

学位論文の要旨

三 重 大 学

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<p>主論文の題名</p> <p>Cardiorenal protective effects of sodium-glucose cotransporter 2 inhibition in combination with angiotensin II type 1 receptor blockade in salt-sensitive Dahl rats</p> <p>主論文の要旨</p> <p>The kidney plays a central role in regulating the salt sensitivity of blood pressure (BP). We hypothesized that sodium-glucose cotransporter 2 (SGLT2) inhibition and angiotensin II type 1 receptor (AT₁R) blockade can synergistically reduce renal sodium reabsorption by beneficially effects on these transporters, leading to lower BP and ameliorating cardiorenal damage.</p> <p>Dahl salt-sensitive rats were treated orally for 8 weeks with a normal salt diet (0.3% NaCl), a high-salt diet (8% NaCl), high-salt diet with ipragliflozin (0.04%), high-salt diet with losartan (0.05%), or high-salt diet with a combination of ipragliflozin and losartan. The combination treatment significantly reduced BP and increased daily urine sodium excretion compared with losartan or ipragliflozin monotherapy, leading to greater improvement in BP salt sensitivity than ipragliflozin monotherapy. The combination treatment significantly ameliorated glomerulosclerosis and reduced cardiomyocyte hypertrophy compared with each monotherapy. The protein expression levels of Na⁺/H⁺ exchanger isoform 3 (NHE3) and Na⁺-K⁺-Cl⁻ cotransporter 2 (NKCC2) in the kidney were significantly decreased with losartan monotherapy and combination treatment, but not with ipragliflozin monotherapy.</p> <p>Inhibition of SGLT2 in combination with an angiotensin II receptor blocker effectively improved BP salt sensitivity by reducing renal NHE3 and NKCC2 expression levels, which eventually led to improvement of BP salt sensitivity and cardiorenal protection.</p>			