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Endothelin-1 Receptor Blockade Induced Upregulating of RAAS Expression in Terms of Blood Pressure Regulation

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Introduction: The renin-angiotensin-aldosterone system (RAAS) and the endothelin (ET) system are the most potent vasoconstrictors that contribute to blood pressure elevation. However, despite vast body of investigations, only limited information exists in their reciprocal relationships. **Aim:** To compare the expression level of RAAS in C57BL/6 mice with or without endothelin-1 receptor antagonist bosentan and the potential value in blood pressure regulation. **Methods and results:** Bosentan (10 mg/Kg/d) and placebo were given to two groups of male C57BL/6 mice (N=5) seperately from 6- to 12-week old. After that, mRNA of liver, kidney and lung was isolated. Northern blot analysis demonstrated that the expression levels of AGT (angiotensinogen) in liver (P=0.0126), renin in kidney (P=0.002), ACE (angiotensin-converting enzyme) in lung (P=0.0041) were up-regulated in mice with bosentan. Another 15 male C57BL/6 mice were divided into 3 groups (N=5): mice in group A were given AT1 blocker valsartan (10 mg/Kg/d), mice in group B were given bosentan (10 mg/Kg/d), mice in group C were given both valsartan and bosentan (10 mg/Kg/d respectively). All mice admitted drug from 6- to 12-week old. No SBP (systolic blood pressure) difference can be found between groups before drug admitting. Six weeks after mono-therapy with valsartan, SBP was a little lowered (126.3±2.1 vs 121.9±3.5 mmHg, P=0.0425). Mono-therapy with bosentan little effect SBP (125.9±2.5 vs 122.3±3.2 mmHg, P=0.0827). While dual blockade with valsarvan and bosentan significantly lowered SBP (126.8±2.7 vs 102.6±2.8 mmHg, P<0.001). **Conclusion:** We conclude that RAAS components will be up-regulating under ET (endothelin) blockade situation. Dual blockade of RAAS and ET system is benefit for blood pressure control.

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What is the Importance of Hypertension in the Preoperative Clinical Evaluation in Patients Aged Over 50 Years?

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Introdution: Preoperative clinical evaluations are routinely performed by cardiologists in patients with chronic arterial hypertension. The hypertension history enhances the risk score according to ASA risk, since hypertension is considered a systemic disease. The aim of this study was to determine whether the history of hypertension as isolated co-morbidity changes the results of preoperative tests and surgical outcome compared with no co-morbidity patients. **Methods:** Two hundred seventy five patients (group I) which had mild/moderate hypertension as isolated co-morbidity (64.9±9.7 years; 89% female) were compared with 297 no co-morbidity patients (61.3±10.0 years; 75.4 female) in a prospective design. All patients had normal physical examination, complete preoperative tests (EKG, chest X-ray, glucose, BUN, creatinine, blood cells count and PTa/PTTa) and were submitted to surgical procedure to treat tumor desorders. The results from EKG, chest X-ray and blood tests were compared between the groups as well as the surgical outcome. The age between the groups was adjusted. Adverse outcomes were considered any complications that increased the length of stay in-hospital or death. **Results:**. For whole statistics analysis the age was adjusted. EKG was normal in 216 patients from group I and 259 from group II [78.5 × 87.2%; p=0.069; OR 1.54 (0.97 - 2.46)]. Chest X-ray was normal in 229 patients from group I and 265 from group II [83.3 × 89.2%; p=0.248;OR 1.35 (0.81 - 2.24)] while the blood tests were normal in 244 patients from group I and 277 from group II [88.7 × 93.3%; p=0.131; OR 1.58 (0.87 - 2.87)]. In relation to surgical outcome, 268 patients from group I and 291 from group II had normal in-hospital evolution [(97.5 × 98.0%; p=0.544; OR 1.42 (0.46 - 4.37)]. Conclusion. The results demonstrated that patients with mild/moderate hypertension behaved themselves in a similar way with the no co-morbidity patients, suggesting that patients with arterial hypertension aged over 50 years do not have additional risk in relation to no co-morbidity patients.

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Relationship Among Resistin, Insulin Resistance, and Hypersensitivity C-Reaction Protein in Primary Hypertensive Patients

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Introduction: To study the relationship among resistin, insulin resistance and hyper-sensitivity C-reaction protein (hsCRP) in primary hypertensive patients. **Methods:** The basic information was collected in fifty hypertensive patients without diabetic history and forty normal people as control. Blood pressure, waist circumference and hip circumference were measured. Then blood samples were taken from them for measurement of biochemical indicators. Fasting serum resistin was tested by enzyme linked immunosorbent assay (ELISA). Insulin resistance index (IRI) was applied to estimate insulin resistance. **Results:** The levels of waist circumference, blood pressure, IRI, hsCRP and serum resistin were significantly higher in the hypertensive patients than those in normal control group (P<0.05). Pearson relation analysis showed that the resistin level of the hypertensive patients was positively correlated with waist circumference (r=0.391, P<0.05), systolic blood pressure (r=0.425, P<0.05), IRI (r=0.608, P<0.05) and hsCRP (r=0.447, P<0.05). In normal control group, the resistin level was positively correlated with IRI (r=0.406, P<0.05) and hsCRP (r=0.452, P<0.05). Multiple factor Logistic regression analysis showed that waist circumference (OR=1.042, P<0.05), IRI (OR=1.368, P<0.05), hsCRP (OR=1.129, P<0.05)and resistin (OR=1.082, P<0.05)were associated with hypertension. **Conclusion:** The results suggest that the presence of resistin is associated with systemic inflammation and insulin resistance of hypertensive patients. It implies that the resistin may play pivotal roles in the pathogenesis and development of hypertension through systemic inflammation and insulin resistance.

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Dynamic Response to Olmesartan Medoxomil

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Exercise induces a physiologic elevation on blood pressure, an effect highly dependent on continued training, abnormal elevations are considered independent predictors of future hypertension or risk markers for target cardiovascular organ damage. Patients with apparently well controlled blood pressure at rest often show abnormal blood pressure (BP) responses to physical activity. **Aim:** To study the effect of Olmesartan Medoxomil both at rest and during exercise, we analysed a set of well controlled hypertensive patients, not treated with ARBs, with a baseline exercise test showing hypertensive response. **Methods:** Hypertensive response (HR) was defined as an escalation in BP during exercise equal or beyond 210/110 mm Hg. Following the first exercise test 104 patients meeting the inclusion criteria (subjects with negative exercise test for ischemia with hypertensive response to exercise, not treated with ARBs) and willing to take part in the study were enrolled. To estimate the effect on the pressure response to exercise medical therapies were adjusted adding Olmesartan; a second exercise test was performed within 6 weeks, following the same protocol. **Results:** up to 58% were males, with a mean age of 58±10 years old, 25% had previous history of coronary heart disease, 68% showed adequate BP control at rest. Antihypertensive prescriptions included beta-blockers (45%), calcium channel blockers (29%), ACE inhibitors (21%), diuretics (29%) and alpha blockers (16%). Baseline exercise duration was 9±3 minutes, reaching 9±3 METs on average. A total of 32 patients received 40 mg/day of Olmesartan, and 72 had 20 mg. daily. The second test performed with identical protocol lasted 9.8±3 minutes on average (p<0.05) and rendered 9.5 +2.3 METs (p<0.05). Baseline BP was significantly lower (138±17/78 +13 mm Hg; p<0.05). Only two patients showed peak BP reached the upper normal limits, the average systolic pressure was 178±22 and diastolic was 95±20 mm Hg (comparison of paired means p<0.01). **Conclusion:** hypertensive patients often show abnormal increases in blood pressure induced by physical exercise. Adequate blood pressure control at rest does not necessarily imply dynamic control. Olmesartan was very well tolerated, showed antihypertensive efficacy on resting, exercise and post exercise blood pressure thus modifying an independent cardiovascular risk marker.

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Study of Autoantibodies Against AT1 Receptors and α1 Adrenoceptors in Hypertension with Acute Coronary Syndromes

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Itroduction: The pathogenesis of hypertension is very complicated, and its complications are the main risk factors of cardiovascular death. Hypertension and the associated risk factors can promote the formation and development of atherosclerosis plaque to the great and middle arteries. The article is to observe the effects of autoantibodies against AT1 receptors and α1 adrenoceptors on the tension of isolated coronary vascular ring, and to evaluate the function and possible mechanisms of the two autoantibodies in the hypertensive patients combined with acute coronary syndromes. **Methods:** The peptides from the second extracellular loop of AT1 receptors and α1 adrenoceptors were synthesized and used as the antigens to detect the autoantibodies of sera from 120 hypertensive patients with acute coronary syndromes,253 patients with hypertension and 188 normotensives and by SA-ELISA;To observe the effects of autoantibodies against AT1 receptors and α1 adrenoceptors on changes of the tension of isolated coronary artery rings in Wistar male rats. **Results:** The positive rates of the autoantibodies against AT1 receptors and α1 adrenoceptors in the hypertensive patients with acute coronary syndromes (43.3% and 41.7%, respectively) were significantly higher than those in the normotensives group (7.2% and 10.6% respectively, P<0.01) and the hypertension group (35.2% and 34.4% respectively, P<0.05);The purified autoantibodies against AT1 receptors and α1 adrenoceptors induced agonist-like vasoconstriction on coronary artery rings in a dose-dependant manner, and the vasoconstrictive roles equal to the Ang II's and phenylephrine's 46.4% and 24.4% respectively, these roles can be blocked either by Losartan and Prazosin or by the related antigens. **Conclusions:** The frequency of the autoantibodies against AT1 receptors and α1 adrenoceptors increased markedly in hypertensive patients combined with acute coronary syndromes, and these autoantibodies induced vasoconstrictive effects on coronary artery rings in vitro indicating that they might be involved in the coronary artery vasoconstriction and the coronary artery remodeling during the pathogenesis of acute coronary syndromes.