involvement could drive to develop high blood pressure without significant changes in GFR in this experimental model of glomerulopathy.

Key Words: Blood pressure; immune-complex; polysaccharides; polyvinyl alcohol

K021
ANGIOTENSIN II-INDUCED ALTERATIONS IN G-PROTEINS IN RENAL PREGLOMERULAR ARTERIOLES FROM YOUNG GENETICALLY HYPERTENSIVE RATS
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Alterations in signaling pathways that regulate cAMP in renal preglomerular arterioles (PA) may lead to enhanced renal responsiveness to angiotensin II (Ang II) in young SHR. Consequently, we examined the effects of low dose Ang II on the expressions of $\alpha_i$, $\alpha_o$, and $\alpha_q$ in PA from SHR and correlated these alterations to changes in renal vascular resistance (RVR), mean arterial pressure (MAP) and renal cyclic AMP excretion (UcAMP.V). Young prehypertensive (5–6 week old) SHR and WKY rats were treated with Ang II (35 ng/kg/min, s.c) or its vehicle using osmotic minipumps for 7 days. Urine was collected over the last 24 hours. Baseline MAP and renal blood flow were then measured in anesthetized rats and RVR determined. PA were isolated by iron oxide method. Expressions of $G_{\alpha_i1,2}$, $G_{\alpha_i3}$, $G_{\alpha_o}$ and $G_{\alpha_q}$ in membranes were evaluated by Western immunoblotting. Baseline MAP were not significantly different between SHR and WKY rats. RBF was significantly lower and RVR was significantly higher in SHR compared to WKY rats. Ang II significantly increased MAP and RVR in SHR but not in WKY rats. Compared to WKY rats, PA from SHR exhibited higher basal expression of $G_{\alpha_i1,2}$, $G_{\alpha_i3}$ and $G_{\alpha_o}$. Chronic infusion of Ang II downregulated the expression of $G_{\alpha_i1,2}$, $G_{\alpha_i3}$ and $G_{\alpha_o}$ in SHR PA but upregulated these proteins in WKY. Basal levels of $G_{\alpha_q}$ were similar in PA from the two strains and were downregulated by Ang II similarly. Basal UcAMP.V was significantly lower in SHR compared with WKY rats. Chronic Ang II infusion significantly increased UcAMP.V in SHR as well as WKY rats. These data suggest that elevated levels of $G_{\alpha_i}$ proteins may be directly associated with a blunted adenyl cyclase-cAMP cascade in PA in early hypertension. Furthermore, the ability of Ang II to downregulate the expression of $G_{\alpha_i}$ in young SHR but not in young WKY PA may be important for enhanced renal sensitivity to Ang II in SHR.

Key Words: SHR; kidney; hypertension; G proteins

K022
EFFECT OF COMBINATION THERAPY (ANG II ANTAGONIST, VALSARTAN AND A CALCIUM CHANNEL BLOCKER) IN A HYPERTENSIVE MODEL OF DIABETIC NEPHROPATHY
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Recently, it has been suggested that in the context of diabetes and hypertension, more aggressive blood pressure targets should be considered. To achieve these levels of blood pressure control, it is likely that combination therapy will need to be used. The present study has explored the role of the addition of either a dihydropyridine or a non-dihydropyridine calcium channel blocker (CCB) to Ang II antagonist based treatment in an experimental model of hypertension and diabetes. The doses chosen for the combination therapy groups were lower than those used with monotherapy in order to achieve similar antihypertensive efficacy. Diabetic (streptozotocin induced) SHR were randomised to no treatment, valsartan (30 mg/kg/day), the non-dihydropyridine CCB verapamil (20 mg/kg/day), the dihydropyridine CCB amlodipine (6 mg/kg/day), a combination of valsartan and amlodipine (20 mg + 4 mg/kg/day respectively) or valsartan and verapamil (20 mg + 15 mg/kg/day respectively). Serial measurements of systolic blood pressure (BP) and albumin excretion rate (AER) were performed monthly (data are shown at week 16 for AER and mean of wk 20–28 for BP). This model was associated with hypertension (control, 217 ± 8, diabetic, 200 ± 5 mmHg) which was reduced by most treatments to a similar degree (valsartan 165 ± 3, amlodipine 164 ± 2, verapamil 182 ± 4, valsartan + amlodipine 151 ± 3 and valsartan + verapamil 169 ± 5 mmHg). Diabetes was associated with a progressive increase in AER (control 1.5 vs diabetic 17 mg/24 hr). Valsartan retarded the increase in AER (11 mg/24 hr). Similar efficacy was observed in the valsartan + amlodipine combination (9 mg/24 hr) but not with amlodipine alone (16 mg/24 hr) despite similar effects on blood pressure. No advantage of verapamil versus amlodipine either as monotherapy or in combination with valsartan was observed. The present study indicates that the combination of an Ang II antagonist and a dihydropyridine CCB is an effective regimen at reducing blood pressure and albuminuria in the context of diabetes and hypertension.

Key Words: Diabetes; valsartan; calcium channel blocker; nephropathy

K023
EFFECTS OF FOSINOPRIL AMLODIPINE COMBINATION ON MICROALBUMINURIA IN HYPERTENSIVE PATIENTS WITH TYPE 2 DIABETES
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Aim of this study was to compare the effects of fosinopril and amlodipine alone or in combination on urinary albumin excretion (UAEx) in NIDDM hypertensives with microalbuminuria. We studied 209 microalbuminuric hypertensive...