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Author's Reply to Correspondence: "Effect of Tolvaptan Treatment on Acid-Base Homeostasis in ADPKD Patients"

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Effect of Tolvaptan Treatment on Acid - Base Homeostasis in ADPKD **Patients**



To the Editor: We read with great interest the recent report of Heida et al.1 on the impact of tolvaptan on acid-base status in autosomal dominant polycystic kidney disease (ADPKD) patients. The authors hypothesized that V2 receptor antagonism may induce a state of metabolic alkalosis by activation of V1 receptors through increased circulating vasopressin, which in turn would stimulate renal net acid excretion (NAE). The authors found no changes in plasma bicarbonate after tolvaptan administration and therefore concluded that tolvaptan does not affect renal NAE.

Recent studies^{2,3} indicate, however, that urinary citrate is superior to plasma bicarbonate for the detection of subtle acid-base alterations. We previously observed that ADPKD patients treated with tolvaptan exhibit a significant reduction in renal NAE, with an increase in urinary citrate.4 These changes were associated with increased net gastrointestinal alkali absorption (NGIA; a marker of alkali intake) but unaltered urinary sulfate (a marker of acid intake), suggesting that lower NAE may be due to higher alkali intake or gut alkali absorption in patients taking tolvaptan. Thus, our data suggest that tolvaptan treatment is associated with changes in renal NAE and hence acid-base homeostasis in ADPKD patients. The underlying mechanisms, however, remain to be elucidated.

- 1. Heida JE, Gansevoort RT, Meijer E. Acid-base homeostasis during vasopressin V2 receptor antagonist treatment in autosomal dominant polycystic kidney disease patients. Kidney Int Rep. 2021;6:839-841.
- 2. Gianella FG, Prado VE, Poindexter JR, et al. Spot urinary citrate-to-creatinine ratio is a marker for acid-base status in chronic kidney disease. Kidney Int. 2021;99:208-217.
- 3. Goraya N, Simoni J, Sager LN, et al. Urine citrate excretion as a marker of acid retention in patients with chronic kidney disease without overt metabolic acidosis. Kidney Int. 2019;95: 1190-1196.
- 4. Bargagli M, Dhayat NA, Anderegg M, et al. Urinary lithogenic risk profile in ADPKD patients treated with tolvaptan. Clin J Am Soc Nephrol. 2020;15:1007-1014.

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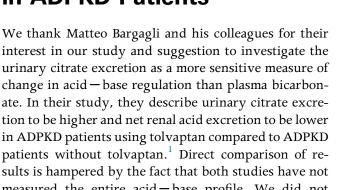
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change in acid — base regulation than plasma bicarbonate. In their study, they describe urinary citrate excretion to be higher and net renal acid excretion to be lower in ADPKD patients using tolvaptan compared to ADPKD patients without tolvaptan. Direct comparison of results is hampered by the fact that both studies have not measured the entire acid-base profile. We did not measure urinary citrate and net renal acid excretion, which would have been valuable additions, and Bargagli and colleagues did not measure plasma pH, bicarbonate, and pCO2. However, results of these 2 studies are consistent in their rejection of our primary hypothesis. Tolvaptan does not seem to induce an increase in bicarbonate reabsorption in the investigated patients.

1. Bargagli M, Dhayat NA, Anderegg M, et al. Urinary lithogenic risk profile in ADPKD patients treated with tolvaptan. Clin J Am Soc Nephrol. 2020;15:1007-1014.

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