SMOKING TREATMENT INCREASE SERUM AGES LEVEL AND HAVE EFFECTS ON EXPRESSION OF ICAM-1 IN VASCULAR ENDOTHELIAL CELLS OF RAT

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Objective To investigate whether smoking can increase serum advanced glycosylation end products (AGEs) level and have effects on expression of intercellular cell adhesion molecule-1 (ICAM-1) in vascular endothelial cells of rat.

Methods Male SD rats (n=138) were randomly assigned to five groups according to duration of smoking treatment: 2-week group, 4-week group, 6-week group, 8-week group, smoking cessation group. The rats of following groups, that is 2w, 4w, 6w and 8w groups were further randomly divided into five subgroups according to intervention condition: control subgroup, smoking treatment for 1 h/per day subgroup, smoking treatment for 0.5 h/per day subgroup, aminoguanidine hydrochloride subgroup, puerarin subgroup, the rats of smoking cessation group were further randomly divided into three subgroups according to duration of smoking cessation: smoking cessation 2 weeks subgroup, smoking cessation 4 weeks subgroup and smoking cessation 6 weeks subgroup. The rats of 2w, 4w, 6w and 8w groups were sacrificed after smoking treatment for 2, 4, 6 and 8 weeks respectively; the rats of smoking cessation group were sacrificed after smoking treatment for 8 weeks and then cease-smoking for 2, 4, and 6 weeks respectively. Serum AGES levels of each rat were assayed by fluorescent method. ICAM-1 mRNA and protein of vascular endothelial cells were determined by semiquantitative RT-PCR (Reverse transcription PCR) and immunohistochemistry.

Results Serum AGES levels of all SM1 subgroups rats were increased after smoking treatment for 2 weeks (p<0.01), and reached peak at 4 weeks (p<0.001), then declined at 6 weeks and 8 weeks, but did not recover back to normal level; the increasing trend was depressed by aminoguanidine hydrochloride and puerarin. Levels of serum AGES declined in smoking cessation rats, and were significantly lower at 4 weeks than those before smoking cessation (p<0.001). With the increased duration of smoking, ICAM-1 mRNA and protein of vascular endothelial cells were up-regulated, both aminoguanidine hydrochloride and puerarin depress the up-regulation. The expression of ICAM-1 mRNA and protein of vascular endothelial cells also declined after smoking cessation, and they were significantly lower in rats of smoking cessation of 4 weeks subgroup than those before smoking cessation (p<0.05).

Conclusions Smoking treatment increase serum AGEs level in rat. Cigarette-induced AGEs play roles in the increased expression of ICAM-1 in vascular endothelial cells of rat with smoking treatment. Aminoguanidine hydrochloride, puerarin and smoking cessation contribute to the decrease of serum AGES level and the expression of ICAM-1 in vascular endothelial cells of rat.
a dose-dependent and time-dependent manner, with maximal effect at a concentration of $10^{-8}$ mol/l at 12 h (in the level of protein secretion from the cells, $p<0.01$) or 24 h (in the level of protein expression in the cells, $p<0.001$), which could also be inhibited by these inhibitors ($p<0.01$ in all groups).

**Conclusion** Urotensin II may stimulate the expression of monocyte chemoattractant protein-1 in rat aortic adventitial fibroblasts, through its receptor and the $Ca^{2+}$ channel, protein kinase C, mitogen-activated protein kinase, calcineurin and Rho kinase signal transduction pathways, contributing to the vascular inflammation.

**e0157 RNA INTERFERENCE TARGETING ACE AND AT1R GENE REDUCED BLOOD PRESSURE AND IMPROVED MYOCARDIAL REMODELLING IN SHR**

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**Introduction** Angiotensin-converting enzyme (ACE) and angiotensin II (Ang II) Type 1 receptor (AT1R) have been shown to play an important role in the pathogenesis of hypertension.

**Objective** To investigate the effects of RNA interference (RNAi) AT1R and ACE on blood pressure and myocardial hypertrophy in spontaneously hypertensive rats (SHR).

**Methods** SHRs were treated with normal saline as vehicle controls, with Ad5-EGFP as vector controls, with recombinant adenoviruses Ad5-EGFP-ACE-shRNA carrying shRNA for ACE as ACE-RNAi, Ad5-EGFP-AT1R-shRNA carrying shRNA for AT1R as AT1R-RNAi, and Ad5-EGFP-ACE-AT1R-shRNA carrying shRNA for ACE and AT1R as ACE-AT1R-RNAi. WKY rats were taken as normotensive controls treated with normal saline. Systolic blood pressure of the caudal artery was recorded. Serum levels of ACE and Ang II were measured by radioimmunoassay. Cardiac angiotensin II type 1 and type 2 receptor (AT1R and AT2R) protein were determined by immunoblotting and brain natriuretic peptide (BNP) mRNA was semi-quantified by reverse transcription-PCR (RT-PCR).

**Key findings** The SBP in SHR-Los was reduced until age 46 weeks, but returned to untreated SHR levels in SHR-Aml from 30 weeks onwards. Compared to untreated SHR, the LVMi and CVF in SHR-Los were markedly decreased until week 46, and the LV ejection fraction (LVEF) (SHR-Los vs SHR: 83.1±2.3% vs 79.5±1.9%, p<0.05) and cardiac BNP mRNA expression were improved, whereas comparable LVMi and elevated CVF were found in SHR-Aml, and the LVEF fell significantly below that of untreated SHR at week 46 (SHR-Aml vs SHR: 74.4±4.3% vs 79.5±1.9%, p<0.05), with cardiac BNP mRNA expression increasing slightly. Compared to untreated SHR, the plasma and myocardium Ang II and Aldosterone (Aldo) were measured by radioimmunoassay. Cardiac angiotensin II type 1 and type 2 receptor (AT1R and AT2R) protein were determined by immunoblotting and brain natriuretic peptide (BNP) mRNA was semi-quantified by reverse transcription-PCR (RT-PCR).

**Conclusion** To compare the effectiveness of transient prehypertensive treatment with losartan versus amlodipine in spontaneously hypertensive rats (SHR) on long-term blood pressure and cardiac protection. Main methods SHR were prehypertensively (weeks 4–10 of age) treated with losartan (SHR-Los: 20 mg/kg/day), amlodipine (SHR-Aml: 10 mg/kg/day) or saline (n=24 each group). Rats were followed up until week 46. Systolic blood pressure (SBP) was measured by tail-cuff method. Cardiac parameters including Left ventricular (LV) mass index (LVMI), collagen volume fraction (CVF) and LV function were assessed by histomorphometry and echo-cardiography. Plasma and myocardium angiotensin II (Ang II) and aldosterone (Aldo) were measured by radioimmunoassay. Cardiac angiotensin II type 1 and type 2 receptor (AT1R and AT2R) protein were determined by immunoblotting and brain natriuretic peptide (BNP) mRNA was semi-quantified by reverse transcription-PCR (RT-PCR).

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