

## Loss to Analysis—a Problem in CKD Trials

Randomized trials of treatment for chronic kidney disease (CKD) have important quality shortcomings—including a high rate of loss of patients from the analysis, according to a study in the *American Journal of Kidney Diseases*.

The researchers performed a systematic evaluation of loss to analysis for primary outcomes of randomized controlled trials of patients with CKD undergoing dialysis or kidney transplantation. The analysis included

196 trials published in 2007 and 2008. Studies in which not all randomized patients were included in the primary outcome analysis were considered to have loss to analysis.

Twenty-seven percent of the trials specified no clear primary outcome. Five percent did not report numbers of patients randomized and analyzed, while 12 percent used time-to-event analysis. Of the remaining 110 studies, 58 percent had some loss to analysis. The median loss to analysis was 10

percent, with a range of one to 41 percent.

Fifty-four percent of trial reports said that analysis was by intention to treat. Yet 44 percent of studies making this claim did not include all randomized patients in the analysis. Imputation of missing data was reported by five percent of studies. Studies without loss to analysis tended to have smaller sample sizes: 128 versus 229.

Randomized trials of treatment for CKD pose unique challenges. Based on

the new review, many CKD studies do not meet current standards for clinical trial reporting. Many trials do not specify a primary outcome of interest; those which do have high rates of data loss to analysis. Efforts to improve the quality of CKD randomized trials should include increased attention to transparency and reporting loss to analysis. [Deo A, et al: Loss to analysis in randomized controlled trials in *CKD*. *Am J Kidney Dis* 2011; 58: 349–355]. ●

## Low Sodium Beats Dual Blockade for Nondiabetic Nephropathy

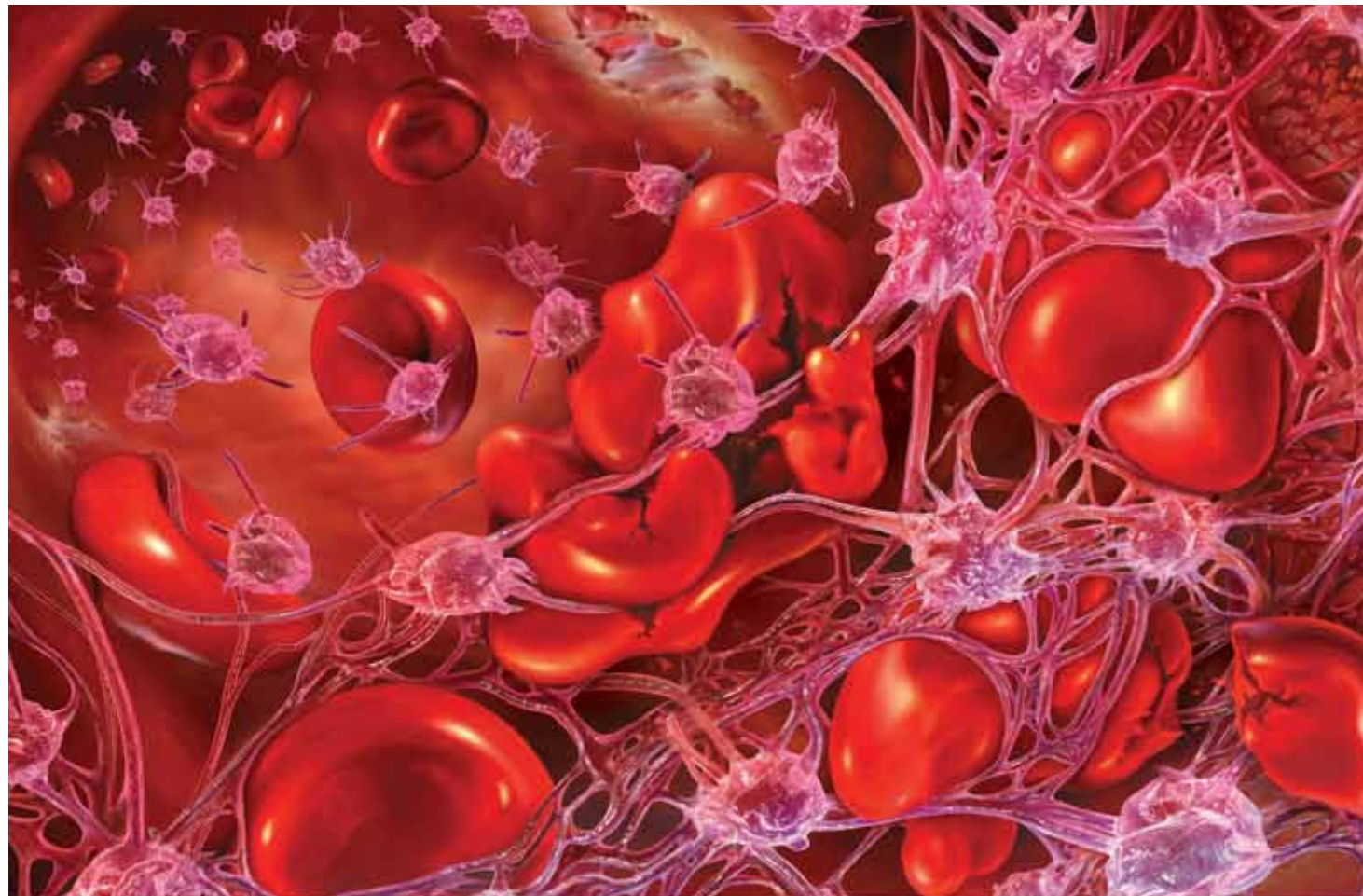
In patients with nondiabetic nephropathy, guideline-based reductions in sodium intake are more effective than the combination of lisinopril and valsartan in lowering proteinuria and blood pressure, reports a trial in the *British Medical Journal*.

The randomized controlled trial included 52 outpatients with nondiabetic nephropathy. In four 6-week periods, patients were treated with the angiotensin receptor blocker (ARB) valsartan 320 mg/d or placebo (in random order) plus a low- and regular-sodium diet (in sequential order): target intake 50 versus 200 mmol Na<sup>+</sup>/d. Patients took the angiotensin-converting enzyme (ACE) inhibitor lisinopril 40 mg/d throughout the study.

Mean urinary sodium excretion was 106 mmol Na<sup>+</sup>/d on the low-sodium diet and 184 mmol Na<sup>+</sup>/d on the regular-sodium diet. Proteinuria decreased from 1.68 g/d on ACE inhibitor plus regular-sodium diet, to 1.44 with ACE inhibitor plus ARB, to 0.85 with ACE inhibitor plus low-sodium diet, to 0.67 g/d with ACE inhibitor plus ARB plus low-sodium diet. The 51 percent reduction in proteinuria with ACE inhibitor plus low-sodium diet was significantly greater than the 21 percent reduction with ARB plus ACE inhibitor.

Mean systolic blood pressure was 134 mm Hg with ACE inhibitor plus regular-sodium diet. There was a 2 percent reduction on ACE inhibitor plus ARB, compared to a 7 percent reduction with ACE inhibitor plus low-sodium diet. Adding dual blockade to low-sodium diet did not produce further significant reductions in proteinuria or blood pressure.

The results suggest that adding a low-sodium diet to an ACE inhibitor reduces proteinuria and blood pressure to a greater extent than the combination of ACE inhibitor and ARB in patients with nondiabetic nephropathy. Efforts to reduce sodium intake to recommended levels will enhance the efficacy of renoprotective strategies in this group of patients. [Sलगman MC], et al: Moderate dietary sodium restriction added to angiotensin converting enzyme inhibition compared with dual blockade in lowering proteinuria and blood pressure: randomised controlled trial. *BMJ* 2011; 343: d4366]. ●



# CATaHUSTROPHIC

**In atypical Hemolytic Uremic Syndrome (aHUS), chronic uncontrolled complement activation causes systemic thrombotic microangiopathy (TMA), which can result in sudden and progressive vital organ failure and premature death<sup>1-5</sup>**

**Chronic uncontrolled complement activation causes the continuous activation of platelets and endothelial cells, leading to systemic TMA.<sup>3,6</sup> Systemic, complement-mediated TMA can lead to sudden, fatal complications and progressive failure of vital organs, including the kidneys, heart, and brain.<sup>1-4,7</sup>**

**aHUS is a devastating and life-threatening disease of chronic uncontrolled complement activation.<sup>1,2,5</sup> To learn more, please visit [www.aHUSsource.com](http://www.aHUSsource.com).**

References: 1. Loirat C, Noris M, Fremeaux-Bacchi V. Complement and the atypical hemolytic uremic syndrome in children. *Pediatr Nephrol*. 2008;23:1957-1972. 2. Noris M, Caprioli J, Bresin E, et al. Relative role of genetic complement abnormalities in sporadic and familial aHUS and their impact on clinical phenotype. *Clin J Am Soc Nephrol*. 2010;5:1844-1859. 3. Fang CJ, Richards A, Liszewski MK, Kavanagh D, Atkinson JP. Advances in understanding of pathogenesis of aHUS and HELLP. *Br J Haematol*. 2008;143:336-348. 4. Sallée M, Daniel L, Piercecchi MD, et al. Myocardial infarction is a complication of factor H-associated atypical HUS. *Nephrol Dial Transplant*. 2010;25:2028-2032. 5. Loirat C, Garnier A, Sellier-Leclerc AL, Kwon T, Plasmatherapy in atypical hemolytic uremic syndrome. *Semin Thromb Hemost*. 2010;36:673-681. 6. Ståhl AL, Vaziri-Sani F, Heinen S, et al. Factor H dysfunction in patients with atypical hemolytic uremic syndrome contributes to complement deposition on platelets and their activation. *Blood*. 2008;111:5307-5315. 7. Neuhaus TJ, Calonder S, Leumann EP. Heterogeneity of atypical haemolytic uraemic syndromes. *Arch Dis Child*. 1997;76:518-521.

**ALEXION**

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