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OUABAIN-LIKE FACTOR AND ACUTE SALT LOADING IN LOW-REIN HYPERTENSION
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In these years an ouabain-like factor (OLF), structurally similar to cardionic glycoside ouabain, has been isolated in human plasma. OLF has been implicated in states of volume expansion and in essential hypertension, especially as a factor of salt sensitivity of blood pressure. On the other hand, salt sensitivity has been described particularly in low-renin hypertension.

Aim of this study was to determine the response of plasma OLF to acute sodium expansion in low renin hypertension. To this purpose, an acute intravenous sodium load (two litres saline in four hours) was performed in 14 subjects with low-renin hypertension.

OLF was measured in plasma extracts (C18 extracted samples) by a radioimmunoassay (previously described except for having employed filter separation of bound/free 3H ouabain and compared with other endocrine parameters (aldosterone, ANP, cortisol, ACTH).

Variable responses to the saline load were observed in the individual patients for blood pressure, which significantly increased (p<0.05 for both diastolic and systolic levels).

Only a modest non significant change was observed after four hours saline infusion for OLF (mean±SEM; 894±207 pm against 749±171 pm ouabain equivalents before treatment, whereas plasma aldosterone showed a significant decrement (p<0.0007), paralleled by an increase in ANP levels (p<0.0007). A positive relationship was observed between OLF and ACTH (p<0.02).

In conclusion, our results do not support the hypothesis that ouabain-like factor is stimulated in low renin hypertension by acute volume expansion obtained with intravenous saline loading; ACTH could be a factor modulating OLF secretion in this condition.

Key Words: Ouabain-Like-Factor, Salt, Renin

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IN SALT-SENSITIVE HYPERTENSION STATINS PROTECT END-ORGAN INJURY VIA INCREASED NO PRODUCTION AND DECREASED REACTIVE OXYGEN SPECIES
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The balance between nitric oxide (NO), angiotensin (Ang) II and super-oxide (O$_2^-$) is critical for maintenance of cardiovascular homeostasis. Hypertensive Dahl salt-sensitive (DS) rats are NO deficient due to eNOS downregulation and decreased NO bioavailability linked to a functional upregulation of Ang II, which results in increased O$_2^-$, endothelial dysfunction, and cardioenral injury. It has been reported that statins upregulate eNOS, inhibit oxidative stress and downregulate AT1 receptor. Here we investigated whether atorvastatin (ATO, 30 mg/kg/day; by gavage for 10 weeks) would upregulate eNOS, increase NO bioavailability and prevent the increase in O$_2^-$ in DS rats, thereby reducing end-organ injury. DS rats were divided into 5 groups: NS, fed 0.5% NaCl diet; HS, fed 4% NaCl diet; HS+ATO, fed 4% NaCl diet plus ATO; HS/NS, fed 4% NaCl diet for 6 weeks following 0.5% NaCl diet for 4 weeks; HS/NS+ATO, fed 4% NaCl diet for 6 weeks following 0.5% NaCl diet plus ATO for 4 weeks. HS rats developed hypertension (SBP 200 ± 8 vs 150 ± 2 mmHg in NS; P<0.05), impaired endothelium-dependent relaxation to acetylcholine (EDR), functional upregulation of endothelin (ET)-1, left ventricular (LVH, 30%), aortic (23%) hypertrophy, and proteinuria (16%), accompanied by downregulation of aortic eNOS activity (0.7 ± 0.2 vs 1.8 ± 0.3 nmol/min/g protein in NS; P<0.05) and increased aortic O$_2^-$ (2632 ± 316 vs 1176 ± 112 counts/min/mg in NS; P<0.05) and plasma 8-F$_2$-isoprostanes (97.2 ± 12.3 pg/ml vs 57.3 ± 13 pg/ml in NS, P<0.05). ATO (HS+ATO) prevented the decrease in eNOS activity (1.5 ± 0.3 nmol/min/g protein) as well as the increase in O$_2^-$ (1192 ± 243 counts/min/mg) and plasma 8-F$_2$-isoprostanes (58.4 ± 15.2 pg/ml), reduced LVH and proteinuria, and normalized EDR, vascular response to ET-1, and aortic hypertension, although reduction in SBP was modest (174 ± 8 mmHg). Switch to NS alone (HS/NS) did not ameliorate SBP (205 ± 7 mmHg), EDR or end-organ injury and minimally reduced O$_2^-$ production (1974 ± 171 counts/min/mg). Combination of ATO and removal of high salt (HS/NS+ATO) normalized aortic eNOS (1.56 ± 0.17 nmol/min/g protein), as well as SBP (152 ± 2 mmHg), LVH, and proteinuria. These novel findings indicate that in salt-sensitive hypertension the concomitant upregulation of vascular eNOS and inhibition of oxidative stress may importantly contribute to the protection against end-organ injury afforded by statins.

Key Words: Statins, Nitric Oxide Synthase, Oxidative Stress

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RACE DIFFERENCES IN STRESS-INDUCED PRESSURE NATRIURESIS AND LEFT VENTRICULAR GEOMETRY
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Objective: The incidence and prevalence of essential hypertension and associated target organ damage is much greater in African-Americans compared to European-Americans. We hypothesize that impaired stress-induced pressure natriuresis among African-Americans contributes to these differences by increasing the cardiovascular load experienced by African-Americans in response to stress. We define impaired stress-induced pressure natriuresis as an increase in blood pressure without an adequate compensatory increase in sodium excretion to help return blood pressure to pre-stress levels. The purpose of this study was to test this hypothesis.

Methods: The 256 African-American and 113 European-American youths (mean age 16±1 yrs) were placed on a controlled sodium diet to bring them into similar levels of sodium balance prior to testing. The stress protocol consisted of a 2 hour baseline period, followed by a one hour period during which the subjects played a competitive video game task and a two hour recovery period. Hemodynamic measurements were obtained at 15 minute intervals; urine samples were obtained hourly. Echocardiograms were obtained on a sub-sample of 110 subjects (59 African-American, 51 European-American).

Results: The condition (baseline, stress, recovery) by race interaction was significant for mean blood pressure (P=0.02) but not for sodium excretion. African-Americans had higher blood pressure throughout the protocol (P=0.001 for each). This was coupled with lower sodium excretion during stress (P=0.07) and recovery (P=0.0001), despite similar levels at baseline. These results demonstrate impaired stress-induced pressure natriuresis among the African-Americans. Furthermore, this response pattern was associated with cardiac remodeling in this group as evidenced by greater relative wall thickness (0.38 v 0.35%; P=0.001).

Conclusion: These results are consistent with our hypothesis. As such, they provide support for an interactive model of salt and stress in the development of essential hypertension and its sequelae in this salt-sensitive population.

Key Words: Race, Pressure Natriuresis, LV Geometry