high in the United States (United Nations Office on Drugs and Crime, 2015) with an estimated 22.2 million people aged ≥ 12 years reported to use marijuana in 2014 (Center for Behavioral Health and Statistics Quality, 2015; United Nations Office on Drugs and Crime, 2015). Recent changes in the legal status of marijuana for both medical and recreational purposes in many states would, therefore, lead to an inevitable increase in the prevalence of marijuana use.

Although medical marijuana has been reported to confer therapeutic benefits against glaucoma and multiple sclerosis (Watson et al., 2000), there is growing evidence that general marijuana use may be harmful to overall health. Marijuana use has been associated with an

increased risk of addiction, psychological health problems, problematic behavior, and respiratory illnesses (Fergusson et al., 2006; Macleod et al., 2004; Tan et al., 2009). Moreover, exposure to marijuana smoke has been implicated in the occurrence of nasal congestion, sneezing, and anaphylaxis (Ocampo and Rans, 2015).

Allergy to marijuana has also garnered much attention recently because both personal and occupational exposure to marijuana has been associated with hypersensitivity reactions and sensitization to plant-derived foods (de Larramendi et al., 2008; Nayak et al., 2013; Perez-Bustamante et al., 2007; Prasad et al., 2009; Stokes et al., 2000). Although allergic reactions are uncommon, the potential of marijuana use and cultivation to cause allergy should be considered.

In this study, we aimed to investigate whether marijuana use was associated with sensitization to specific allergens based on data from the National Health and Nutrition Examination Survey (NHANES). Specifically, we assessed sensitization to 19 specific allergens including

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molds, mites, plants, pets, arthropods, rodents, and foods among adults based on whether or not they used marijuana in the past 30 days.

2. Methods

2.1. Data and study population

This study used the data of the 2005–2006 NHANES, which is a representative cross-sectional survey of the civilian non-institutionalized population in the United States. The study protocols and all testing procedures for the NHANES were approved by the Institutional Review Board of the National Center for Health Statistics. Both oral and written consent were obtained from all participants.

The NHANES only provided drug use statistics for participants aged 20–59 years; therefore, the original population included 3409 participants (aged 20–59 years) in the study. Of these, we included 2743 participants who completed a questionnaire on marijuana use and underwent a complete panel of allergen-specific immunoglobulin E (IgE) tests. Another 72 individuals were excluded because information for at least one of the variables of interest was unavailable, leaving a total of 2671 adults for inclusion in the final analyses.

2.2. Measures

A person was considered as a current marijuana user if they had a positive response to the question: “During the past 30 days, for how many days did you use marijuana?” Participants who reported marijuana use for at least one day in that period were defined as marijuana users.

For the allergen-specific IgE tests, serum levels of specific IgE were analyzed in peripheral blood sample of participants using the Pharmacia Diagnostics Immuno-CAP 1000 System (Pharmacia Diagnostics, Kalamazoo, MI). Specific allergens included 15 aeroallergens [*Alternaria alternata*, *Aspergillus fumigatus*, Bermuda grass (*Cynodon dactylon*), birch (*Betula verrucosa*), cat dander, cockroach (*Blattella germanica*), dog dander, dust mite (*Dermatophagoides farinae* and *D. pteronyssinus*), mouse urine proteins, oak (*Quercus alba*), ragweed (*Ambrosia elatior*), rat urine proteins, Russian thistle (*Salsola kali*), and rye grass (*Lolium perenne*)] and four food allergens [egg white, cow’s milk, peanut (*Arachis hypogaea*), and shrimp (*Pandalus borealis*)]. The specific allergen of interest, which was covalently coupled to the ImmunoCAP, reacted with the specific IgE in the serum sample of the participant. After washing the non-specific IgE, an enzyme-labeled antibody was added to form a complex, which was incubated. Unbound anti-IgE was then washed, and the remaining bound complex was then incubated with a developing agent. Higher response values indicated the presence of more allergen-specific IgE in the samples. Sensitization by specific IgE was defined as a level of ≥ 0.35 kU/L (Min and Min, 2015).

The following confounding variables were obtained: age (20–29, 30–39, 40–49, or 50–59 years), race/ethnicity (non-Hispanic white, non-Hispanic black, Mexican-American or other), sex (male or female), and family income ($< \$20,000$ or $\geq \$20,000$). Participants were categorized as current smokers, former smokers, or never smokers based on the history of smoking and as ‘yes’ or ‘no’ response to whether they currently consumed alcohol. Body mass index (BMI) was calculated by dividing weight by the square of height and was classified as < 30 kg/m² or ≥ 30 kg/m². A history of allergic disease was defined as a positive response to the following question – “Has a doctor or other health professional ever told you that you have allergies?” Hypertension was defined as a systolic blood pressure of ≥ 140 mm Hg and diastolic blood pressure of ≥ 90 mm Hg, the use of antihypertensive drugs or previous physician-diagnosed hypertension. Diabetes was defined as a fasting plasma glucose level of ≥ 6.99 mmol/L, a non-fasting plasma glucose level of ≥ 11.1 mmol/L, current insulin use or a prior physician diagnosis of diabetes. The presence of thyroid and liver diseases were based on diagnosis by a physician or health professional. Blood lead and

cadmium levels were included as biomarkers of exposure to heavy metals.

2.3. Analysis

The prevalence of sensitization to specific allergen between marijuana users and non-users was compared with chi square test. Logistic regression analyses were conducted using the SURVEYLOGISTIC procedures to assess the association between allergen sensitization and marijuana use. The model provided odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs) for sensitization to each allergen, compared with marijuana non-user as the reference group. Statistical models were adjusted for all confounding variables.

3. Results

3.1. Characteristics by marijuana use status

Of the 2671 study participants, 316 (11.8%) were current marijuana users. Compared with marijuana non-users, marijuana users were more likely to be young, non-Hispanic black, male, and current smokers, and current drinkers. They were found to have an average family income of $< \$20,000$, BMI of < 30 kg/m², high blood lead (1.85 μ g/dL vs. 1.52 μ g/dL; p-value = 0.0003) and cadmium (0.89 μ g/L vs. 0.47 μ g/L; p-value < 0.0001) levels, and have neither diabetes nor thyroid disease. We found no differences regarding the history of allergy, hypertension, or liver disease between marijuana users and non-users. In addition, compared with participants not sensitized to allergens, those sensitized to at least one allergen were more likely to be young, non-Hispanic black, male, and non-smokers, and were also more likely to have a history of allergies and high blood lead (1.62 μ g/dL vs. 1.52 μ g/dL; p-value = 0.0093) and cadmium (0.47 μ g/L vs. 0.56 μ g/L; p-value = 0.0077) levels. There were no differences between the two groups in any other variable (Table 1).

3.2. Proportion and likelihood for sensitization to allergens by marijuana use status

The proportion of marijuana users with sensitization to allergens not related to cannabis varied from 3.0% for rodents and egg to 32.2% for *D. pteronyssinus* and was significantly higher than that of marijuana non-users, except for Bermuda grass, white oak, Russian thistle, cockroach, egg, and milk. Compared with marijuana non-users as the reference group, the AOR of sensitization to allergens among marijuana users was significantly greater for antibodies against *Alternaria alternata* (AOR = 1.67; 95% CI, 1.04 – 2.70), *D. farinae* (AOR = 1.68; 95% CI, 1.27 – 2.22), *D. pteronyssinus* (AOR = 1.65; 95% CI, 1.32 – 2.06), ragweed (AOR = 1.84; 95% CI, 1.30 – 2.59), rye grass (AOR = 1.49; 95% CI, 1.12 – 1.97), Bermuda grass (AOR = 1.55; 95% CI, 1.03 – 2.33), oak (AOR = 1.76; 95% CI, 1.14 – 2.70), birch (AOR = 2.09; 95% CI, 1.23 – 3.55), peanut (AOR = 1.91; 95% CI, 1.25 – 2.92), and cat dander (AOR = 1.51; 95% CI = 1.13 – 2.03). The results suggested that marijuana exposure via usage or cultivation may be associated with an increased risk of sensitization to allergens unrelated to cannabis (Fig. 1).

4. Discussion

In this study, we aimed to investigate whether marijuana use was associated with sensitization to specific allergens in adults from a representative sample of the US population. After adjusting for covariates, marijuana users were more likely than non-user to be sensitized to molds (*Alternaria alternata*) dust mite (*D. farinae* and *D. pteronyssinus*), plants (ragweed, rye grass, Bermuda grass, oak, birch, and peanut), and cat dander than non-users. These results therefore indicate that marijuana exposure via use or cultivation may be associated with an

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