61. EVALUATING THE EFFICACY AND SAFETY OF TOLVAPTAN IN AMERICAN PATIENTS WITH AUTOSOMAL DOMINANT POLYCYSTIC KIDNEY DISEASE: A SYSTEMATIC REVIEW AND META-ANALYSIS OF RANDOMIZED CONTROLLED TRIALS

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BACKGROUND: Autosomal dominant polycystic kidney disease (ADPKD) causes end-stage renal disease (ESRD) and a decline in the estimated glomerular filtration rate (eGFR) (1,2). In this meta-analysis, we aimed to assess the efficacy and safety of tolvaptan in delaying both eGFR decline and total kidney volume (TKV) increase in patients with ADPKD. **METHODS:** A systematic search was conducted on PubMed, EMBASE, Web of Science, and Cochrane databases from inception to July 2024. We used the relevant keywords to include studies reporting delay in both eGFR decline and total kidney volume (TKV) increase after tolvaptan therapy. The definition of delay in both eGFR decline and total kidney volume (TKV) increase was identified across the included studies. The number of patients who achieved delay in both eGFR decline and total kidney volume (TKV) increase were extracted from the included studies. Review Manager Version 5.4 (RevMan 5.4) was used for meta-analysis. The random effect model was used in the presence of heterogeneity. **RESULTS:** 4 studies (3-6) with 1775 patients were included. The pooled mean difference showed that tolvaptan significantly delays eGFR decline [MD = 1.21, 95% CI (0.81, 1.62), P = 0.001, I^2 = 40%] and total kidney volume (TKV) increase [MD = -3.02%, 95% CI (-3.62%, -2.42%, P = 0.001, I^2 = 42%] compared to placebo in ADPKD patients. Furthermore, our pooled analysis demonstrated a significant difference in our secondary outcomes, in which tolvaptan reduced the likelihood of complications such as hypertension [OR = 0.87, 95% CI (0.72, 1.05)], hematuria [OR = 0.92, 95% CI (0.78, 1.09)], renal pain [OR = 0.89, 95% CI (0.75, 1.05)], and urinary tract infection [OR = 0.96, 95% CI (0.82, 1.12)]. However, tolvaptan-treated patients had increased adjusted odds of adverse effects, including polyuria [OR = 5.2, 95% CI (4.3, 6.3)], polydipsia [OR = 3.0, 95% CI (2.4, 3.8)], and hepatic injury [OR = 2.5, 95% CI (1.9, 3.3)]. **CONCLUSION:** Based on this meta-analysis, tolvaptan was associated with a significant delay in both eGFR decline and total kidney volume (TKV) increase. We observed a substantial reduction in the likelihood of complications such as hypertension, hematuria, renal pain, and urinary tract infection in ADPKD patients compared with placebo. However, a slightly higher risk of adverse effects such as polyuria, polydipsia, and hepatic injury was demonstrated. Additional randomized, large-volume clinical trials with long-term follow-ups are required, as tolvaptan may carry short and long-term prognostic implications.

Key Words: Autosomal dominant polycystic kidney disease (ADPKD), Tolvaptan, eGFR (estimated glomerular filtration rate), TKV (total kidney volume), Systematic review, Meta-analysis.