Marijuana and Cannabinoids in ESRD and Earlier Stages of CKD

Joshua L. Rein, DO, and Christina M. Wyatt, MD

Marijuana is the most commonly used recreational drug in the United States, and legal recreational and medicinal use of marijuana has increased during the last decade. As of June 2017, twenty-nine US states and the District of Columbia have medical marijuana programs. Eight states and the District of Columbia also allow for recreational use (Fig 1), although marijuana remains illegal under federal law. Legal marijuana sales in the United States are projected to grow to more than $20 billion by 2020. Canada also has a well-established medical marijuana program and is expected to legalize recreational marijuana in 2018. Advanced chronic kidney disease (CKD) and end-stage renal disease (ESRD) are chronic conditions with significant associated morbidity and mortality. Patients experience substantial symptom burden that is frequently undertreated due to adverse medication side effects. This article reviews the available evidence for the use of medical marijuana to manage chronic pain, nausea/vomiting, anorexia/cachexia, and pruritus, all of which are frequently reported by patients with advanced CKD or ESRD. Potential adverse health effects of medical and recreational marijuana use are also discussed. Regardless of personal, social, and political beliefs, marijuana use is becoming mainstream, and nephrologists should be aware of the potential impact on our patient population. Further research is warranted to investigate the renal impact of marijuana use on kidney disease outcomes, and the risks and benefits of medical marijuana use on symptoms of advanced CKD and ESRD.

INDEX WORDS: Marijuana; cannabis; synthetic cannabinoids; medical marijuana; end-stage renal disease (ESRD); chronic kidney disease (CKD); chronic pain; nausea; anorexia; cachexia; pruritus; transplantation; recreational drug use.
sclerosis–related spasticity. In addition to pharmaceutical cannabinoids, more than 170 synthetic cannabinoids have been developed for use in laboratory research, some of which have been adopted as drugs of abuse.

Potential Impact of Marijuana and Cannabinoid Use on the Kidney

It is unknown whether and to what extent marijuana use might affect kidney disease. Both CB1 and CB2 are expressed throughout the body, including in podocytes, mesangial cells, and tubular epithelial cells. In animal models, overactivation of CB1 in podocytes promotes diabetic nephropathy, whereas blocking CB1 decreases albuminuria and renal fibrosis. Activation of CB2, which in general has opposing effects, has been shown to reduce albuminuria and podocyte loss, whereas knockout of CB2 worsens kidney function in a mouse model of diabetic nephropathy. Cannabinoids also have diuretic properties. THC activation of CB1 has been reported to increase urine output in rats, possibly by inhibiting the Na/K/2Cl cotransporter NKCC2 and a sodium/hydrogen exchanger in the thick ascending limb.

Data for the relationship between marijuana use and kidney disease in humans are scarce. Cross-sectional studies using nationally representative data have demonstrated lower odds of metabolic syndrome and diabetes among marijuana users compared with nonusers; however, renal outcomes were not evaluated. In a prospective cohort of 647 men attending the hypertension clinic at a single Veterans Administration medical center, any self-reported history of recreational drug use was associated with a significant increase in risk for kidney function decline (serum creatinine increase > 0.5 mg/dL) over a median of 7 years. Although marijuana was the most commonly reported drug, marijuana use was not significantly associated with kidney function decline. The nonsignificant trend associated with marijuana use may reflect concomitant use of other drugs, including cocaine or psychedelics, which were independently associated with kidney function decline. Similarly, a small cross-sectional study found elevated β2-microglobulin concentrations in 2 of 42 cannabinoid users, but not in control patients. Although this could suggest subtle proximal tubular injury with cannabinoid use, the authors did not control for comorbid conditions or concomitant drug or medication use.

Electrolyte concentration abnormalities have been reported with the use of other recreational drugs, but do not appear to be an important complication of isolated marijuana use. Hypophosphatemia was observed in a case series of 6 men with cannabinoid hyperemesis syndrome, an uncommon complication of long-term marijuana overuse. Alkalemia-induced transcellular shift of phosphate from hyperventilation or vomiting was hypothesized as a possible mechanism.
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