and polarity switch, which maybe the main mechanism in the initiation and progression of atherosclerosis.

GW26-e0984

Calorie Restriction Attenuates Monocrotaline-induced Pulmonary Arterial Hypertension in Rats

Mingge Ding,[1,2] Jingyi Lei,[1] Yinxian Qu,[1] Enqing Fu[2]
[1]Department of Geriatrics, Xi'an Central Hospital; [2]Department of Respiratory Medicine, Tangdu Hospital, Fourth Military Medical University

OBJECTIVES Calorie restriction (CR) is one of the most effective nonpharmacological interventions protecting against cardiovascular disease such as hypertension in the systemic circulation. The aim of this study is to investigate whether CR could attenuate pulmonary arterial hypertension (PAH).

METHODS The PAH model was developed by subjecting the rats to a single subcutaneous injection of monocrotaline (MCT, 60 mg/kg). The CR rats received 90% of the average caloric intake of ad libitum-fed animals before MCT injection for 2 weeks, followed by 65% of the caloric intake of the control rats after MCT injection for 3 weeks.

RESULTS Five weeks of short-term CR reduced gain in body weight significantly, while it did not alter tibia length compared with controls, indicating that CR did not affect growth. CR lowered mean pulmonary arterial pressure (mPAP: 21.1±2.1 vs. 30.4±2.0 of MCT control, n=6, $P<0.05$) and reduced vascular remodeling (cross-sectional medial wall area/total arterial cross-sectional area: 74.3±4.2 vs. 90.1±3.9 of MCT control, n=6, $P<0.05$) and right ventricular hypertrophy (right ventricle /(left ventricle+septum): 0.33±0.03 vs. 0.44±0.02 of MCT control, n=6, $P<0.01$) in PAH rats at 3 weeks after MCT injection. Meanwhile, CR attenuated endothelial dysfunction as evidenced by increased relaxation in response to ACh. The beneficial effects of CR were associated with restored SIRT1 expression and eNOS phosphorylation and reduced eNOS acetylation in pulmonary arteries of PAH rats. To further clarify the role of SIRT1 in the protective effects of CR, adenoviral vectors for overexpression of SIRT1 (Ad. SIRT1) was administered intratracheally at 1 d before MCT injection. Ad. SIRT1 exhibited similar preventive effects on mPAP (24.1±2.8 vs. 33.4±2.2 of MCT+ Ad. GFP, n=6, $P<0.05$) and endothelial function, and increased eNOS phosphorylation and reduced eNOS acetylation in the absence of CR. Moreover, SIRT1 overexpression attenuated the increase in mPAP in hypoxic pulmonary hypertension (HPH) animals after 2 weeks of hypoxia (20.1±1.8 vs. 28.4±2.1 of HPH+Ad. GFP, n=6, $P<0.05$).

CONCLUSIONS The present data demonstrate that CR may serve as an effective treatment of PAH, and targeting the SIRT1/eNOS pathway may improve treatment of PAH.

GW26-e1238

Increased Expression of Na+-Ca2+ Exchanger in Patients With Chronic Atrial Fibrillation

Tao Li, Wenjun Huang, Liang Mao, Xuehui Fan, Xiaorong Zeng
Department of Electrophysiology, Institute of Cardiovascular Research,Luzhou Medical College

OBJECTIVES This aim of this study was to measure the mRNA and protein expression levels of NCX1. Moreover, we plan to observe the difference of NCX1 level between the patients with chronic atrial fibrillation and the patients with sinus rhythm.

METHODS The protocol of this study was approved by Ethics Review Board of Luzhou Medical College. Written letters of consent were obtained from all members, and all of the procedures were done in accordance with the Declaration of Helsinki and relevant policies in China. Specimens of right atrial appendage were obtained from patients who accepted cardopulmonary bypass. There were no statistical differences in age and gender. NCX1 mRNA level was obtained from 14 patients with sinus rhythm (SR group) and 25 patients with chronic atrial fibrillation (AF group). The protein extractions were detected by western blotting. NCX1 protein level was obtained from 24 patients with sinus rhythm (SR group) and 28 patients with chronic atrial fibrillation (AF group). The expression of mRNA were detected by quantitative real-time PCR. The data was analyzed with $2^{-\Delta\Delta CT}$ method. The statistical analysis was done using independent-samples T test by SPSS 17.0.

RESULTS The mRNA expression levels of NCX1 were increased in AF group compared with SR group. The expression of NCX1 in chronic atrial fibrillation patients was 48.14% higher than that of sinus rhythm patients ($P < 0.05$). The relative expression of NCX1 protein in AF group was 1.39±0.52, while it was 0.76±0.22 in SR group ($P < 0.05$).

CONCLUSIONS The mRNA and protein expression level of NCX1 was significantly up-regulated in patients with chronic atrial fibrillation. It may demonstrate that NCX1 are involved electrical remodeling of chronic atrial fibrillation. These finding provide a new insight into mechanisms of chronic atrial fibrillation. Meanwhile, NCX1 may become a new treatment target of chronic atrial fibrillation.

GW26-e1369

Noval Arg1114Cys, Glu1142Lys mutations in beta myosin heavy chain gene in Chinese pedigrees with familial hypertrophic cardiomyopathy

Xin Shi, Jia Lin, Junhua Yang
First Affiliated Hospital, Soochow University

OBJECTIVES To screen MYH7 gene mutation in Chinese pedigrees with familial hypertrophic cardiomyopathy (FHCM) and to analyse the correlation between genotype and phenotype.

METHODS Specimens of peripheral blood were collected from thirteen probands of Chinese pedigrees with hypertrophic cardiomyopathy (HCM) and 100 normal control subjects. The genome DNA was extracted. The 3 ~ 27 exons in the functional region of the MYH7 gene were amplified with PCR and the products were sequenced. The results were analyzed and mutation sites were determined. Further genetic testing and clinical investigation were done on the other members of the families with the positive results. The correlation between genotype and phenotype was analyzed.

RESULTS Arg1114Cys and Glu1142Lys mutations were identified in exon 26 in two pedigrees, and were found cosegregate with the disease. No similar mutations were identified in controls. The two mutations were found for the first time at home and abroad and the two pedigrees had different clinical phenotype. Six members carried the Arg1114Cys mutation in the pedigree, and three of them were diagnosed as HCM, all female, were the proband(59 years old), the proband's mother(82 years old) and second sister(56 years old),ECG all showed ST-T abnormal, echocardiography all demonstrated the significantly thickness of ventricular septal, the max thickness varied in 16-20mm,one with left ventricular outflow tract light degree obstruction, the other two with no obstruction in left ventricular outflow tract. The proband's third sister (50 years old) and her son, daughter (17, 28 years old) were all not HCM patients but carried the mutation, ECG and echocardiography were normal. In the pedigree carried the Glu1142Lys mutation, 2 members were diagnosed as HCM,1 carried the mutation(the proband), male, 32 years old, ECG shows ST-T abnormal, echocardiography demonstrated the max thickness of ventricular septal was 32mm,left ventricular outflow tract with middle degree obstruction. Another HCM patient was the proband's father, dead suddenly in 2012. The proband's daughter and sister didn't found mutation, ECG and echocardiography were all normal.

CONCLUSIONS Few mutations occurred in the rod domain of MYH7, about 20%. The two mutations found in the research were both in exon 26 in the rod domain. The pedigree carried Arg1114Cys mutation had a low rate of penetrance, a light degree of myocardial hypertrophy, mild symptoms, a slow progress and good survival prognosis. The pedigree carried Glu1142Lys mutation had a severe degree of myocardial hypertrophy, high risk of sudden cardiac death and an unfavorable prognosis.