

The Effect of Tolvaptan on BP in Polycystic Kidney Disease: A *Post Hoc* Analysis of the TEMPO 3:4 Trial

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Abstract

Background: The V2 receptor antagonist tolvaptan is prescribed to patients with autosomal dominant polycystic kidney disease to slow disease progression. Tolvaptan may alter BP *via* various acute and chronic effects.

Methods: To investigate the magnitude and time course of the effect of tolvaptan use on BP, we conducted a *post hoc* study of the TEMPO 3:4 trial, which included 1445 patients with autosomal dominant polycystic kidney disease randomized 2:1 to tolvaptan or placebo for 3 years. We evaluated systolic and diastolic BP, mean arterial pressure, hypertension status, and use and dosing of antihypertensive drugs over the course of the trial.

Results: At baseline, BP did not differ between study arms. After 3 weeks of tolvaptan use, mean body weight had decreased from 79.7 to 78.8 kg, and mean plasma sodium increased from 140.4 to 142.6 mmol/L (both $P<0.001$), suggesting a decrease in circulating volume. We observed none of these changes in the placebo arm. Nonetheless, BP remained similar in the study arms. After 3 years of treatment, however, mean systolic BP was significantly lower in participants receiving tolvaptan versus placebo (126 versus 129 mm Hg, respectively; $P=0.002$), as was mean diastolic BP (81.2 versus 82.6 mm Hg, respectively; $P=0.01$). These differences leveled off at follow-up 3 weeks after discontinuation of the study medication. Use of antihypertensive drugs remained similar in both study arms during the entire study.

Conclusions: Long-term treatment with tolvaptan gradually lowered BP compared with placebo, which may be attributed to a beneficial effect on disease progression, a continued natriuretic effect, or both.

Clinical trial registry name and registration number: TEMPO 3:4, [NCT00428948](#).