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OUABAIN-LIKE FACTOR AND ACUTE SALT LOADING IN LOW-RENIN HYPERTENSION
Sylwana Balcan, Enza Fommei, Giuseppina Niccolini, Annalisa Iervasi, Tina Prontera, Pietro Di Cecco, Paolo Gazetti, Silvano Masini. Clinical Chemistry, Institute of Clinical Physiology, Pisa, Italy; Cardiovascular Medicine, Institute of Clinical Physiology, Pisa, Italy.

In these years an ouabain-like factor (OLF), structurally similar to cardiac 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<0.001). 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
Ming-Sheng Zhou, Edgar A Jaimés, Leopoldo Raji. Department of Medicine, Division of Nephrology-Hypertension, and Vascular Biology Institute, University of Miami, School of Medicine, Veterans Affairs Medical Center, Miami, FL.

The balance between nitric oxide (NO), angiotensin (Ang) II and superoxide (O2-) is critical for maintenance of cardiovascular homeostasis. Hypertensive Dahl salt-sensitive (DS) rats are NO deficient due to eNOS downregulation and decreased NO availability linked to a functional upregulation of Ang II, which results in increased O2-, endothelial dysfunction, and cardiorenal 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 O2- 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 O2- (262 ± 316 vs 1176 ± 112 counts/min/mg; P<0.05) and plasma 8-iso prostanes (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 O2- (1192 ± 243 counts/min/mg) and plasma 8-iso prostanes (58.4 ± 15.2 pg/ml), reduced LVH and proteinuria, and normalized EDR, vascular response to ET-1, and aortic hypertrophy, 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 O2- 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