Challenges and Considerations in Metformin Use for ADPKD: A Commentary on Recent Findings

Dear Editor,

We are writing to provide our perspective on the recently published study by Venkatasubramanian *et al*.[1] The authors' investigation into the efficacy of metformin in nondiabetic patients with autosomal dominant polycystic kidney disease (ADPKD) adds to the growing body of literature exploring novel therapeutic avenues for this challenging condition. The study's findings, particularly the observation that metformin did not significantly slow the progression of the disease as measured by changes in estimated glomerular filtration rate (eGFR) and height-adjusted total kidney volume (htTKV), are consistent with previous trials such as the Trial of Administration of Metformin in Polycystic Kidney Disease (TAME-PKD) study and the work of Brosnahan *et al*.[2] However, this study stands out for its focus on a low-risk cohort (Mayo Class 1A-C) and its attempt to elucidate metformin's potential renoprotective effects in a more uniform population with well-preserved renal function at baseline.[1] The metformin's proteinuria-reducing capacity and protection from renal cancers in the diabetic population is mentioned due to its vascular endothelial growth factor (VEGF) induction pathway.[3–5] Besides that, type 2 diabetes patients experience renoprotective effects in terms of eGFR change with the flozin group of drugs.[6] The readers couldn't see the benefits of metformin intervention due to baseline differences during the recruitment. The study's results raise important questions about the role of metformin in ADPKD management, particularly regarding its long-term impact and the challenges in maintaining therapeutic doses in this population. Only 46.1% of participants in the metformin arm tolerated the total dose, highlighting the need for further research into optimizing dosing regimens, possibly through personalized medicine approaches that account for individual tolerability and disease characteristics.

Moreover, the study's findings underscore the potential limitations of short-term follow-up in capturing the full extent of metformin's effects. The nonsignificant differences observed may be a function of the study's duration rather than the inefficacy of the intervention. Therefore, as the authors suggest, extended follow-up studies with larger sample sizes are crucial to determine whether metformin could offer meaningful clinical benefits in the ADPKD population.[1]

In conclusion, while this study adds valuable data to the ongoing discourse on metformin's role in ADPKD, it also highlights the need for further investigation. Future studies should focus on more extended follow-up periods, personalized dosing strategies, and a more comprehensive assessment of patient-reported outcomes to understand the potential of metformin in this context.

Conflicts of interest

There are no conflicts of interest.

Amol N Patil[1], Mahendra Pratap Singh[2], Pramod Rawat[3], Sanjit Sah[4], Prakasini Satapathy[5]

[1]Department of Pharmacology, PGIMER, Chandigarh, [2]Center for Global Health Research, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences, Saveetha University, Chennai, [3]Department of Biotechnology, Graphic Era (Deemed to be University), Dehradun, India [4]Department of Pediatrics, Sanjeevani Hospital, Kalyanpur, Siraha, Nepal [5]University Center for Research and Development, Chandigarh University, Punjab, India

Corresponding author: *Amol N Patil, Department of Pharmacology, PGIMER, Chandigarh, India. E-mail: patil.amol@pgimer.edu.in*

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