








Letter to editor

Additional Considerations in the Treatment of Diabetic Nephropathy Based on the KDOQI Clinical Practice Guideline

Consideraciones adicionales en el tratamiento de la nefropatía diabética basado en las guías de práctica clínica KDOQI

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Dear Editor:

We have read with interest the paper published by Mottls, *et al.* “KDOQI US Commentary on the KDIGO Clinical Practice Guideline for Diabetes in CKD”, in the American Journal of Kidney Diseases, where the authors and the KDOQI group comment on the KDIGO guidelines (Kidney Disease: Improving Global Outcomes) published in 2020.

Obesity is a risk factor for the development and progression of CKD, which has been shown in numerous studies [1]. The mechanism of how this occurs is not completely understood, but several putative mechanisms proposed via adiposity, include low adiponectin high leptin and resistin, causing inflammation, insulin resistance, RAAS activation and oxidative stress, leading to CKD; in addition, it also causes diabetes mellitus, hypertension, and cardiovascular

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disease [1]. Obesity is a persistent inflammatory state, and inflammation has been shown to play an important role in the development and progression of diabetic kidney disease [2], hence controlling obesity has become a key component as a preventative strategy in the development of kidney disease.

The KDOQI guidelines highlight the necessity of innovative approaches for the multidisciplinary care of these patients, given the discovery of new cardiorenal-protective therapies. We are grateful to Mottls, *et al.* [3] for their valuable input, however, we believe additional information should be considered. Regarding GLP-1 analogues, KDOQI reports that they have no class effect, and that their cardiovascular benefits are restricted to GLP-1 agonists derived from native GLP-1; nonetheless, there is data regarding GLP-1 agonists derived from exendin. In a post hoc analysis of the EXSCCEL trial, the positive effect of exenatide on GFR decline was more relevant in patients with high albuminuria compared to the ones with normal albuminuria [4].

In another post hoc analysis of the EXSCCEL trial, exenatide reduced the composite of sustained deterioration of GFR of 30 to 40 % or reaching ESRD [5]. The AMPLITUDE trial with epeglenatide reported cardiovascular benefits with reduction of MACE; and in addition, benefits in renal outcomes [6]. Given this, we consider that there may be a class benefit. Regarding SGLT-2 inhibitors, the evidence of renal benefit is reported in patients with proteinuria, but little in atypical phenotypes. SGLT-2 inhibitors reduce blood pressure via intravascular volume depletion and glycosuria, effect that is independent of baseline renal function [7]. Treatment with SGLT-2 inhibitors reduces markers of inflammation in tubular cells [7]. The DAPA-CKD trial revealed renal benefits in patients with chronic kidney disease and microalbuminuria, regardless of diabetes [8]. We consider that it is important to incorporate the different patient phenotypes in the guidelines, considering the different mechanisms that can lead to renal injury. Treatment with these new therapies should be considered to preserve renal function, as with obese patients, reducing the morbidity and mortality associated with the progression of CKD.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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