Antioxidants Therapy for Patients with Chronic Kidney Disease: A Question of Balance

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Oxidative stress reflects an imbalance between an excessive generation of oxidant compounds and reduced antioxidant defenses. Findings from prospective cohort studies suggest a possible etiopathogenetic role of oxidative stress in cardiovascular disease (CVD) among patients with coronary artery disease and chronic kidney disease (CKD) [1, 2], while clinical trials using antioxidants failed to demonstrate beneficial effect in patients with increased CVD risk and CKD [3, 4]. The discrepancy observed in these findings warrants explanation. Oxidative stress levels are increased in patients with CKD due to increased production and decreased renal clearance of reactive oxygen species, as well as a dysfunctional antioxidant defense system [5, 6]. This increased production and reduced antioxidant defense capability may be due to multiple etiologies, including traditional CVD risk factors and inflammation [7]. Therefore, treatment for reducing oxidative stress in CKD patients should target multiple levels. We and others propose 4 major challenges in antioxidant therapy for CKD patients: (1) the optimal control of the etiology may not be easily achieved; therefore, oxidative stress can regenerate during antioxidant therapy; (2) the optimal dose of antioxidants for targeting specific levels of oxidative stress remains to be fully evaluated; (3) in the presence of high oxidative stress,

many antioxidants can be oxidized to pro-oxidative substances that can cause oxidative stress; therefore, the choice of antioxidant may affect the success of the treatment; and (4) the efficacy of a combination of antioxidants acting at multiple levels of the antioxidant system is unknown. It is plausible that combination therapy targeting multiple levels may be more effective.

In this issue of the American Journal of Nephrology, Ilori et al. [8] reported the association of oxidative balance score (OBS) and CKD among 19,461 participants in the Reasons for Geographic and Racial Differences in Stroke Study with a median follow-up of 3.5 years. The OBS was calculated by combining 13 a priori-defined pro-oxidants and antioxidants by using a baseline dietary and lifestyle assessment. Diet, medications, and lifestyle are major exogenous sources of both antioxidants and pro-oxidants [9]. The study findings suggested that a higher OBS (which is reflective of higher antioxidant levels) was associated with a lower prevalence of CKD. However, there was no significant association between OBS and end-stage renal disease (ESRD) incidence in the multivariable analyses, which may be due to an insufficiency of statistical power, given the small number of incident ESRD cases. The OBS has also been shown to correlate inversely with all-cause mortality in other popula-

tions [10]. These findings suggest the potential usefulness of an integrated approach to evaluate the balance between exogenous oxidants and antioxidants in CKD risk evaluation and prediction. In addition, antioxidant supplements might provide kidney protection. Furthermore, an evaluation of exogenous oxidants in guiding antioxidant therapy may be valuable for individualized care in CKD patients. Finally, controlling and modifying exogenous oxidants via diet and lifestyle modification in

individuals with reduced kidney clearance would be a promising approach, especially when combined with antioxidant therapy. Further studies in these important areas are warranted.

Disclosure Statement

We have no conflict of interest to declare.

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