NORMOTENSIVE WISTAR-KYOTO AND SPONTANEOUSLY HYPERTENSIVE RATS

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The effects of intravenous injection (12 µg/kg) of rat atriopeptin III (rANP III) on glomerular angiotensin II (AII) receptor binding properties and plasma AII concentration were examined in anesthetized Wistar-Kyoto (WKY) and spontaneously hypertensive (SHR) rats. WKY glomeruli had two classes of receptor: high affinity-low capacity (Kd 0.97±0.15 (M±SD)nM, Bmax 88±7 fm/mg), and low affinity-high capacity (Kd 7.6±1.7nM, Bmax 413±64 fm/mg). By seventy minutes after intravenous bolus injection on rANP III into WKY rats, only the low affinity-high capacity receptor (Kd 4.8±0.5nM, Bmax 375±59 fm/mg) remained. Plasma AII concentration (134±19 pg/ml) in WKY decreased significantly (p<0.01) after injection of rANP III compared to 224±116 pg/ml in control rats. By contrast, SHR glomeruli had only a low affinity-high capacity class of AII receptor (Kd 3.2±0.2nM, Bmax 450±82 fm/mg) and rANP III injection did not alter the binding properties of this AII receptor (Kd 2.7±0.6nM, Bmax 370±57 fm/mg). Plasma AII concentration of SHR injected with rANP III (159±85 pg/ml) was not significantly different from that in control SHR (198±90 pg/ml). The Kd and Bmax of glomerular AII receptors in SHR control rats were significantly greater than those of WKY control rats. There were marked increases in sodium excretion in WKY and SHR rats after injection of rANP III but no significant difference between SHR and WKY. These findings suggest that glomerular AII receptors from SHR are less sensitive to AII than those from WKY rats: however, after rANP III injection, WKY AII receptor also become less sensitive to AII. The changes in glomerular AII receptors following rANP III may contribute to differences in hemodynamics and sodium homeostasis mediated by angiotensin II in this genetic model of hypertension.

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INHIBITORY EFFECT OF 12-O-TETRADECANOYL-PHORBOL-13-ACETATE ON ANGIOTENSIN II-INDUCED PHOSPHOINOSITIDE TURNOVER IN CULTURED VASCULAR SMOOTH MUSCLE CELLS

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In vascular smooth muscle cells (VSMC), angiotensin II (Ang II) has been shown to stimulate phosphoinositide turnover and produce inositol 1,4,5 trisphosphate (IP₃) and diacylglycerol (DG). IP₃ and DG serve as second messengers for Ca²⁺ mobilization from intracellular storage sites and activation of protein kinase C (PKC), respectively. Although Ca²⁺ is known to activate calmodulin dependent myosin light chain kinase and induce muscle contraction, the role of PKC in the action of Ang II has not been defined.

Since recent study has shown that PKC activating phorbol esters inhibit thrombin-induced phosphoinositide turnover in platelets, we examined the effect of 12-O-tetradecanoyl-phorbol-13-acetate (TPA), a potent activator of PKC, on Ang II-induced phosphoinositide turnover in cultured rabbit aortic VSMC.

Ang II markedly stimulated ³²P incorporation into phosphatidylinositol (PI), which was blocked by [Sar¹, Ala⁸]-Ang II, a receptor antagonist. This reaction was inhibited by TPA

in a dose-dependent manner. The dose required for the inhibition of ³²P incorporation into PI was similar to that for the activation of PKC.

The results suggest that DG produced during Ang II receptor activation may feedback to inhibit phosphoinositide turnover and IP₃ generation through activation of PKC, thus leading to a decrease in the responsiveness of VSMC to Ang II.

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THE EFFECTS OF α-BLOCKADE ON CIRCADIAN VARIATION OF INTRA-ARTERIAL BLOOD PRESSURE AND HEART RATE IN HYPERTENSIVE PATIENTS USING A NEW PORTABLE RECORDER

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A new portable recorder (size 14 × 11 × 5 cm, weight 600g) with digital memory for recording intra-arterial blood pressure (BP) and R-R interval on the electrocardiogram at every 10 seconds throughout 24 hours have been developed. Using this recorder, 24-hour systolic BP, diastolic BP and heart rate were obtained (total 8,640 points) in 17 hypertensive patients (male 14, female 3, included 3 patients with malignant hypertension, mean age 50 ± 2 yrs) under unrestricted conditions. The data were analyzed by a computer. The measurements were performed before and after the treatment for 7 days by α-blockade (Bunazosin, 2 mg × 3/day, n = 8), α-β-blockade (Labetalol, 150 mg × 3/day, n = 3). Dilevalol, 200 mg × 2/day, n = 3) and β-blockade (Propranolol-LA, single dose of 120 mg/day, n = 3). The results were as follows: (1) The mean BP during early morning (before morning drug administration) was reduced more in Bunazosin group (-14 ± 4%) than in Propranolol group (-6 ± 2%), although its reduction of daytime was not different between the two groups. (2) The early morning BP was reduced in Labetalol and Dilevalol group significantly. It is concluded that our new portable recorder is easy to handle and useful in evaluating the effects of antihypertensive drugs on circadian variation. Bunazosin significantly reduced the early morning increase in BP, relating to α-sympathetic activity, and did not show a reflex increase in heart rate.

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PRESSOR MECHANISM OF DIGITALIS-LIKE SUBSTANCE (II) -EFFECTS OF INTRAVENOUS ADMINISTRATION OF DIGOXIN ON PRESSOR RESPONSE TO NOREPINEPHRINE IN NORMOTENSIVES-

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To clarify the role of digitalis-like substance