

deficiency have been implicated in development of left ventricular failure, little is known about the role of L-carnitine in the right ventricular failure in pulmonary arterial hypertension.

METHODS Experimental pulmonary hypertension develops in male Sprague-Dawley rats subjected to a single subcutaneous injection of monocrotaline (60 mg kg⁻¹, MCT group). Compared with the vehicle group, by day 21, MCT group developed higher right ventricular systolic pressure (34±5 mmHg versus 19±4 mmHg; P<0.001) and right ventricular hypertrophy (0.51±0.13 versus 0.28±0.05; P<0.001). In MCT group, L-carnitine levels were significantly decreased in both the right ventricular myocardium (159±47 nmol/g vs 435±76 nmol/g, P<0.05) and plasma (7±3 μmol/l vs 16±10 μmol/l, P<0.05), indicating L-carnitine deficiency was associated with the right ventricular failure. To evaluate whether supplementation with L-carnitine could attenuate right ventricular failure, we treat the rats received monocrotaline with either L-carnitine (500mg kg⁻¹ day⁻¹, L-carnitine MCT group) or saline (saline MCT group) for 14 days.

RESULTS In comparison with saline MCT group, the mean pulmonary arterial pressure and the right ventricular systolic pressure decreased by 34% (P=0.04) and 25% (P=0.01) in the L-carnitine MCT group, respectively. The right ventricular hypertrophy index and right ventricular free wall thickness decreased by 25% (P=0.02) and 14% (P=0.03) in the L-carnitine MCT group, respectively. Furthermore, the myocardial PET/CT demonstrated that SUV_{RV} / LV of L-carnitine MCT group reduced by 15% when compared with saline MCT group (P<0.05).

CONCLUSIONS The L-carnitine deficiency may aggravate development of pulmonary hypertension. Supplementation with L-carnitine could improve pulmonary arterial hypertension by reversing energy metabolism dysfunction of right ventricular failure.

GW26-e1573

Apelin: An Endogenous Peptide Essential for Cardiomyogenic Differentiation of Mesenchymal Stem Cells via Activating Extracellular Signal-Regulated Kinase 1/2 and 5

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OBJECTIVES Growing evidence has shown that apelin/APJ system functions as a critical mediator of cardiac development as well as cardiovascular function. Here we investigated the role of apelin in the cardiomyogenic differentiation of mesenchymal stem cells derived from Wharton's jelly-derived mesenchymal stem cells (WJ-MSCs) and undescribed functional link between MAPK/ERK signaling cascade and apelin/APJ axis in vitro.

METHODS We used RNA interference methodology and gene transfection technique to regulate the expression of apelin in WJ-MSCs, which were divided into four groups: (A) WJ-MSCs; (B) apelin-silenced WJ-MSCs; (C) apelin-regained WJ-MSCs and the control group. All groups were treated with an effective cardiac differentiation protocol including 5-azacytidine and bFGF, except the control group. Cells were analyzed by real-time RT-PCR, Western blot, Immunofluorescence and Calcium flux assay. MEK1/2 inhibitor PD0325901 and MEK5 inhibitor BIX02189 were used to regulate ERK1/2 and ERK5 in apelin-silenced WJ-MSCs with/without supplementary apelin-13 during Cardiomyogenic Differentiation.

RESULTS Four weeks after induction, cells in group A and C assumed a stick-like morphology and myotube-like structures except apelin-silenced cells and the control group. The silencing of apelin decreased the expressions of several critical cardiac progenitor transcription factors (Mesp1, Mef2c, NKX2.5) and cardiac phenotypes (cardiac α-actin, β-MHC, cTnT and connexin-43). Meanwhile, endogenous compensation of apelin contributed to differentiating into cells with characteristics of cardiomyocytes in vitro. Remarkably, our experiment indicated that apelin up-regulated cardiac specific genes in Wharton's jelly-derived mesenchymal stem cells via activating ERK1/2 and ERK5.

CONCLUSIONS Our study indicated that apelin was essential for cardiomyogenic differentiation of WJ-MSCs via activating MEK1/2-ERK1/2 and MEK5-ERK5, which were involved in MAPK signaling pathway. Down-regulation of apelin in WJ-MSCs decreases the expression of several critical cardiac progenitor transcription factors and cardiac phenotypes.

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Liqihuoque Pills Ameliorates Atrial Fibrillation via Prevention Atrial Fibrosis in Rats

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OBJECTIVES Liqihuoque pills (LQHX) is a compound Miao medicine in China used for treatment of cardiovascular diseases, and can decrease acute myocardial infarct and refusion injury in cat and rat. This study was to investigate whether LQHX ameliorates atrial fibrillation by prevention atrial fibrosis in the isoproterenol-induced myocardial infarct in rats. his study was to investigate whether LQHX ameliorates atrial fibrillation by prevention atrial fibrosis in the isoproterenol-induced myocardial infarct in rats.

METHODS Myocardial infarct (MI) rat model was induced by subcutaneous injection of 120 mg/kg/d isoproterenol for 2 days. We studied a normal control group and 4 groups of rats undergoing isoproterenol-induced MI 1 week prior to treatment: isoproterenol (ISO) group, and ISO combined with LQHX (ISO+LQHX) group. The three ISO+LQHX groups were administered LQHX (187.5 mg/Kg, 75 mg/Kg, 37.5mg/Kg respectively) by gavage for 4 weeks after 7d for ISO treatment. After treatment for 4 weeks, cardiac function were measured by echocardiography and the histopathological changes of cardiac tissue was observed via Masson's staining. AF inducibility and duration were detected by transesophageal programmed electrical stimulation AF inducing technology. The atrial conduction velocity was detected by multi-electrodes arrays measurements. The expression of type I and III collagen and the changes of transforming growth factor β1 (TGF-β1) in left atrial were detected by western blot.

RESULTS LQHX (at the dose of 37.5 mg/Kg) significantly improved left systolic functions, resulting in improved LV ejection fraction (64.6±4.42% vs 57.9±5.66%; P<0.05), LV internal dimension in systole (4.74±0.51 mm vs 5.73±0.48 mm; P<0.01). LQHX-treated rats had lower rates of AF inducibility (70%, 56%, 50% in LQHX groups vs. 90% in ISO group), and shorter AF duration. Masson's trichrome staining in ISO treated group reveals increased left atrial fibrosis (63.4±5.8%), while treatment with LQHX resulted in reversal of atrial fibrosis, and in the lower dose of LQHX group (37.5 mg/Kg) could decreased the left atrial fibrosis areas to (15.3±2.4)%. LQHX (at the dose of 75 mg/Kg and 37.5 mg/Kg) also obviously reduced the expression of type I and III collagen in left atrium and markedly inhibited TGF-β1 protein expression.

CONCLUSIONS LQHX pills reduced the AF inducibility rate and duration after ISO induced myocardial infarct by inhibiting left atrial fibrosis, and associate with inhibition type I and III collagen and TGF-β1 protein expression in left atrium of rat heart. It obviously suggests that LQHX could be an effective Chinese drug for the prevention atrial fibrillation induced by post-MI myocardial remodeling.

GW26-e2289

The impacts of renal sympathetic activation on atrial fibrillation: the potential role of the autonomic cross talk between kidney and heart

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OBJECTIVES The aim of our study was to investigate the roles of renal sympathetic nerve stimulation (RSS) on atrial fibrillation (AF) and cardiac autonomic nervous activity.

METHODS RSS was performed using electrical stimulation on the left renal artery at the 30 volts for 3 hours. Twenty-eight dogs were randomly assigned to the proximal renal sympathetic stimulation (RSS) group (P-RSS, N=7), middle RSS group (M-RSS, N=7), distal RSS group (D-RSS, N=7), and the control group (sham RSS, N=7). Effective refractory period (ERP) and the window of vulnerability (WV) were measured. SLGP and LSG function were determined. Neural activities were recorded from the SLGP and LSG. C-fos and nerve growth factor (NGF) protein expressing in the SLGP and LSG were examined. Serum inflammatory cytokines were assayed.

RESULTS

- (1) Only P-RSS caused pronounced blood pressure rises, induced a significant decrease in ERP, and generated a marked increase in WV and ERP Dispersion (all P < 0.05).
- (2) P-RSS significantly facilitated SLGP and LSG function.
- (3) The frequency and amplitude of the neural activity in the SLGP and LSG were markedly increased by P-RSS.