GW26-e4409

Association of PS gene polymorphism and soluble P-selectin levels in atrial fibrillation thromboembolism population in Xinjiang

Ling Bai, Muhuyati
Cardiac Center, the First Affiliated Hospital of Xinjiang Medical university, Urumqi, China

OBJECTIVES To investigate the association between the polymorphism of P choose element (p.selectin, PS) and soluble P-selectin levels in atrial fibrillation (AF) thromboembolism in Han and Uigur population of Xinjiang.

METHODS Using ELISA method determination of plasma level of sPs. The frequency distributions of SNP sP-selectin gene promoter (-2123C/G) and SNP in exon region (Thr715Pro) were investigated by PCR-restriction fragment length polymorphism and direct DNA sequence analysis among 302 Xinjiang Uigur and 340 age- and sex-matched Han people.

RESULTS Cases sPs exist significant difference serum level and the control group. The frequencies of the -2123C/G allele among the Uigur population had no significant differences from those of the Han population. Thr715Pro did not show any polymorphism in the two populations.

CONCLUSIONS The sP-selectin gene polymorphisms are associated with serum sP-selectin levels or thromboembolic events, suggesting that the patients with nonvalvular AF and thromboembolic events may have genetic susceptibility.

GW26-e4447

The study on microcirculatory disturbance and no-reflow phenomenon mechanism after coronary artery autologous microthromboembolism in rats

Yupeng Bai, Liqun Hu, Jie Wu, Bo Gao, Ye Gu
Department of Cardiology, Wuhan Puai Hospital, Huazhong University of Science and Technology

OBJECTIVES To research microcirculatory disturbance and no-reflow phenomenon mechanism in the model of coronary thrombotic microembolism in rats.

METHODS 5mg dried auto-microthrombotic particulates dissolved in 0.2 ml saline (CME group) or 0.2 ml saline (SHAM group) was injected into temporarily clamped aorta of male Sprague-Dawley rats. After auto-microthrombotic particulates injection, serum c-troponin I, a von Willebrand factor (3 hours, 24 hours, 1 days, 28 days) was determined, no-flow area was evaluated by Thioflavin-S (3 hours), myocardial leukocyte infiltration (24 hours, 7days and 28days), myocardial expressions of TNF-α and IL-6 (24 hours, 7 days and 28 days) were measured by immunohistochemical Analysis and Western Blot Analysis, Arteriole density (AD) was calculated by immunohistochemical analysis. Cardiac function was evaluated by transthoracic echocardiography and hemodynamic measurements.

RESULTS After automicrothrombotic particulate injection, serum c-troponin I and von Willebrand factor levels, the no-flow area as evaluated by Thioflavin S, myocardial leukocyte infiltration levels, myocardial expressions of tumor necrosis factor and interleukin-6, were all significantly increased whereas cardiac function as evaluated by echocardiography and hemodynamic measurements were significantly reduced compared with the SHAM group ($P < 0.05$). Number of arterioles with diameter between 10～50 μm, especially for arterioles with diameter between 20～50 μm was significantly lower in CME group at 3 hours post injection($P < 0.05$).

CONCLUSIONS Aortic automicrothrombotic particulate injection could induce coronary microembolism in rats, and this model could be of value in improving the understanding of pathophysiology of no-reflow phenomenon mechanism: coronary microembolism / coronarymicrothrombosis—endothelial damage and dysfunction / arteriolar spasm - no reflow - infarctlets - inflammatory reaction-myocardial remodeling and cardiac dysfunction.

GW26-e4506

Losartan cannot weaken the change of PGC-1α/NT-PGC-1α altered by Metformin in myocardial cells

Jinghai Hua, Changhua Liu, Zhuheng Liu, Wenyan Lai, Dingli Xu
Department of Cardiology, Nanfang Hospital, Southern Medical University, Guangzhou

OBJECTIVES It has shown that the expression of intracellular PGC-1α/NT-PGC-1α was regulated by a variety of factors. However, it is completely unknown whether Metformin and angiotensinII can alter the expression of PGC-1α/NT-PGC-1α. Here we attempted to explore the change in myocardial cells.

METHODS SD neonatal rat cardiomyocytes after isolation, cells were seeded and corresponded to line drug stimulation, then the target protein expression were detected with Immunofluorescence and Western blotting.

RESULTS Metformin and angiotensinII can enhance the expression of PGC-1α/NT-PGC-1α in myocardial cells. Whereas, Losartan cannot weaken the change altered by metformin, but can abirritate the effect mediated by angiotensin II. Additionally, its expression also could be influenced by other factors, such as seeded in low glucose or serum-free state, low temperature and the prolongation of the culture time.

CONCLUSIONS The mechanism of metformin augmenting the expression of PGC-1α/NT-PGC-1α is not RAAS pathways but others in myocardial cells.

GW26-e0208

Naturally occurring multiple-modified low density lipoprotein (LDL)

Alexander N. Orekhov,[1,2] Natalia V. Elizova,[1,2] Alexandra A. Melnichenko,[1,2] Vasily P. Karagodin,[1,2] Veronika A. Myasoedova,[1,2] Andrey V. Zhelankin,[3] Sergey S. Trubinov,[2] Varvara A. Orekhova,[1,2] Vasily V. Sinyov,[3] Valeria A. Barinova,[3] Anastasia V. Ryzhkova,[3] Yuri V. Bobryshev,[1,2] Igor A. Sobenin[3]
[1]Institute of General Pathology and Pathophysiology, Moscow, Russia; [2]Institute for Atherosclerosis Research, Moscow, Russia; [3]Russian Cardiology Research and Production Center, Moscow, Russia

OBJECTIVES Electronegative LDL, small dense LDL, and desialylated LDL circulating in the blood of patients were obtained by different methods. Naturally, the question arises what are the similarities and differences between these forms of LDL modification. We believe that multiple modified LDL particle (small, dense, electronegative, desialylated, etc.) occurs in blood.

METHODS Ex vivo experiments have revealed mechanisms of multiple modification of LDL in the blood. Fraction of native LDL was isolated from blood plasma of healthy subjects. Blood serum of patients with assessed atherosclerosis was also obtained. LDL and serum were mixed and incubated for various periods at 37°C.

RESULTS After 1 hour incubation of native LDL with atherosclerotic serum desialylated LDL appears. After 3 hours, LDL becomes able to cause accumulation of cholesterol in cultured cells. After 6 hours, LDL demonstrates reduction of neutral lipids and phospholipids as well as reduction in its size. After 36 hours, an increase in the electronegativity of the lipoprotein particle is detected. After 48-72 hours, loss of α-tocopherol, increase of susceptibility to oxidation, and accumulation of lipid peroxidation products in LDL are observed. Thus, multiple modification of LDL is a cascade of sequential changes in lipoprotein particle, namely: desialylation, loss of lipids, size reduction, increase of electronegative charge, lipid peroxidation in LDL. Desialylation of LDL particle is one of the first or primary events of atherogenic modification. We have established that the reason of LDL desialylation is trans-sialidase. We found trans-sialidase activity in the blood of patients with atherosclerosis and other cardiovascular diseases. We have shown that human neuraminidases 2 and 4 possess trans-sialidase activity. On the other hand, selective inhibitors of viral sialidases suppress trans-sialidase activity in the blood of atherosclerotic patients.

CONCLUSIONS Thus, trans-sialidase causing atherogenic desialylation of LDL may be of both endogenous and exogenous origin. Supported by Russian Ministry of Education and Science (Project RFMEFI61614X0010).