J005 EFFECTS OF CHRONIC INGESTION OF LEAD ON BLOOD PRESSURE IN WISTAR-KYOTO RATS
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Of all the heavy metals, for example, cadmium, mercury and lead, lead (Pb) is the most ubiquitous because of its widespread use by humans in various substances in the past. Lead has been implicated as a causal factor in (essential) hypertension, and these substances in the past. We intended to explore any lead-induced changes in blood pressure in these normotensive WKY rats. As expected, lead-induced changes in blood pressure [-160 mmHg] as they become 3 months old. We found a strikingly graduated response to the chronic intake of Pb in raising blood pressure - (i) controls (no Pb) [-122mmHg], (ii) 4.75ppm Pb [-132 mmHg], (iii) 8.75ppm [-141mmHg], (iv) 17.5 mmHg [-148mmHg], and (v) 35 ppm [-156mmHg]. Several neurophysiological and biochemical correlates - as gathered from these experiments - will be discussed (Supported in part by NIH Training Grant EF07290 to Michael Amuneké).

Key Words: Lead, hypertension, neurochemical correlates

J006 REDUCTION IN POST-DOCA NACL VENOUS PRESSURE AND RENAL INJURIES IN AQUEDUCT BLOCKED DAHL RATS
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In our previous report, AV3V lesion prevents DOCA-NaCl hypertension. In the current study, effects of hydroxychloroquine on the kidney and venous pressure were investigated. DOCA-hypertension was induced in 33 Dahl R rats (6 weeks of age) with 150 mg/Kg DOCA, 1% NaCl and 1% Pb drinking water for 4 weeks. After 7 days of recovery from the DOCA and Pb NaCl with 0.5% low NaCl chow and tap water, the rats were divided into sham and aqueduct blocked groups with matched mean blood pressure (BP) and weight. After 4 weeks of recovery from the surgery on the same low NaCl diet, sham group showed much higher BP than that of the truly blocked rats (161 ± 3.2 vs. 146 ± 2.5 mm Hg). After 4-weeks on the 8% high NaCl diet for both groups, sham group's BP showed a further increase (186 ± 2.6 vs. 154 ± 3.7, p < 0.0001). After 11 weeks, on the high NaCl diet, tail venous pressure in the sham group showed much higher than that of the blocked group rats, 29 ± 5 vs. 13 ± 0.5 mm H2O (p < 0.0001), indicating the end stage of the kidney and heart failure. Another set of studies was performed with strain 5 (DS) rats. In a kidney cross-section, 54 DS rats on a 0.3% low NaCl diet for 14 weeks averaged 156 glomeruli. Aqueduct blocked 34 DS rats on a 6% high NaCl diet averaged 141 glomeruli, while 23 sham blocked DS rats on a 6% NaCl averaged 102 glomeruli (28% reduction, p < 0.001). Dilatation of tubular casts in a kidney cross-section averaged 48, 223, 488, respectively, 54% reduction in the blocked group as compared with the sham group on the 9% NaCl diet (p < 0.0001). Average BP was 15 mm Hg higher in the sham group on the high NaCl diet that may partially explain the reduction of glomeruli and increased tubular casts. Shah group rats' dry kidney weight was significantly higher than that of blocked ones, 0.56 ± 0.34 grams (p < 0.005). All of these results indicate that the Sylvian aqueduct block appears to reduce the NaCl-signal, and prevent post-DOCA hypertension as well as vessel and kidney injuries.

Key Words: Sylvian Aqueduct, Hydrochloroquine, NaCl Signal, DOCA Hypertension, Venous Pressure, Renal Injury.

J007 ACETYLSALICYLIC ACID TREATMENT IMPROVES THE ENDOTHELIOUM-DEPENDENT VASORELAXATIVE RESPONSE IN SPONTANEOUSLY HYPERTENSIVE RATS

The aim of this study was to analyze if the vasoconstrictor cidoorganeme-dependent mechanisms could be involved in the impaired endothelium-dependent vasorelaxing response associated with spontaneous hypertension. Also, we wanted to investigate the possible role of platelet in these mechanisms. The work was developed by using spontaneously hypertensive rats (SHR, 16-weeks-old) with MAP of 180±7 mmHg, lightly treated with acetylsalicylic acid (ASA, 1 mg/kg weight/day during 4 days) and Wistar rats (16-weeks-old) with MAP 110 ± 5 mmHg. Endothelial nitric oxide synthase (eNOS) expression was analyzed by Western blot. Platelet activation was measured at plasma levels of TGFβ. ASA-treatment did not modify MAP in SHR (+ASA: 177±5 mmHg, p NS). SHR showed an impaired vasorelaxing response to acetylcholine with respect to that found in normotensive rats. ASA-treated SHR normalized the hypotensive response to acetylcholine. This effect was not observed when SHR were treated with a specific thromboxane A2 receptor antagonist. The eNOS protein expression was higher in aorta isolated from ASA-treated SHR than that observed in non-treated SHR. The treatment also decreased TGFβ plasma levels in SHR (42.2 vs 18.04 ng/mL). We conclude that treatment with ASA normalized the endothelium-dependent vasorelaxative response in SHR by a thromboxane A2-independent mechanism and increases the expression of the eNOS isoform. Inactivation of platelets could be a possible mechanism involved in the beneficial effect of ASA in SHR. Further studies will delineate the relationship between the ASA-dependent increase on eNOS expression and the improvement of the hypotensive endothelium-dependent response in spontaneous hypertension.

Key Words: SHR - Acetylsalicylic acid - endothelial response - eNOS

J008 ERYTHROPOIETIN RECEPTOR GENE EXPRESSION IN CULTURED RAT VASCULAR TISSUE. MS Hu, GB Lira, N Jangseth, HU Wang*, CC Tan, JD Barrett, P Eggeaua, F Dominguez, and DBN Lee. Departments of Medicine, Sepulveda VA MC and Drew/UCLA Medical Center, Los Angeles, and the National University of Singapore, Singapore

We have reported erythropoietin (EPO)-induced hypertension in normotensive Wistar rats and that completely abrogated by ACh inhibition. In addition, EPO directly stimulates the transcription of renin, angiotensinogen, angiotensin II type 1 (AT1) and type 2 (AT2) receptors and growth factors, such as TGF-β, IGF-II, EGF, fibronectin, and PDGF in cultured rat vascular smooth muscle cells (VSMC). We postulate EPO acts on vascular tissue through its receptor (EPO-R). However, the presence of EPO in VSMC of normotensive Wistar rats has not been reported and although EPO has been demonstrated in human capillary endothelial cells (EC) and in human umbilical veins EC, its presence in systemic vascular EC under culture conditions is not known. We reverse transcribed mRNA of cultured Wistar VSMC and EC, and carried out PCR to amplify EPO cDNA using oligonucleotide primers specific to the EPO gene. Various primer pairs were utilized to distinguish between different splice variants, which have been shown to exist in the rat. Each primer pair was used at least twice to confirm the presence of EPO mRNA in all VSMC and EC tested. Two splice variants were detected, one with an insert between exon V and VII, and a second with an insert between exon VII and VIII. Thus, the effect of EPO on vascular tissue renin system components and growth factors may be mediated through EPO-R. 

Key Words: Endothelial cells, EPO receptors, hypertension, VSMC