Adverse events during dual RAAS blockade in diabetic nephropathy

Combination therapy with an ACE inhibitor and an angiotensin receptor anatgonist is associated with an increased risk of serious adverse events, among patients with diabetic nephropathy, according to investigators from the US.[1]

The VA NEPHRON-D* study was a multicentre, double-blind, randomised, controlled study designed to evaluate the efficacy of losartan 100 mg/day in combination with lisinopril (10–40 mg/day) compared with losartan alone in slowing the progression of proteinuric diabetic kidney disease. Patients (n = 1448) with type 2 diabetes mellitus, a urinary albumin-to-creatinine ratio of ≥300 and an estimated glomerular filtration rate (GFR) of 30.0–89.9 mL/min/1.73m^2 were included in the study. The study was stopped early (median follow-up of 2.2 years) because of safety concerns.

The rate of serious adverse events was significantly higher in the combination therapy group compared with the monotherapy group (98 vs 82 events per 100 person-years). Moreover, combination therapy increased the risk of acute kidney injury (12.2 vs 6.7 events per 100 person-years; $p < 0.001$) and hyperkalaemia (6.3 vs 2.6 events per 100 person-years; $p < 0.001$). There were no significant differences between treatment groups in mortality. Combination therapy did not significantly improve the primary endpoint of the first occurrence of a decline in the estimated GFR compared with monotherapy.

In an accompanying editorial Dr Dick de Zeeuw from the Department of Clinical Pharmacology, University of Groningen, commented that it is clear that dual RAAS blockade treatment cannot be recommended in patients with diabetes. However, dual RAAS blockade may be appropriate in certain subgroups if future trials can demonstrate renal and cardiovascular benefits without major increases in potassium levels or other side effects.[2]

* Veterans Affairs Nephropathy in Diabetes

1. Fried LF, et al. Combined Angiotensin Inhibition for the Treatment of Diabetic Nephropathy. New England Journal of Medicine 369: 1892-1903, No. 20, 14 Nov 2013. Available from: URL: http://dx.doi.org/10.1056/NEJMoa1303154.
2. de Zeeuw D. The End of Dual Therapy with Renin-Angiotensin-Aldosterone System Blockade? New England Journal of Medicine : 9 Nov 2013. Available from: URL: http://dx.doi.org/10.1056/NEJMe1312286.

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