Helping Patients With ESRD and Earlier Stages of CKD to Quit Smoking

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Among the many adverse effects of tobacco exposure is the increased risk for progression of kidney disease. Individuals with chronic kidney disease (CKD), who already face increased cardiovascular event rates compared to the general population, are at even greater risk if they smoke. Despite these risks and the increased focus on smoking cessation in the general population in recent years, national guidelines have not specifically targeted individuals with CKD. There are similarly sparse data specific to individuals with CKD regarding the safety and efficacy of evidence-based smoking cessation modalities. This review aims to identify the risks of nicotine dependence in individuals with CKD and the potential benefits of smoking cessation; discuss current strategies for smoking cessation, including behavioral and pharmacologic therapies such as varenicline; and extrapolate these interventions to the unique challenges of this population. Much of the data presented stem from evidence for the general population but are described with additional consideration in dosing of nicotine replacement therapy, as well as non-nicotine pharmacotherapy and treatment modality for individuals with CKD.

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Case Presentation: *A 67-year-old man with a history of cerebrovascular accident with left upper and lower residual hemiparesis presents for evaluation of elevated serum creatinine concentration. He has a history of hypertension, which was untreated until his cerebrovascular accident event. Serum creatinine concentrations ranged between 0.9 and 1.2 mg/dL until he underwent 4-vessel coronary artery bypass surgery 1 year ago. Since then, his serum creatinine concentration has increased and is now between 1.3 and 1.6 mg/dL. Urinalysis results are normal and albumin-creatinine ratio is 13 mg/g. He does not have diabetes and his last hemoglobin A_{1c} concentration was 5.4%. He smokes 2 packs of cigarettes per day. He quit smoking for several months after the cerebrovascular accident event, but relapsed after his divorce 4 years ago and states that he now feels unable to quit despite being motivated to do so. On examination, blood pressure is 128/70 mm Hg and he has no edema. Medications include metoprolol, 50 mg, twice daily; losartan, 25 mg, daily; and furosemide, 40 mg, daily. The patient is extremely anxious about needing dialysis in the future and asks what he can do to prevent kidney failure.*

Background

Approximately 20% of the world's population smokes cigarettes, and tobacco use is a major contributor to disease burden.[1] In 2013, six million deaths worldwide were attributable to tobacco use, making tobacco use a leading cause of death even in developed countries despite its decreasing prevalence.[2] Meanwhile, the growing use of noncombustible tobacco products such as electronic cigarettes over recent years, particularly among current smokers and young adults,[3] introduces new questions about the effects of these products on long-term health. Harm begins with a single cigarette and smoking has demonstrated a dose-dependent association with all-cause mortality even after accounting for other behavioral and social determinants of health.[4] Smoking is a known risk factor for multiple chronic conditions, including cardiovascular disease, lung disease, and cancers.

Smoking was first described as a risk factor for chronic kidney disease (CKD) in individuals with diabetes, and more recent evidence has shown that it is a risk factor for the development of CKD in the general population.[5] Furthermore, of individuals with kidney disease requiring dialysis, ~15% report current tobacco use.[6] Despite these risks, little evidence on smoking cessation in this vulnerable population exists. Much of our understanding stems from the general population, but we offer a more detailed understanding of the mechanisms of harm in individuals with CKD who smoke and the associated outcomes, review best practices and evidence-based guidelines for smoking cessation, provide information for renal dosing of pharmacotherapies, and share recent evidence on noncombustible products such as electronic cigarettes.

Mechanisms of Harm From Smoking in CKD

Observational studies demonstrate that smoking adversely affects kidney function, but the

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biological mechanisms through which this occurs remain incompletely understood. A study of kidney biopsies from smokers and nonsmokers shows histopathologic differences between the 2 groups: smokers have a 2-fold increase in the degree of myointimal hyperplasia of small arteries.[7] Studies of the mechanisms of kidney injury from smoking can provide background for nephrologists interested in understanding the unique importance of smoking cessation in their at-risk patients and patients with established CKD.

Both non–hemodynamic- and hemodynamic-mediated changes may cause kidney damage in smokers.[8,9] Proposed non–hemodynamic-mediated mechanisms through which smoking causes kidney damage include oxidative stress, decreased bioavailability of nitric oxide, increased endothelin 1 concentration, tubular cell damage, and increased vasopressin secretion.[9] Insulin resistance, which has been associated with smoking[10] and reduced glomerular filtration rate,[11] may also contribute adversely to kidney function over time. A heightened inflammatory state has also been shown to result from cigarette smoking[12] and to be associated with declining kidney function.[13]

Hemodynamic-mediated changes include a transient but significant increase in blood pressure from smoking initiation.[14,15] These transient increases in systemic blood pressure have been associated with kidney disease progression.[16–20] The role of sympathetic overactivity as a direct mediator of smoking-induced changes in renal hemodynamics was examined in a study of occasional smokers without kidney disease who were pretreated with prazosin and atenolol.[21] Pretreatment with prazosin compared to placebo showed no difference in glomerular filtration rate, filtration fraction, renal plasma flow, or renal vascular resistance. In contrast, pretreatment with atenolol compared to placebo led to smaller decreases in active renin, glomerular filtration rate, and renal vascular resistance after smoking onset. These results suggest that β-adrenergic–mediated mechanisms and effects on the renin-angiotensin system may be partly responsible for smoking-induced changes in kidney hemodynamics. This hypothesis is also supported by data that showed a protective effect of angiotensin-converting enzyme inhibitors in the progression of kidney disease in patients who smoke.[22]

Outcomes From Smoking in Individuals With CKD

Individuals with CKD have increased risk for cardiovascular disease,[23] and smoking is a well-established risk factor for cardiovascular disease.[24] However, the risks of smoking specific to individuals with established kidney disease are less apparent because there have been no randomized controlled trials and the quality of evidence is weak. A relatively small number of observational studies have examined the risk for mortality, CKD progression, and vascular events associated with smoking among patients with CKD (Table 1). Two multicenter prospective cohort studies indicated that smoking adversely affects mortality and cardiovascular events in patients with CKD; however, there is significant heterogeneity between studies and the association of smoking with CKD progression remains unclear. Although more evidence regarding the outcomes of smokers with CKD is warranted, the various outcomes described in Table 1 provide some evidence for nephrologists to identify active smokers in their patients and offer evidence-based therapeutic options.

Benefits of Smoking Cessation

Smoking cessation decreases proteinuria in patients with CKD and type 2 diabetes and slows progression to end-stage renal disease (ESRD).[22,25–27] Despite the benefits from smoking cessation in patients with CKD, scant data for these patients are available in guidelines on smoking cessation. Certain subgroups are addressed in national guidelines, including pregnant women, black and minority ethnic groups, children and adolescents, individuals with mental illness or substance use disorders, and individuals with cardiovascular disease. No smoking cessation guidelines specific to individuals with CKD exist.[28] Nevertheless, it is reasonable to assume that the benefits of smoking cessation (ie, decreased mortality, improved lung function, and reduced rates of cardiovascular disease, stroke, and cancer) for the general population and other chronic disease conditions are also applicable to individuals with CKD.

Smoking Cessation Interventions

Overview

Data regarding the effectiveness of accepted modalities for smoking cessation applied to individuals with CKD are similarly lacking but can be extrapolated from recommendations for the general population. These recommendations vary by country, particularly in regard to recommended use of specific pharmacotherapies. The available smoking cessation guidelines from English-speaking countries are further detailed in Table 2. As discussed later, meta-analyses suggest that the best outcomes are achieved when behavioral interventions are used in combination with pharmacotherapies. Steps for smoking cessation are outlined in Figure 1.[29]

Advice and Behavioral Therapies

Successful intervention begins with identifying smokers and offering appropriate interventions based on the individual's level of motivation to quit. A recommended method endorsed by many of the clinical guidelines is the "5 A's" method: ask, advise, assess, assist, and arrange.[30] Spending as little as 1 minute on each component is effective. The first A (ask) can be automated in the era of electronic health records. The National Health Interview