Association Between Combination of Anti-Hypertensive Drugs and Adverse Outcomes in Patients with Chronic Kidney Disease; The Results from the KNOW-CKD Study

Seon Yeong LEE1, Ki Heon Nam1, Jung Tak Park2, Tae-Hyun Yoo3, Kook Hwan Oh4, Shin-Wook Kang4, Kyu Hun Choi4, Curie Ahn3, Tae-Ik Chang3, Seung Hyeok Han4
1Department of Internal Medicine, Severance Hospital, Korea, Republic of
2Department of Internal Medicine, Seoul National University Hospital, Korea, Republic of
3Department of Internal Medicine, National Health Insurance Service Ilsan Hospital, Korea, Republic of

Objectives: Renin-angiotensin system blockers (RASBs) are the cornerstone therapy in patients with CKD. However, blood pressure (BP) is not well controlled with RASBs alone. Accordingly, there has been growing interest in the combination therapy of RASBs with other BP-lowering drugs that can improve clinical outcome better in these patients.

Methods: Among 2,238 CKD patients in the KNOW-CKD study, we studied 1,907 patients who were taking anti-hypertensive drugs. Patients were classified into 4 groups: RASBs only; RASBs+calcium channel blockers (CCBs); RASBs+beta-blockers (BBs); and RASBs+CCBs+BBs. Diuretics were liberally used among 4 groups. The study endpoints were a composite of ≥50% decline in eGFR or ESRD, and a composite of cardiovascular events (CVEs) or death.

Results: During a median follow-up of 3.2 years, 310 (16.3%) and 132 (6.9%) patients reached the composite renal outcome and the composite of CVEs or death, respectively. In the fully adjusted multivariable Cox models, risk of renal outcome was significantly higher in patients with RASBs and CCBs (HR, 1.55; P=0.002) and in patients with triple therapy (HR, 2.00; P<0.001) as compared to RASBs only. However, there were no differences in risk of CKD progression among dual or triple combination therapies and combination of RASBs with CCBs had similar risk to that with BBs. In addition, combined use of RASBs and BBs was significantly associated with a 2.95-fold and a 2.67-fold increased risk of CVEs or death as compared to RASBs only (HR, 2.95; P<0.001) and combination of RASBs and CCBs (HR, 2.67; P=0.001). This association was consistently observed in patients without prior history of CVEs and in those without use of diuretics.

Conclusions: Risk of CKD progression was similar between CCBs and BBs when added to RASBs. However, risk of CVEs or death was significantly higher in combined use of RASBs and BBs than in combined use of RASBs and CCBs.