Endothelin-1 (ET) may participate in both maternal vasoconstriction and placental hypoperfusion that are present in preeclampsia (PE), but its source is unknown. In 18 preeclamptic (3rd trimester), 9 of which with “pure” PE, and 9 normotensive (NT), ET in plasma was measured. We characterized pharmacologically and anatomically (by radioligand-binding and autoradiographic techniques) the ET binding sites in placental bed tissues and evaluated placental ET gene expression by RT-PCR. In PE vs. NT, higher plasma levels of NA and of ET (26.9 ± 3.3 vs. 9.4 ± 1.3 pg/ml, *p < 0.05) were found. Placental bed tissues bound I-ET1 with very low Kd values. The Scatchard analyses of the results showed in PE a significant (*p < 0.001) increase both of the affinity (Kd = 0.18 ± 0.03, PE vs. 0.39 ± 0.03 nM, NT) and of the density (Bmax = 78.60 ± 1.40, PE vs. 63.30 ± 1.70 fmol/mg tissue, NT) of ET binding site which was confirmed in autoradiography studies (higher silver content density in the intima of the spiral arteries walls and in the myometrium of PE v NT). However, relative ET-mRNA levels respectively in central and peripheral areas of placenta were similar (p > 0.40) in NT (0.56 ± 0.16 and 0.77 ± 0.09) and in PE (0.48 ± 0.10 and 0.74 ± 0.13). We conclude that in PE the placenta may not be the main source of the increased maternal circulating levels of ET. Meanwhile, ET high plasma levels along with the increased density and affinity of ET-binding sites in placental bed, may participate in the utero-placental hypoperfusion of PE. Supported by PRAXIS XXI SAU 1302/95.

Key Words: Preeclampsia; endothelin; placenta; hypertension

F010
E-SELECTIN LEVEL MAY BE A USEFUL CLINICAL MARKER FOR ENDOTHELIAL DAMAGE IN HYPERTENSION
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It is well known that atherosclerosis is caused by aging hypertension, diabetes mellitus, hyperlipidemia, smoking and hereditary disposition. Selectin is glycoprotein and has three subtypes (E-selectin, P-selectin, L-selectin). Especially that selectin is considered first step of leukocyte attachment to vascular wall. The cell-surface expression of these molecules in response to pathophysiological stimuli mediates the interaction between the endothelium and blood cells central to the development of atherosclerosis. We measured serum soluble E-selectin, P-selectin and L-selectin by ELISA in 86 normal subjects and 36 never-treated essential hypertensive patients without diabetes mellitus, hyperlipidemia and obesity. Moreover, we detected protein of E-selectin by western blot analysis after exposed to cyclic stretch in cultured human aortic endothelial cells (HAEC) and human glomerular endothelial cells (HGEC). With immunohistochemistry, we found that E-selectin expressed in HAEC and HGEC. There was no correlation between each selectin level and age, sex and body mass index. We found no difference of serum soluble P-selectin (255.9 ± 18 ng/ml versus 298 ± 17 ng/ml) and L-selectin (990 ± 26 ng/ml versus 942 ± 57.9 ng/ml) level between normal and hypertensive subjects, but serum soluble E-selectin level was significantly higher in hypertensives than in controls (47.8 ± 3.4 ng/ml versus 73 ± 12.9 ng/ml *p < 0.01). Stretching increased protein expression of E-selectin from HAEC and HGEC.

Those results suggested that soluble E-selectin level might be a useful clinical marker for endothelial damage in hypertension.

Key Words: Blood pressure; cell adhesion molecules; E-selectin

F011
MYOCARDIAL FIBROSIS IN DOCA-SALT HYPERTENSIVE RATS: EFFECT OF ENDOTHELIN ETA RECEPTOR ANTAGONISM
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Cardiovascular remodeling associated with hypertension is characterized by increase of cardiomyocyte volume and changes in extracellular matrix, particularly collagen deposition. To test the hypothesis that endothelin-1 contributes to fibrosis of the heart in some models of experimental hypertension, we studied cardiac collagen in deoxycorticosterone acetate-salt hypertensive rats (DOCA-salt), in which the endothelin system is activated, and the effect of the ETA-selective endothelin receptor antagonist, A-127722. A-127722 (30 mg/kg per day) was administered for 4 weeks to DOCA-salt rats. Cardiac fibrosis was evaluated after Sirius Red F3BA staining of paraffin embedded sections. Systolic blood pressure was 105 ± 6 mmHg in unilaterally nephrectomized rats (UniNx), 202 ± 3.2 mmHg in DOCA-salt (p < 0.01 vs UniNx) and 182 ± 3.1 mmHg in ETA-treated DOCA-salt (p < 0.01 vs DOCA-salt or UniNx). In DOCA-salt, collagen density was significantly increased in subendocardial (4-fold, *p < 0.01) and midmyocardial regions (3-fold, *p < 0.05) but not in the subepicardial myocardium of the left ventricle. The administration of ETA-receptor antagonist to DOCA-salt normalized collagen to baseline value. Subendocardial and midmyocardial collagen density was significantly increased in DOCA-salt hypertensive rats. Both were corrected by ETA receptor antagonism, although blood pressure was only slightly lower and cardiac hypertrophy was unaffected in treated rats. This suggests a role for endothelin-1 in cardiac collagen deposition in mineralocorticoid hypertension, which may have pathophysiological and pharmacological implications in hypertensive heart disease.

Key Words: Collagen; mineralocorticoid hypertension; heart

F012
ANTIOXIDANT TREATMENT REVERSES VASCULAR REMODELING, BUT NOT MYOGENIC TONE IN MESENTERIC RESISTANCE ARTERIES OF STROKE-PRONE SPONTANEOUSLY HYPERTENSIVE RATS (SHRSP)
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