separated from whole blood. NADPH-oxidase activity was measured by reduction of cytochrome C. Phospholipase A\textsubscript{2} activity was measured by the release of arachidonic acid from prelabeled cells. Cells were incubated with MEK inhibitors U0126 (0.1μM-5μM), or with p38 MAP-kinases inhibitor SB 202190 (0.5μM-10μM) for 30 min in 37°C prior to stimulation with angiotensin II (10^{-5}M). The activation of ERK1/2 and p38 MAP-kinase was determined by western blot analysis with anti-active antibodies. Angiotensin II stimulated a time-dependent activation of both type of MAP-kinases ERK2 and p38. ERK activation was immediate, and was detected 30 sec after stimulation, peaked at 3 min and decreased thereafter. Phosphorylation of p38 MAP kinase was detected in unstimulated cells slightly increased at 3 min and stayed elevated for, at least, 15 min. Activation of NADPH-oxidase in angiotensin II-stimulated neutrophils and monocytes was inhibited in a dose dependent manner by both the p38 MAP-kinases inhibitor, SB 202190, and the MEK inhibitor, U0126. The p38 MAP kinase inhibitor, SB 202190, completely inhibited phospholipase A\textsubscript{2} activity stimulated by angiotensin II in correlation with its effect on NADPH oxidase activity. In contrast the MEK inhibitor, U0126, did not affect phospholipase A\textsubscript{2} activity stimulated by angiotensin II. Our results demonstrated that both types of MAP-kinases, ERK and p38 mediate the activation of NADPH-oxidase by angiotensin II in phagocytic cells. While p38 MAP-kinase mediate the phospholipase A\textsubscript{2} activity, ERK does not participate in phospholipase A\textsubscript{2} activation and its role in NADPH-oxidase activation remains to be elucidated.

Key Words: Angiotensin II, NADPH-Oxidase, Phagocytes

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PARAMETERS OF THE RESPIRATORY SYSTEM FUNCTION IN PATIENTS WITH ESSENTIAL HYPERTENSION TREATED WITH ATENOLOL AND LOTREL
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Fifty patients were observed for the purpose of comparison the effect of β1 adrenoblockers (β1 AB) and ACE inhibitors (ACE) on the state of the respiratory system function for the treatment of patients with essential hypertension (EH). Patients of the 1st group (26) took ATENOLOL (SANOFI) 25 mg twice a day, and patients of the 2nd group (24) took LOTREL (NOVARTIS) 5 mg twice a day for ten days. Parameters of the respiratory system function were examined by the method of computer spirometry before and after the treatment. Such predictive and active parameters of computer spirometry as Maximum Voluntary Ventilation (MVV), Forced Vital Capacity (FVC), Forced Expiratory Volume after 1s (FEV\textsubscript{1}), FEV\textsubscript{1} as % of Inspiratory Vital Capacity (FEV\textsubscript{1}/V\textsubscript{CIN}), FEV\textsubscript{1} as % of FVC (FEV\textsubscript{1} E), and Peak Inspiratory Flow (PIF) were not significantly different between both groups before β1 AB and ACE administration (p>0.05). The data of active parameters mentioned above were decreased in the 1st group of the patients on the fifth day of ATENOLOL test (p>0.05). On the background of LOTREL treatment such active parameters of respiratory system function as MVV, FEV\textsubscript{1}/V\textsubscript{CIN}, FEV\textsubscript{1} E, were uncertainly higher than for the patients who were taking ATENOLOL (p>0.05).

Conclusions: The usage of LOTREL (NOVARTIS) for the patients with essential hypertension and pathology of the respiratory system function is safer and admissible in comparison with β1 adrenoblockers.

Key Words: Lotrel, Atenolol, Spirography

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DIFFERENT ANTIOXIDANT EFFECTS OF ATI RECEPTOR ANTAGONIST AND LONG-ACTING CA ANTAGONIST ON SMOOTH MUSCLE CELL PHENOTYPIC MODULATION IN INTRAMYOCARDIAL ARTERIES FROM STROKE-PRONE SHR
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To clarify the mechanisms underlying vascular remodeling and oxidative stress in hypertension, we compared the effects of anti hypertensive drugs on vascular remodeling and smooth muscle (SM) cell phenotype of intramyocardial arteries, and NAD(P)H oxidase essential subunit, p22phox as well as superoxide dismutase (SOD) in heart from 12-week-old male stroke-prone spontaneously hypertensive rats (SHRSP). SHRSR were divided into 4 groups: Control, angiotensin-converting enzyme inhibitor, Cilazapril (10 mg/kg/day), angiotensin II type-1 receptor antagonist, E4177 (30 mg/kg/day) or long-acting calcium antagonist; Amlodipin (5 mg/kg/day). All rats were fed 0.9% NaCl and treated for 6 weeks. All drugs significantly and equally reduced not only blood pressure, but also inhibited left ventricular hypertrophy and perivascular fibrosis compared to the Controls. Additionally, all drugs significantly up-regulated contractile-type SM myosin heavy chain (MHC), SM2, and SOD. In contrast, all drugs significantly down-regulated synthetic-type SM-MHC (SMemb), and nuclear factor-kB compared to the Controls. Furthermore, E4177 significantly inhibited wall-to-lumen ratio, synthetic-type SM-MHC (NMHC-A), p22phox and oxidative stress assessed by TBARS more than did the other drugs. Thus, all of drugs might have antioxidant action mediated via modulation of enzyme systems that may generate free radicals. It is also suggested that NAD(P)H oxidase-mediated oxidative stress and angiotensin II type 1 receptor may play an important role in vascular remodeling and phenotypic modulation of SM cells in intramyocardial small arteries from SHRSP.

Key Words: Vascular Smooth Muscle, Antioxidation, Angiotensin II Type1 Receptor

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INTRARENAL RENIN INNSUPPRESSIBILITY IN HEALTHY BLACKS ON HIGH SALT DIET
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On a high salt (HS) diet we have reported differences in the kidneys of healthy blacks and caucasians: renal perfusion is 10% lower in age-matched healthy blacks compared to caucasians; renal vasoconstriction is blunted in blacks to Ang II; the renal vasodilator response to captopril is significantly larger in blacks compared with caucasians (p<0.001) despite similar PRA levels in the HS state; and the renal vasoconstrictive response to Ang II corrects to a similar level to caucasians after captopril.

To ascertain if these differences exist in low salt (LS) state as well, we compared the responses of 16 healthy blacks to Ang II and the renal vasodilator response to captopril. There was no differences between the 2 groups. Likewise, captopril caused a significant vasodilator response in both groups (98±21 and 117±27 ml/min/1.73m\textsuperscript{2}) respectively; again with no difference between the 2 groups. The PRA levels were similar (4.8±0.97 vs 3.5±0.64 ng/ml/hr in blacks and caucasians respectively). Activation of the RAS is
Aldosterone to renin ratio (ARR) is an indicator of inappropriate aldosterone activity in hypertension. Since aldosterone may induce vascular fibrosis and contribute to deteriorate vascular compliance we hypothesised that the ARR would relate to aortic stiffness as measured by carotid-femoral pulse wave velocity.

Plasma sampling from 60 (32 males) untreated hypertensives, aged 46 + 2 (s.e.m.) years, with body mass index 29 + 2 kg/m2, were done for plasma renin activity (PRA, ng/ml/h) and plasma aldosterone (ALD ng/dl) measurements (by RIA). AAR was calculated by dividing ALD by PRA. Each patient underwent noninvasive measurement of carotid-femoral pulse wave velocity (PWV, m/s, with COMPLIOR). Linear and multiple correlations between PWV and casual systolic BP (SBP), diastolic BP, BMI and ARR values were assessed. Values of PWV (10.6 + 0.3 m/s), SBP (157 + 3 mm Hg), DBP (96 + 2 mm Hg) and of ARR (22.2 + 2.1) were obtained. PWV was significantly correlated with age (r=0.48, p<0.01), SBP (r=0.44, p<0.01), DBP (r=0.34, p<0.02), and with ARR (r=0.47, p<0.01). In a multiple regression analysis, age, casual SBP, casual DBP and ARR emerged as significant (p<0.01) independent predictors of PWV, predicting respectively (adjusted R squared) 22%, 19%, 11% and 21% of the variation of PWV values. We conclude that there was an independent and significant correlation between AAR and aortic pulse wave velocity, suggesting that in hypertensives inappropriate aldosterone activity may be involved in the increase of aortic stiffness.

Key Words: Pulse Wave Velocity, Arterial Stiffness, Aldosterone to Renin Ratio

The main idea was to estimate the parameters of neurohormonal system before and under ACE inhibitors treatment.

72 hypertensives (30 m., 36 f., mean age 58,4+7,6 years) were treated by Ramipril ( R ) (Hoechst-Maarian-Roussel), 5-20 mg o/d or Enalapril ( E ) (Merk Sharp & Dohme) 20-40 mg o/d during 6 months without special choice. Plasma renin activity (PRA), plasma aldosterone level (PA), 24 hours urinary excretion of aldosterone, adrenaline and noradrenaline as well as morphofunctional parameters ejection fraction (EF) and left ventricular mass (LVM) were measured before and after 6 months of drug uptake.

After 6 months of ACE treatment PRA increased on 56.2% (p<0.01), PA decreased on 7.1% (p<0.05); 24 hours urinary aldosterone, adrenaline and noradrenaline excretion significantly reduced on 26.5% (p<0.01), 14.4% (p<0.05) and 17.2% (p<0.05) respectively, EF increased on +13.6% (p<0.05), LVM decreased on 14.6% (p<0.05).

Conclusion: In patients with arterial hypertension there are changes in neurohormonal status and morphofunctional parameters. There were no differences between R and E in neurohormonal and morphofunctional changes. High relationships were found between noradrenaline urinary excretion and EF (r=0.72; p<0.05) and between degree of decrease plasma aldosterone level and degree of decrease of left ventricular mass (r=0.56, p<0.02) under the long-term ACE inhibitor treatment.

Key Words: ACE Inhibitor, Neurohormonal, Treatment

The effects of aldosterone are typically ascribed to the activation of an intracellular receptor that mediates its effects by regulating expression of target genes. In addition to genomic effects, however, there is increasing evidence for rapid, non-genomic effects. The acute effect of aldosterone on vascular tone was unknown. Therefore, we studied the immediate effects of aldosterone on alpha-adrenoceptor-mediated function in aortic ring segments from 10-week-old male Wistar Rats and in primary bovine aortic endothelial cell (BAEC) cultures. Ring segments were incubated (2 min) with aldosterone followed by administration of a submaximal constricting dose of phenylephrine (100 nM). Aldosterone (1 PM-100 nM) caused a biphasic attenuation of phenylephrine-mediated vasoconstriction in endothelium-intact preparations (to a maximal reduction of 25±4% of control phenylephrine-mediated constriction at an aldosterone concentration of 10 pM). In contrast, in endothelium-denuded vessels, aldosterone mediated a monophasic dose-dependent enhancement of vasoconstrictor response (Emax: 24±4% above control, Emax: 0.57±0.6 pM, n=5). Further, in endothelium-intact vessels, L-NMMA (10 μM) blocked the effect of aldosterone to attenuate vasoconstriction, suggesting that the effect of aldosterone was NO synthase-dependent. In BAEC, aldosterone caused an increase in MAP kinase (ERK1/2) and p70 S6 kinase phosphorylation by 10 pM. Cytosensor analysis showed that aldosterone treatment did not affect H+ flux. Overall, these data support a novel non-genomic endothelial-dependent effect of aldosterone paralleling ERK1/2 and p70 S6 kinase activation, which could be important in acute regulation of peripheral vascular resistance.

Key Words: Aldosterone, Endothelial, Nitric Oxide