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REACTIVE HYPEREMIA AND CARDIOVASCULAR PERFORMANCE IN ATHLETES REGULARLY TRAINED
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Regular physical exercise induces beneficial effects on the cardiovascular system. To evaluate the relationships between endothelial function, evaluated as post ischemic reactive hyperemia, and physical performance (as maximal oxygen consumption, VO2max), we studied 15 healthy male volunteers, (mean age 26.4 ± 5 years; B.P. 107/75 ± 27/6 mmHg) used to perform a mixed aerobic and anaerobic exercise, 3 times weekly for 90 minutes.

All the participants underwent the following measurement: 1) reactive hyperemia at the forearm, after 4 minutes of ischemia, measured by strain-gauge plethysmography; 2) flow mediated dilatation in the brachial artery, measured by ultrasound method (Vivid 7, G.E., linear probe 10MHz) after 4 minutes of ischemia; 3) cardiopulmonary response to the exercise test, according to Bruce protocol, on treadmill (Benchmark Exercise System Test, Morgan) with measurement of lactic acid serum concentration; 4) Body composition, as free fat mass and fat mass with Akern Bia 101.

Reactive hyperemia 30 second after ischemia, a nitric-oxide related phase increased by 220% (10-519%). Such increase was negatively correlated with free fat mass (r= -0.47), but not with age, blood pressure or lactic acid concentration. On the other hand reactive hyperemia was negatively related to the increase in SBP during exercise test (r= -0.57, p=0.03) and positively with the levels of serum haemoglobin (r=0.43) and haematocrit (r=0.41), even after correction for free fat mass. VO2max was not related to % increase in reactive hyperemia (r=-0.33), but was related to the flow-mediated dilatation of brachial artery at 30 seconds after ischemia (r=0.66, p < 0.01).

In conclusion, our data suggest that, in well trained young adults, the cardiopulmonary response to maximal exercise test was significantly related to the flow-mediated dilatation of the brachial artery, but not to reactive hyperemia at 30 second. It is therefore possible to conclude that plethysmographic reactive hyperemia and flow-mediated dilatation of the brachial artery are the expression of different aspects of the vascular reactivity to the endothelium depended post-ischemic involving different haemodynamic and neuro-hormonal components.

Key Words: Physical performance, flow mediated dilatation, plethysmography

P-97

THE EFFECTS OF NIMODIPINE ON CORONARY FLOW, NITRITE OUTFLOW AND SUPEROXIDE ANION RELEASE IN ISOLATED RAT HEART
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The effects of Ca2+ channel antagonist nimodipine (also known as phosphodiesterase-1 inhibitor-PDE1) were examined on coronary flow, endothelial NO production (nitrite outflow) and superoxide anion production. The experiments were performed on isolated rat hearts from male Wistar albino rats (BM about 200 g, 8 weeks) and perfused with buffer at constant pressure. The nitrite outflow and superoxide anion release were estimated by spectrophotometry. The coronary autoregulation (CA) was investigated with follow-up of coronary perfusion pressure (CPP) changes from 40 to 120 cm H2O. After first sequence of CPP changes (basic protocol), the hearts were perfused with nimodipine (in concentration known to elicit PDE1 inhibition, 2 mM) alone or in combination with nitric oxide synthase inhibitor (L-NAME, 30 mM). During control state the hearts exhibit CA between 50 and 90 cm H2O; with basal coronary flow at 60 cm H2O of 4.42±0.71 ml/min. Basal nitrite outflow and superoxide anion release (O2) were 0.64±0.18 nmol/min/g wt and 19.72 nmol/min/g wt, respectively. Nimodipine induced significant vasodilatation at all values of CPP (from 26 % to 36 %). Nimodipine-induced dilatation was accompanied with significant decrease of nitrite outflow at all values of CPP (from 59 % at 40 cm H2O to 40 % at 120 cm H2O) and with significant increase of O2 release (from 186 % at 40 cm H2O to 117 % at 120 cm H2O). However, perfusion with L-NAME completely reversed the effects of nimodipine-induced inhibition. Nimodipine-induced dilatation was decreased under L-NAME (from 3 % at 40 cm H2O to 11 % at 120 cm H2O) without changes in autoregulatory range. Nitrite outflow was significantly increased under L-NAME until 90 cm H2O (from 69 % at 40 cm H2O to 36 % at 90 cm H2O) as well as O2 release was significantly decreased at all CPP-values (from 50 % at 40 cm H2O to 43 % at 120 cm H2O).The findings show that effects of nimodipine on coronary flow should be significantly influenced by NO and O2 release in isolated rat heart.

Key Words: Nimodipine, nitrite outflow, superoxide anion release

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AMBULATORY PULSE PRESSURE (PP) AND ENDOTHELIUM DYSFUNCTION OF HYPERTENSION
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The objective of this study was to investigate the relationship between ambulatory pulse pressure (PP) and endothelium dysfunction of hypertension. 555 patients (275 men, 280 women) with mild to moderate essential hypertension (EH) who were initially untreated were studied (age 47.1±12.7 years). 24h ambulatory blood pressure monitoring and two-dimensional echocardiography were applied. According to the ambulatory pulse pressure, we divided the patients with EH into four groups. Group A: pp<-50mmHg; Group B: 50mmHg<pp<50mmHg; Group C: 50mmHg<pp<60mmHg; Group D: pp>60mmHg. And the patients with EH were divided into 3 groups by age. Group I: 40y<age<50y; Group II: 50y<age<60y; Group III: age≥60y. Because the endothelium function is highly influenced by age, we used univariate analysis. The ambulatory pulse pressure was correlated with the level of plasma nitric oxide (NO) (r=-0.269; p<0.01), endothelin (ET) (r=0.314; p<0.01) and ET/NO (r=-0.377; p<0.01). ET/NO is significantly increased in the high PP group (group D) than in the normal PP one (group A). In conclusion, endothelium dysfunction was associated with increased PP. Compared with clinic PP, ambulatory PP monitoring may be a better way to estimate endothelium dysfunction.

Key Words: Endothelium dysfunction

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THE IMPACT OF SUBCHRONIC LEAD POISONING ON THE VASCULAR EFFECT OF NITRIC OXIDE IN RATS
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Lead-induced arterial hypertension is recently suggested as resulting mainly from an attenuation of vascular nitric oxide (NO) effect due to an
increase of reactive oxygen species in vessels wall. The aim of this study was to evaluate the impact of poisoning with lead in hypertensive doses (50 or 100 ppm in drinking water for three months) on the basal and stimulated released NO effect in isolated and perfused rat mesenteric bed according to the red-ox system activity in aorta and levels of NO and endogenous vasoactive agents (endothelin-1 and prostaglandin E2) in the blood. Unexpectedly, rats given 50 ppm of lead have demonstrated an increase of maximal vascular response to Nω-nitro-L-arginine (p<0.01) and acetylcholine (p<0.05), the shift to the left of the dose-response curve for ACh and a decrease of plasma endothelin-1 (p<0.05) concentration in comparison to controls. Lipid peroxides and glutathione in aorta and blood nitric oxide concentrations were significant increased in rats given both 50 and 100 ppm of lead. We conclude, that lead in small hypertensive dose, in contrast to higher hypertensive dose, enhances vascular effect of NO in rat mesenteric bed.

Key Words: Poisoning by lead, nitric oxide, endothelin

P-100
PEPTIDE INTERACTION IN REGULATING VASCULAR NOS
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The aim of this study was to examine the role of the serine/threonine kinase, Akt, signaling pathway in mediating interactions between angiotensin II (Ang II) and insulin-like growth factor-1 (IGF-1) in the regulation of nitric-oxide synthase (NOS) activity in vascular smooth muscle cells (VSMC). To investigate the role of Ang II, aortic and heart tissue obtained from transgenic rats overexpressing the mouse Ren-2 gene (hypertensive mREN rats) and Sprague-Dawley (SD) rats were treated with the AT1 receptor agonist, Valsartan (30 mg/kg/day). In VSMC obtained from the 2 models, exposure to IGF-1 (100 nM) for 10 min resulted in increased NO activity and NO production. IGF-1 treatment induces Akt phosphorylation at Ser473 and Thr308, as well as Akt kinase activity. Pretreatment with Ang II (100 nM) for 5 min substantially decreased these IGF-1 effects; NOS activity was decreased in mREN rats compared to SD animals. Following the treatment of mREN animals with Valsartan for 2 weeks, the NOS activity was found to be similar to the levels in SD controls. Akt phosphorylation at Ser473 was attenuated in aortic tissue in untreated mREN when compared to SD, while no differences were found in the phosphorylation at Thr308 between the two strains. In heart tissue the level of Akt phosphorylation at Ser473 was increased in Valsartan treated animals compared to untreated mREN. These results demonstrate a role for Akt in the Ang II/IGF-1 regulation of NOS in VSMC and cardiac tissue, and show that the AT1 block was successful in correcting some of the abnormalities.

Key Words: Insulin-like growth factor-1, angiotensin II, nitric-oxide synthase

P-101
DOES ALLOPURINOL PREVENT SIDE EFFECTS OF CYCLOSPORINE A TREATMENT?
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Side effects of cyclosporine A (CsA) treatment, such as vasoconstriction and reduced renal plasma flow, are partly endothelium-dependent. Allopurinol improves endothelial function in diabetic and hypertensive patients. We examined the effects of allopurinol-application (50 mg/kg over 14 days) on arterial blood pressure, renal blood flow and vasoreactivity of CsA-treated (8 mg/kg over 14 days) Wistar rats.

Mean arterial pressure (MAP) of CsA-treated rats was 106 ± 4 mmHg (MAP of CsA + allopurinol-treated rats: 103 ± 4 mmHg), renal plasma flow was 6.3 ± 1.5 ml/min in CsA-treated rats as compared to 5.3 ± 1.1 ml/min in rats treated with CsA + allopurinol. Bolus injection of norepinephrin (0.1 mg/kg) increased MAP to 168 ± 9 (CsA-group) and to 128 ± 8 mmHg (CsA + allopurinol-group). The elevation of blood pressure was significantly higher in the CsA-treated-group than in the CsA+allopurinol-treated animals (62 ± 6 vs. 24 ± 5 mmHg, p<0.05), while renal plasma flow decreased to 1.3 ± 0.5 (CsA-group) and to 3.5 ± 0.7 ml/min respectively (CsA + allopurinol-group). The difference of the decrease of renal plasma flow between the groups was significant (p<0.05).

Allopurinol seems to have beneficial effects on vasoreactivity and renal blood flow in CsA-treated animals and might attenuate CsA-induced nephrotoxicity.

Key Words: Cyclosporine A, allopurinol, vascular Reactivity

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TEMPOL PREVENTS AND RECOVERS GLUCOCORTICOID-INDUCED HYPERTENSION
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The aims of present study were to investigate the effects of Tempol (4-hydroxy-2,2,6,6-tetramethylpiperidine-N-oxyl), a membrane-permeable superoxide scavenger, on prevention and reversal of glucocorticoid (GC)-induced hypertension in the rat. Two models were used, adrenocorticotropic hormone (ACTH) treatment which produces hypertension through increase in corticosterone secretion, and the synthetic GC dexamethasone (Dex). Male Sprague-Dawley rats (n=10 in each group) were treated with saline, ACTH (200 µg/kg/day, s.c.) or Dex (10 µg/kg/day s.c.) for 12 days. Tempol (1 mM in drinking water) was given from treatment Day 8 (reversal study) or from 4 days prior to treatment (prevention study). Systolic blood pressure (SBP) was measured by tail cuff. Plasma F2-isoprostane concentrations were assayed as a marker of oxidative stress.

Results were expressed as mean ± SEM. Both GC treatments increased SBP (ACTH: 119 ± 5 to 142 ± 5 mmHg, P < 0.0005. Dex: 122 ± 5 to 136 ± 3 mmHg, P < 0.05). ACTH increased plasma F2-isoprostanes (8.4 ± 1.2 saline vs 12.9 ± 1.6 nM ACTH, P < 0.05). Tempol on T8 reversed ACTH hypertension (118 ± 3 mmHg, P < 0.05) and tended to reverse Dex-induced hypertension (122 ± 4 mmHg, P' = 0.057). Tempol alone did not alter SBP, but Tempol pre-treatment partially prevented both ACTH (123 ± 2 mmHg, P' < 0.05) and Dex (128 ± 4 mmHg, P' < 0.05) induced hypertension.

Conclusions: 1) ACTH-induced hypertension is associated with increased oxidative stress; 2) Tempol reversed and partially prevented ACTH-induced hypertension in the rat, independent of improvement in systemic oxidative stress; 3) Tempol partially reversed and prevented Dex-induced hypertension.

Key Words: Glucocorticoids, hypertension, antioxidant