CLINICAL RESEARCH STUDY

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Marijuana Use and Renal Function Among US Adults

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ABSTRACT

BACKGROUND: In recent years, the number of states that have legalized medical marijuana or retail sales has increased, bringing potential changes of marijuana use pattern among the general population. However, health effects of acute and chronic marijuana use on many relevant health outcomes, including renal function, remain largely unexamined. In this study, we aimed to assess the association between recent and past marijuana use and renal function.

METHODS: We conducted a cross-sectional study among 13,995 US adults aged 18 to 59 years in the National Health and Nutrition Examination Survey from 2007 to 2014. We examined associations between marijuana use and serum creatinine concentration, estimated glomerular filtration rate (eGFR), and odds of having stage 2 or greater chronic kidney disease using weighted multivariable linear regression.

RESULTS: In the study population, 6483 were never users, 5499 were past users, and 2013 were current users. Marijuana use did not have a significant association with serum creatinine, eGFR, or odds of having stage 2 or greater chronic kidney disease. Serum creatinine and eGFR had an increasing trend comparing past and current users with never users that did not reach statistical significance. All associations remained unchanged in the sensitivity analysis restricted to people without cardiovascular disease.

CONCLUSIONS: We did not observe any clinically significant association between current or past self-reported marijuana use and measures of kidney function.

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KEYWORDS: Marijuana use; Renal function

INTRODUCTION

Marijuana is the most commonly used illicit drug in the United States, with an increasing trend of use among middle-aged and older individuals.[1] The most recent National Survey on Drug Use and Health shows that the percentage of past-month marijuana users among people aged 12 years or older in the United States has increased from 7.5% to 8.3% from 2013 to 2015; from 2002 to 2015, the increase in percentage of adult users who are aged more than 26 years is even greater than the increase among those aged 18 to 25 years.[2] As of January 2017, 25 states and the District of Columbia have legalized medical marijuana or retail sales at the state level, bringing potential changes of marijuana use pattern among the general population.[3]

The health effects of acute and chronic marijuana use remain controversial. Some studies have suggested that there may be detrimental health effects of short- and long-term exposure to marijuana, including triggering acute myocardial infarction,[4] impaired pulmonary vascular endothelial function, and changes in pulmonary flow rates.[5] There is also evidence that secondhand exposure to marijuana smoke may impair vascular endothelial function.[6] In contrast, evidence suggests that recent marijuana use may have some beneficial health effects, including lower odds of metabolic syndrome among adults who reported recent use of marijuana compared

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with never users,[7] lower fasting insulin, and improved insulin resistance level.[8]

Physiologic studies suggest that activation of cannabinoid 1 receptors may have adverse effects on the endothelium. Clinical evidence suggests that patients with immunoglobulin A nephropathy, diabetes, and acute interstitial nephritis have highly increased cannabinoid 1 expression.[9] Furthermore, cannabinoid 1 and 2 receptor activation can contribute to atherosclerosis,[10] and blocking cannabinoid 1 receptors after induced myocardial infarction can decrease arterial stiffness and improve systolic and diastolic function.[11] Cannabinoid 1 activation has also been documented to be an important mediator of renal fibrosis in a mouse model, and a cannabinoid 1 knockout model shows significant reduction in renal fibrosis in response to a unilateral ureteral obstruction model.[9] Given that the human kidney mainly expresses cannabinoid 1 receptors,[12] we suspect marijuana use may have adverse effects on renal function.

CLINICAL SIGNIFICANCE

- Marijuana use is increasingly common, and medical marijuana or retail sales have been legalized in 25 states and the District of Colombia.
- No clinically significant association between current or past self-reported marijuana use and measures of kidney function were found. This is relevant and somewhat reassuring given the expanding number of states that have approved medical and recreational use of marijuana.

Long-term ambient fine particulate matter 2.5 exposure from different sources not only negatively affects renal function and increases renal function decline in people with renal disease[13] but also is associated with an increased risk of membranous nephropathy.[14] It is reasonable to suspect that fine particulate matter 2.5 from marijuana combustion may also contribute to renal dysfunction. Therefore, we hypothesized that current and past marijuana use may affect renal function and conducted a study among 13,995 participants in the National Health and Nutrition Examination Survey (NHANES) from 2007 to 2014. We assessed the association between recent and past marijuana use and renal function, measured by serum creatinine concentration and estimated glomerular filtration rate (eGFR).

MATERIALS AND METHODS

Study Population

The NHANES is a cross-sectional, periodic survey conducted by the US Centers for Disease Control and Prevention. Data are collected in 2-year increments using a complex, multistage, stratified, clustered probability sampling design to obtain a national representative sample of the US population. The survey includes an interview, a physical examination, and blood collection to assess the health and nutritional status of noninstitutionalized adults and children in the United States.[15] From 2007 to 2014, 14,017 people aged 18 to 59 years completed specific marijuana use questions in the illicit drug use questionnaire and underwent a physical examination at the mobile examination centers. We further excluded participants with extreme (>4 mg/dL, n = 22) serum creatinine levels, resulting in 13,995 participants in the study population.

Assessment of Marijuana Use

Participants used an audio computer-assisted self-interview system to answer the following questions in the drug use questionnaires:

- "Have you ever, even once smoked marijuana or hashish?" (yes, no, refused, don't know)
- "How long has it been since you last used marijuana or hashish?" (answers were given as number of days, weeks, months, or years).

Each questionnaire was administered at a mobile examination center during the mobile examination center interview. A total of 13,995 participants attended the examination and responded to the first or both questions and were classified as never users (n = 6483), past users (smoked marijuana at least once, but not in the past 30 days, n = 5499), and current users (smoked marijuana at least once within the last 30 days, n = 2013).

Outcomes

Serum Creatinine, Albumin to Creatinine Ratio, and Estimated Glomerular Filtration Rate. Serum creatinine concentration was measured in remote laboratories after blood collection at the mobile examination center and was analyzed by the Beckman UniCel DxC800 Modular Chemistry (Beckman Coulter Inc, Brea, Calif) side with the Jaffe rate method. The calibration was based on an isotope dilution mass spectrometry reference method.[16] Urine albumin and creatinine were measured in remote laboratories after urine collection at mobile examination centers. Urine albumin was analyzed by a solid-phase florescent immunoassay by Sequoia-Turner Digital Fluorometer Model 450 (Sequoia-Turner Corp., Mountain View, Calif), and urine creatinine was analyzed by Roche Cobas 6000 Analyzer (Roche Diagnostics, Indianapolis, Ind).[17,18] Urinary albumin to creatinine ratio (mg/g) was calculated by urine albumin (mg/dL)/urine creatinine (g/dL). We calculated eGFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation,[19] as follows:

$$\text{eGFR (mL/min/1.73 m}^2) = 141 \times \min(Scr/\kappa, 1)^{\alpha} \times \max(Scr/\kappa, 1)^{-1.209} \times 0.993^{Age} \times 1.018 \text{ [if female]} \times 1.159 \text{ [if black]}$$

The *Scr* denotes serum creatinine measured in mg/dL. κ is 0.7 for female patients and 0.9 for male patients, α is –0.329 for female patients and –0.411 for male patients, *min* represents the minimum of Scr/κ or 1, and *max* represents the maximum of Scr/κ or 1. We also calculated eGFR using the