E0038  EFFECTS OF ANGIOTENSIN II ON ATPASES IN AORTIC VASCULAR SMOOTH MUSCLE CELLS FROM WISTAR-KYOTO RATS AND SPONTANEOUSLY HYPERVENTILATIVE RATS

doi:10.1136/hrt.2010.208967.38

Qian-Hui Shang, Gu-Hai Zhang, Qian-Feng Jiang, Wei-Hong Wan. Institute of Clinical Medicine, Zunyi Medical College, Department of Cardiology, Affiliated hospital of Zunyi Medical College; Key Laboratory of cell engineering of Guizhou Province, Zunyi, Guizhou, China

Aim To explore the effects of Angiotensin II on the activities of Ca<sup>2+</sup>-ATPase, Na<sup>+</sup>,K<sup>-</sup>-ATPase and mRNA expression levels of Na<sup>+</sup>,K<sup>-</sup>-ATPase and Ca<sup>2+</sup>-ATPase in cultured thoracic aortic vascular smooth muscle cells (ASMCs) from Wistar-Kyoto (WKY) rats and spontaneously hypertensive rats (SHR).

Methods ASMCs isolated from 14-week-old male WKY rats and SHR were cultured and treated with different concentrations (1×10<sup>-9</sup>, 1×10<sup>-8</sup>, 1×10<sup>-7</sup> mol/l) of Angiotensin II. The activities of Ca<sup>2+</sup>-ATPase, Na<sup>+</sup>,K<sup>-</sup>-ATPase were measured by biochemistry and enzymology. RT-PCR assay was employed to determine the relative levels of PMCA1 and Na<sup>+</sup>,K<sup>-</sup>-ATPase a<sub>1</sub>-subunit mRNA in ASMCs.

Results Low and moderate concentration of Angiotensin II significantly decreased the activity of Ca<sup>2+</sup>-ATPase and PMCA1 mRNA level in ASMCs from SHR. Three different concentrations of Angiotensin II significantly increased the activity of Na<sup>+</sup>,K<sup>-</sup>-ATPase and and down-regulated PMCA1 mRNA level. Three different concentrations of Angiotensin II significantly decreased the activity of Ca<sup>2+</sup>-ATPase and PMCA1 mRNA level in ASMCs from SHR. Three different concentrations of Angiotensin II stimulated the activity of Na<sup>+</sup>,K<sup>-</sup>-ATPase and increased its a<sub>1</sub>-subunit mRNA expression in ASMCs from WKY rats. Low and moderate concentration of Angiotensin II did not affect the activity of Na<sup>+</sup>,K<sup>-</sup>-ATPase in SHR, while high concentration of Angiotensin II significantly suppressed the activity and a<sub>1</sub>-subunit mRNA level of Na<sup>+</sup>,K<sup>-</sup>-ATPase.

Conclusions In WKY rats, Angiotensin II may have biphasic effects on Ca<sup>2+</sup>-ATPase activity and PMCA1 mRNA expression, and may promote the activity and a<sub>1</sub> subunit mRNA expression of Na<sup>+</sup>,K<sup>-</sup>-ATPase in a dose-dependent manner in ASMCs. In SHR, Angiotensin II can inhibit Ca<sup>2+</sup>-ATPase activity and PMCA1 mRNA expression, and only high dose of Angiotensin II can suppress the activity and a<sub>1</sub> subunit mRNA expression of Na<sup>+</sup>,K<sup>-</sup>-ATPase in ASMCs.

E0039  EFFECTS OF Lisinopril ON THE ACTIVITIES AND MRNA EXPRESSION OF ION PUMPS IN AORTIC SMOOTH MUSCLE CELLS FROM SPONTANEOUSLY HYPERVENTILATIVE RATS

doi:10.1136/hrt.2010.208967.39

Qian-Hui Shang, Yu-Huang Guo, Qian Wu, Qian-Feng Jiang, Gu-Hai Zhang. Institute of Clinical Medicine, Zunyi Medical College, Department of Cardiology, Affiliated Hospital of Zunyi Medical College, Zunyi, Guizhou, China; Department of Pharmacology, Zunyi Medical College, Zunyi, Guizhou, China

Objectives To explore the effects of Lisinopril upon the activities of Na<sup>+</sup>, K<sup>-</sup>-ATPase and Ca<sup>2+</sup>-ATPase and mRNA expression levels of Na<sup>+</sup>, K<sup>-</sup>-ATPase a<sub>1</sub>-subunit and plasma membrane Ca<sup>2+</sup>-ATPase isoform 1 (PMCA1) in cultured thoracic aorta vascular smooth muscle cells (ASMCS) isolated from spontaneously hypertensive rats (SHR).

Methods ASMCS were divided into four groups: Wistar-Kyoto (WKY) control, SHR control, Lisinopril (1×10<sup>-7</sup>) intervened SHR group and Lisinopril (1×10<sup>-7</sup>) intervened SHR group. The activities of ion pumps were detected by spectrophotography and mRNA expressions were measured by real-time PCR. The content of Angiotensin II (Ang II) in cells-cultured medium were determined by radioimmunoassay.

Results The activities of Na<sup>+</sup>, K<sup>-</sup>-ATPase, Ca<sup>2+</sup>-ATPase and the mRNA expression levels of Na<sup>+</sup>, K<sup>-</sup>-ATPase a<sub>1</sub>-subunit and PMCA1 in ASMCS from SHR were significantly lower than those from WKY control (p<0.01). Lisinopril significantly increased the activities of Na<sup>+</sup>, K<sup>-</sup>-ATPase and Ca<sup>2+</sup>-ATPase and mRNA expression levels of Na<sup>+</sup>, K<sup>-</sup>-ATPase a<sub>1</sub>-subunit and PMCA1 in ASMCS from SHR (p<0.01). Ang II content of culture medium in ASMCS from SHR was significantly more than those from WKY control (p<0.05). Lisinopril attenuated Ang II content of ASMCS culture medium from SHR (p<0.05).

Conclusions The decreased activities of Na<sup>+</sup>, K<sup>-</sup>-ATPase and Ca<sup>2+</sup>-ATPase may be related to their lower expression of the mRNA in ASMCS from SHR. The Lisinopril may increase the activities of two ion pumps and upregulate the mRNA expression of Na<sup>+</sup>, K<sup>-</sup>-ATPase a<sub>1</sub>-subunit and PMCA1 in ASMCS from SHR through blocking the generation of Ang II.

E0040  THE EXPRESSION OF SIGNAL TRANSDUCTION PATHWAY OF TGF-β1/SMAD IN THE RAT CARDIAC TISSUE WITH TYPE 2 DIABETES AND INTERVENTION BY ATORVASTATIN

doi:10.1136/hrt.2010.208967.40

Yang Xiaohong, Cai Wei, Zhao Bangrong, Lu Jingchao, Liu Fan, Du Jun. Department of Cardiology, The Second Hospital of Hebei Medical University and Institute of Cardio-cerebrovascular Disease of Hebei Province, Shijiazhuang, China

Objective Observation on changes of signal transduction pathway of TGF-β1/Smad in the course of myocardial fibrosis in the rat with type 2 diabetes and preventive effect of atorvastatin.

Methods The experimental type 2 diabetic rats were yielded by injecting streptozotocin (STZ, 30 mg/kg) and fed with high fat and glucose food, then intervention by atorvastatin (20 mg kg<sup>-1</sup> d<sup>-1</sup>) for 12 weeks. Collagen content was observed by Masson staining. RT-PCR was used to observe the gene expression of TGF-β1 in experiment rat hearts. The protein expression and tissue localisation of TGF-β1, Smad2/3, Smad7 and were observed with the immunohistochemistry.

Results The interstitial collagen accumulation and thickened capillary basement membrane in the atorvastatin (Masson stain: 0.80±0.16) administration group was obviously relieved compared with that of the DM (1.36±0.16) group (p<0.01). The expression levels of TGF-β1 mRNA in the DM group was obviously increased compared with that of the control group (1.39±0.10 vs 1.60±0.02, p<0.01). In atorvastatin group the positive cells of Smad7 was obviously relieved compared with that of the DM group (0.57±0.04 vs 1.39±0.10, p<0.01). Immunohistochemistry: the positive expressions of Smad2/3, Smad7 and were observed with the immunohistochemistry.

Conclusion The interstitial collagen accumulation and thickened capillary basement membrane in the atorvastatin (Masson stain: 0.80±0.16) administration group was obviously relieved compared with that of the DM (1.36±0.16) group (p<0.01). The expression levels of TGF-β1 mRNA in the DM group was obviously increased compared with that of the control group (1.39±0.10 vs 1.60±0.02, p<0.01). In atorvastatin group the positive cells of Smad7 was obviously relieved compared with that of the DM group (0.57±0.04 vs 1.39±0.10, p<0.01). Immunohistochemistry: the positive expressions of Smad2/3, Smad7 and were observed with the immunohistochemistry.