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Angiotensin Blockade Beyond Hypertension in Autosomal Dominant Polycystic Kidney Disease

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Autosomal dominant polycystic kidney disease (ADPKD) is the most common inherited kidney disorder, affecting millions of people worldwide.[1] One of the major complications associated with ADPKD is hypertension, which occurs in the majority of affected individuals. The management of hypertension in ADPKD patients is crucial, as it plays a pivotal role in the progression of kidney disease.[1] Renin–angiotensin system (RAS) blockers have emerged as a cornerstone in the management of hypertension in ADPKD patients.[1]

We read the article "Long-Term Experience of a Reference Center on Autosomal Dominant Polycystic Kidney Disease: Associated Demographics, Clinical Presentation, and Kidney Survival in Turkish Population" by Ozler et al[2] with great interest. The article was a retrospective cohort study that aimed to investigate the demographic, clinical, and laboratory characteristics of patients with ADPKD, and the factors associated with kidney survival. It had a very long follow-up period of up to 25 years, which allowed for the observation of the natural course and outcomes of ADPKD.[2] One of the main findings of the article is that the use of RAS blockers, such as angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB), was associated with better kidney survival in ADPKD patients.[2] This article provides valuable insights into the important role of RAS blockers in long-term ADPKD progression.

RAS is a complex hormonal system that regulates blood pressure and fluid balance in the body. In ADPKD, aberrant activation of the RAS is believed to contribute to the development of hypertension and the progression of kidney damage.[3] RAS blockers target different points in this pathway to mitigate its harmful effects. One of the primary benefits of RAS blockers in ADPKD patients with hypertension is their ability to lower blood pressure effectively.[4] Beyond hypertension, RAS blockers may have protective effects on kidney function by reducing proteinuria, cyst growth, inflammation, and fibrosis, which are common complications of ADPKD.[3,4]

However, RAS blockers were associated with minimal effect on kidney function in ADPKD patients in the past.[4,5] Our previous network meta-analysis also found that there were no significant effects of RAS blockers on estimated glomerular filtration rate (eGFR) and serum creatinine by combining randomized controlled trials in ADPKD patients.[6] Moreover, the combination of ACEI and ARB had no significant protective effects on the rate of total kidney volume increase and eGFR in both early and late ADPKD.[4,5] However, it is worth noting that the follow-up time of previous RCTs ranged from 1 to 8 years, while kidney function in the majority of ADPKD patients remained steady until the late stage.[4-6] Therefore, the study by Ozler et al[2] is important, for it for the first time reports a 25-year follow-up, which is long enough to show the benefits of RAS blockers on kidney function in ADPKD patients.

In conclusion, RAS blockers play a crucial role in the management of hypertension in ADPKD patients. The underlying ability to lower blood pressure, reduce proteinuria, slow cyst growth, and provide cardiovascular protection makes them a valuable therapeutic option for long-term kidney benefit. However, more long-term studies of RAS blockers in ADPKD are needed to better illustrate the comprehensive effects of angiotensin blockade beyond hypertension.

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AUTHOR'S RESPONSE

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Thank you very much for your valuable and constructive comments.

Hypertension (HT) is the most common symptom in autosomal dominant polycystic kidney disease (ADPKD). The average age of onset is 27. Approximately 60% of patients have HT before a decrease in glomerular filtration rate.[1,2] Activation of the renin angiotensin-aldosterone system (RAAS) has a very important role in the pathogenesis of HT. Studies have shown that both systemic and intrarenal renin, angiotensin II and angiotensin-converting enzyme (ACE) levels are increased in ADPKD. When patients with ADPKD and HT were compared with patients with other chronic kidney diseases and HT, it was observed that renin, aldosterone, and ACE activities were higher in ADPKD. For this reason, it is thought that in ADPKD, RAAS activation is activated by an additional mechanism in addition to kidney dysfunction.[3-5] In addition to the systemic effects of angiotensin II that occur with the activation of the RAAS system; It is also known that it functions as one of the growth factors that increase the growth of existing kidney cysts.[6] These data suggest that RAAS inhibition may be important in controlling the blood pressure level, reducing the rate of cyst growth and kidney enlargement, and finally slowing the rate of kidney disease progression. In ADPKD, early and effective treatment of HT is very important to slow down kidney disease progression. As you mentioned; previous studies and meta-analyses have yielded mixed results regarding the impact of RAAS blockers on renal function in ADPKD. However, current data have shown that RAAS inhibition is effective in kidney disease progression, similar to the results of our study.

Autosomal dominant polycystic kidney disease often has a slower progression rate than most glomerular diseases. For this reason, in cases where kidney volume is not monitored with magnetic resonance imaging, long follow-up periods are needed when efficiency is monitored with glomerular filtration rate. As you emphasize, our study has a long-term follow-up period to determine factors affecting the progression in ADPKD. We think that the number of participants, as well as the follow-up period, increases the power of the study.

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