water and 60% alcohol (5 ml/kg once per day) by intragastric administration in the first week; 10% alcohol ad libitum as the drinking water and 60% alcohol (10 ml/kg twice per day) by intragastric administration in the second week; 20% alcohol ad libitum as the drinking water and 60% alcohol (15 ml/kg twice per day) by intragastric administration from week 3 to week 16; and 30% alcohol ad libitum as the drinking water and 60% alcohol (15 ml/kg twice per day) by intragastric administration from week 17 to month 6. Animals in the control group received purified drinking water in the same regimen with alcohol treatment. Before and 6 months after initiating the study, left ventricular end diastolic diameter (LVEDD), left ventricular ejection fraction (LVEF), and fractional shortening (FS) were assessed by echocardiography. Six months after the study started, histopathology and ultrastructure of myocardium were examined with light and electron microscopy; mRNA expression of TACE was evaluated by real-time PCR; and protein expression of TACE and TNF-α was analysed using immunohistochemistry and western blot, respectively.

Results

Following 6 months of alcohol feeding, LVEF and FS were reduced (p < 0.05 for all), while LVEDD was augmented in the ACM group (p < 0.05), as compared with the control group. Severe changes in cardiac structure were also seen in the ACM group. The mRNA and protein expression of TACE and the protein expression of TNF-α were up-regulated in the ACM group in comparison with the control group (p < 0.05 for all). In both groups, the protein expression of TACE positively correlated with that of TNF-α (p < 0.01) and LVEDD, whereas it negatively correlated with LVEF (p < 0.05).

Conclusions

TACE is over-expressed in the ventricle of ACM rats, and may involve in the process of ventricular remodelling via cleaving TNF-α. Therefore, TACE may represent a new therapeutic target in the prevention and treatment of ventricular remodelling in ACM.

e0156 UROTENSIN II PROMOTES MONOCYTE CHEMOTACTANT PROTEIN-1 EXPRESSION IN AORTIC ADVENTITIAL FIBROBLASTS 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 intervening condition: control subgroup, smoking treatment for 2 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 depressed 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 augmented expression of ICAM-1 in vascular endothelial cells of rats 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 $10^{-6}$ 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, $p<0.01$), 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-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 determined with ELISA. ACE and AT1R mRNA and protein level were determined by reverse transcription-PCR (RT-PCR).

**Key findings** The SBP in SHR-Los was reduced until age 46 weeks, and returned to untreated SHR levels in SHR-Aml from 30 weeks onwards. Compared to untreated SHR, the LVMI and CVP in SHR-Los were markedly decreased until week 46, and the LV ejection fraction (LVEF) (SHR-Los vs SHR: 83.1±2.0% vs 79.5±1.9%, $p<0.05$) and cardiac BNP mRNA expression were improved, whereas comparable LVMI and elevated CVP 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%, $p<0.05$). Cardiac AT1R protein was down-regulated and AT2R protein was up-regulated, no significant difference of these indices was found between SHR-Aml and untreated SHR. Significance Prehypertensive treatment with losartan was more effective than amlodipine on delaying long-term blood pressure rise and meliorating cardiac structure and function, which might be related to permanent attenuation of circulating and local renin-angiotensin (R-A) systems.

**e0158 TRANSIENT PREHYPERTENSIVE TREATMENT IN SPONTANEOUSLY HYPERTENSIVE RATS: A COMPARISON OF LOSARTAN AND AMLODIPINE REGARDING LONG-TERM BLOOD PRESSURE AND CARDIAC PROTECTION**

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**Aims** 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 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 echocardiography. 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).

**Key findings** The SBP in SHR-Los was reduced until age 46 weeks, and returned to untreated SHR levels in SHR-Aml from 30 weeks onwards. Compared to untreated SHR, the LVEF 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 CVP 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 Aldo levels in SHR-Los at week 46 were remarkably decreased (plasma Ang II: 302±32 vs 452±32 pg/ml; plasma Aldo: 172±20 vs 252±41 pg/ml; cardiac Ang II: 126±11 vs 199±14 pg/100 mg; cardiac Aldo: 497±43 vs 766±46 pg/100 mg, all $p<0.05$), and the cardiac AT1R protein was down-regulated and AT2R protein was up-regulated, no significant difference of these indices was found between SHR-Aml and untreated SHR. Significance Prehypertensive treatment with losartan was more effective than amlodipine on delaying long-term blood pressure rise and meliorating cardiac structure and function, which might be related to permanent attenuation of circulating and local renin-angiotensin (R-A) systems.

**e0159 OSTEOPONTIN IS INVOLVED IN UROTENSIN II INDUCED MIGRATION OF ADVENTITIAL FIBROBLASTS FROM RAT AORTA**

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**Background** Recent studies suggest osteopontin (OPN) plays a critical role in the progression of vascular remodelling, and that Urotensin II (UII) is a potent vasoconstrictor and stimulator of cellular migration. The goal of this study was to test the hypothesis that OPN is involved in UII-induced migration of rat aortic adventitial fibroblasts (AFs), and examine the effect and mechanisms of UII on OPN expression.

**Aims** 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 adenoviral vectors 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 determined with ELISA. ACE and AT1R mRNA and protein level were determined by reverse transcription-PCR (RT-PCR).

**Key findings** The SBP in SHR-Los was reduced until age 46 weeks, and returned to untreated SHR levels in SHR-Aml from 30 weeks onwards. Compared to untreated SHR, the LVEF 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 CVP 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 Aldo levels in SHR-Los at week 46 were remarkably decreased (plasma Ang II: 302±32 vs 452±32 pg/ml; plasma Aldo: 172±20 vs 252±41 pg/ml; cardiac Ang II: 126±11 vs 199±14 pg/100 mg; cardiac Aldo: 497±43 vs 766±46 pg/100 mg, all $p<0.05$), and the cardiac AT1R protein was down-regulated and AT2R protein was up-regulated, no significant difference of these indices was found between SHR-Aml and untreated SHR. Significance Prehypertensive treatment with losartan was more effective than amlodipine on delaying long-term blood pressure rise and meliorating cardiac structure and function, which might be related to permanent attenuation of circulating and local renin-angiotensin (R-A) systems.