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Tolvaptan in Later-Stage Polycystic Kidney Disease

Christian De Tymowski, M.D. and Matthieu Legrand, M.D., Ph.D.

Hôpital Saint-Louis, Paris, France, matthieu.

TO THE EDITOR: Torres et al. (Nov. 16 issue)¹ report a slower decline in the estimated glomerular filtration rate (GFR) with the use of tolvaptan than with placebo in patients with autosomal dominant polycystic kidney disease. The resultant renoprotection is proposed to arise from a decrease in cell proliferation within cysts in the kidneys. An alternative mechanism has a potential therapeutic implication — renoprotection by means of a decrease in the GFR after the activation of tubuloglomerular feedback. The initiation of tolvaptan induced an early but sustained drop in the estimated GFR² and a rapid rise in the estimated GFR after treatment interruption, which suggests direct intrarenal hemodynamic effects. Blocking the V₂ receptors may lead to higher chloride concentrations in the ascending thin limb of Henle's loop,³ activating tubuloglomerular feedback. In addition, tolvaptan increases the level of vasopressin,⁴ which may lead to increased stimulation of V₁ receptors at the macula densa level, which would further activate tubuloglomerular feedback, leading to vasoconstriction of the afferent arteriole.⁵ The presence of such a mechanism would be supported by a decrease of microalbuminuria during tolvaptan treatment. Data regarding whether microalbuminuria changed would be helpful in delineating the renoprotective effects of tolvaptan. Theoretically, such a renoprotective effect may occur concomitantly with therapy with high doses of angiotensin-converting-enzyme (ACE) inhibitors.

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legrand@aphp.fr.

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