

Title: Leukotriene Antagonist Use is Associated with Less Albuminuria and Lower Systolic Blood Pressure in Adults

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Background: Pro-inflammatory mediators known as leukotrienes have been implicated in the development of both chronic kidney disease (CKD) and cardiovascular disease (CVD). Leukotrienes cause endothelial dysfunction which increases glomerular permeability to albumin and causes vascular dysfunction leading to CVD. Animal models have shown that short term inhibition of leukotrienes in mice prevents CKD. We hypothesized that the use of montelukast in healthy adults would associate with less albuminuria and lower systolic blood pressure (SBP).

Methods: Participant data from a total of 51,111 adults was extracted from the National Health and Nutrition Examination Survey 1999-2018 and stratified by montelukast prescription status. We evaluated baseline urine albumin to creatinine ratio (ACR) (mg/g), estimated glomerular filtration rate (eGFR) (mL/min/1.73m²), CKD (defined as urine ACR >30 mg/g or eGFR <60 mL/min/1.73m²), and SBP (mmHg) in participants taking montelukast vs. participants not taking montelukast. Urine ACR was log transformed prior to analysis due to positive skew. Linear and logistic regression was used to examine the association between montelukast use and the primary outcomes.

Results: We identified participants taking montelukast (N=434) and compared them to participants not taking montelukast (N=50,677). The mean age and eGFR were 47.2 ± 19 years and 96.6 ± 23.2 mL/min/1.73m², respectively. Participants taking montelukast were older, had a higher prevalence of diabetes and hypertension, and had a lower eGFR (87.9 ± 21.9 vs. 96.6 ± 23.3 mL/min/1.73m², respectively). After adjustment for age, sex, race, diabetes status, hypertension, body mass index (BMI), eGFR, and use of an ACE inhibitor or angiotensin receptor blocker, montelukast use associated with lower urine ACR (Table). Montelukast use did not associate with eGFR or CKD. After adjustment for demographics, diabetes status, BMI, hypertension, eGFR, urine ACR and use of anti-hypertensive medications, montelukast use associated with lower SBP.

Montelukast Use vs. No Use	β-Estimate (95% CI)	P-value
Urine ACR	-0.13 (-0.22 to -0.04)	0.005
eGFR	-0.50 (-2.1 to 1.05)	0.51
SBP	-1.98 (-3.82 to -0.11)	0.038
	Odds Ratio (95% CI)	P-value
CKD	0.89 (0.66 to 1.21)	0.45

Conclusions: Participants taking montelukast had significantly lower albuminuria and SBP compared to participants not taking montelukast. Thus, leukotriene inhibition may represent a promising avenue for future treatment of CKD and CVD. Further studies are needed to examine the relationship between montelukast use and kidney and cardiovascular disease.