GW25-e0842
Alteration in right heart function upon high-altitude exposure and its roles in Acute mountain sickness
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Objectives: The occurrence and symptom severity of AMS (Acute Mountain Sickness) function parameters variation is consistent with the high-altitude hypoxic environment. (1) Comparisons of the parameter at sea level and high altitude

Conclusions: The echocardiography examinations were performed by ultrasonography using the S5-1 cardiac probe (C590, Philips, USA) by a senior technician. Most of the valuable parameters have been measured including right atrial diameter (RA), right ventricular end-diastolic diameter (RV), pulmonary artery (PA), pulmonary acceleration time (AT), tricuspid blood flow velocity peak E, tricuspid blood flow velocity peak A, the right ventricular outflow tract blood flow to the end time (b), tricuspid blood flow velocity at the peak a peak termination to the next new Tung Chau tricuspid blood the velocity E peak time interval (a) ECG R-wave peak to the right ventricular outflow tract ejection fraction terminate at the time interval (c). Each parameter has been measured four consecutive cardiac cycles. Myocardial performance index (MPI) Tei index, mean pulmonary artery pressure (mPAP), pulmonary vascular resistance (PVR), pulmonary capillary wedge pressure (PCWP), blood flow velocity in the tricuspid peak E / A peak were calculated according the parameters abovementioned.

Results:
(1) Comparisons of the parameter at sea level and high altitude
(2) Among 264 subjects who rapidly ascended to 3700m high altitude, the incidence of AMS was 25.8% (68 out of 196). Compared with plain, basic follow-up observations of 264 subjects’ radical plateau 24h right heart function parameters variation is consistent with the findings in the first chapter. Enter the altitude of 3700m plateau 24h within the E / A ratio (P<0.05) reduced significantly, while Tei index, PVR, mPAP was increased significantly (all P values were less than 0.05). Tei index was higher (P=0.05) in AMS group than that in Non-AMS group, E/a ratio was lower (P<0.05) in AMS group than that in Non-AMS group. However, there were no significant differences in PVR, mPAP between AMS and Non-AMS groups.

Conclusions: The hypobaric hypoxic environment of high altitude would lead to a series of changes in right ventricular functions mainly reflected in increase of systolic function, reduction of diastolic function, as well as increase of right ventricular afterload.

GW25-e0005
Cortistatin inhibited aortic calcification in rats by regulating calcification related genes expression
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Objectives: Artery calcification is an active biomineralization process mediated by calcification-related genes. Therefore, this study aims to investigate the role of cortistatin in rat aortic calcification, and further exploring its molecular mechanism.

Methods: Calcification model was produced by the administration of vitamin D3 plus nicotine in rats to induce aortic calcification. In vitro, Plasma calcium, calcium content of rat aortic tissue and VSMC culture were measured by o-cresolphthalein complex colorimetric method and von Kossa staining, respectively. Plasma phosphorus was tested by malachite green colorimetric method. Calci- nation related gene expression was detected by RT-PCR in aortic tissues and VSMCs. Results: The results from in vivo study showed that VDN increased 1.7 times higher of calcium content, Elastic fiber disorder and interrupt and von Kossa staining positive brown \ black particles in rat aortic tissues in the VDN group as compared to the control group. After CST administration, aortic calcium content, and elastic fiber disorder and brown \ black particles were decreased in the VDN + CST group compared to the control group. Plasma calcium, phosphorus and calcium-phosphorus product has no significant difference between the rats of each group. As compared with the control group, expression of BMP-2 mRNA and Pit-1 mRNA was increased, MGP mRNA expression decreased in rat aortas of the VDN group; After CST treatment, BMP-2 mRNA and Pit-1 mRNA expression were down-regulated, MGP mRNA expression increased in aortic tissues of VDN + CST group compared with VDN group alone. There was not significant difference in OPG mRNA expression of Aortic tissue between each group. In vitro results confirmed that as compared with the control group, calcium content was increased 2.4 times, calcium phosphate brown \ black particles were increased 2.1 times, calcium content was increased 2.8 times, calcification-related gene expression was down-regulated in rat VSMCs incubated with β-GP. After co-incubation VSMCs with β-GP in the presence of different concentrations of CST (10−10 and 10−7mol/L), calcium content were reduced, calcified nodules and brown \ black particles also reduced in the Ca+CST treatment groups of BMP-2 mRNA and Pit-1 mRNA expression fell, MGP mRNA expression increased in the CST treated group than the control groups alone. There were no significant differences between OPG mRNA expressionof rat VSMCs in each group.

Conclusions: CST could reduce calcium deposition of aortic tissues and VSMCs cultures by regulating BMP-2 mRNA and Pit-1 mRNA expression, thereby improving the proliferation of OC and providing experimental evidence of the prevention and cure of CST for artery calcification.

GW25-e1671
The Relaxation effect of Danhong Injection in Vascular smooth muscle cells and its mechanism
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Objectives: Danhong injection (DHI) is composed of two herbs Savia miltiorrhiza and Carthami tinctorius L., it is used for the treatment of cardiovascular related diseases, such as stroke, coronary heart disease and angina pectoris in clinical therapy in China. We have confirmed that DHI could stimulate the production of vaso- dilatory factors in the endothelial cells via prostaglandin/cyclooxygenase-2 but not nitric oxide/endothelial nitric oxide synthase pathway. However, the molecular mechanisms of the effect of DHI in relaxing the vascular smooth muscle cells are unclear. In this study, we further examine whether DHI can exert a relaxation effect in vascular smooth muscle cells and its underlying molecular mechanism.

Methods: The effect of DHI was investigated on rat aortic smooth muscle cells (A7r5).Calcium assay kit was used to detect changes in intracellular calcium while the changes of calmodulin (CaM) mRNA expression was subsequently detected by RT-PCR. Western blotting assay was carried out to quantify the protein expression of protein kinase B (Akt) and phosphorylated-Akt, myosin light chain (MLC) and phosphorylated-MLC. In addition, co-culture system of endothelial cells (EA.hy926) and A7r5 cell was constructed by a transwell, which was simulated with a vascular structure. After treatment of Hy926 cells with DHI for co-culture system, cell-based ELISA was used to observe the cAMP generation in A7r5. Protein expression of Akt, P-Akt, MLC and P-MLC in A7r5 cell co-culture system was detected by Western Blotting. Therefore, Western blotting assay was finally used to detect the effect of DHI in proliferation of A7r5 cell, which is induced by platelet derived growth factor-BB (PDGF-BB).

Results: DHI (1:100) contributed to the decrease of CaM mRNA expression in A7r5 cells but there was no significant change observed in intracellular calcium concentration while the changes of calmodulin (CaM) mRNA expression was subsequently detected by RT-PCR. Western blotting assay was carried out to quantify the protein expression of protein kinase B (Akt) and phosphorylated-Akt, myosin light chain (MLC) and phosphorylated-MLC. In addition, co-culture system of endothelial cells (EA.hy926) and A7r5 cell was constructed by a transwell, which was simulated with a vascular structure. After treatment of Hy926 cells with DHI for co-culture system, cell-based ELISA was used to observe the cAMP generation in A7r5. Protein expression of Akt, P-Akt, MLC and P-MLC in A7r5 cell co-culture system was detected by Western Blotting. Therefore, Western blotting assay was finally used to detect the effect of DHI in proliferation of A7r5 cell, which is induced by platelet derived growth factor-BB (PDGF-BB). In western blot analysis, DHI significantly decreased P-MLC protein expression at a concentration of 1:100, with no significant effect in expression of Akt, P-Akt and MLC proteins in the same cell line. The Transwell co-culture system was well established. DHI (1:100) could increase the secretion of cAMP in A7r5 after treating Hy926 in co-culture system with DHI (1:100). In co-culture system, DHI could still decrease the protein expression of P-MLC in A7r5, while the changes in protein expression of Akt, P-Akt, MLC were also none significant. DHI was also found to suppress the proliferation of A7r5 which was induced by the PDGF-BB (20ng/ml).

Conclusions: Our findings demonstrated that DHI can relax vascular smooth muscle cells. The mechanism included the effect of DHI increasing secretion of cAMP in vascular smooth muscle cells, meanwhile reducing the mRNA expression of CaM and protein expression of P-MLC. In addition DHI can inhibit PDGF-BB-induced A7r5 cell proliferation. Therefore, these effects support the fact that it can be used in treating cardiovascular related diseases.

GW25-e2129
Tumorigenesis of nuclear transfer embryonic stem cells can be induced through differentiation and enrichment after transplantation in the infarcted rat heart
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Objectives: To evaluate the tumorigenic potential of nuclear transfer (nt) mouse embryonic stem cells (mESCs) transplanted into infarcted rat hearts.
Methods: nt-mESCs were cultured using a bioreactor system to develop embryoid bodies. Embryoid bodies were induced with 1% ascorbic acid to differentiate into cardiomyocytes. nt-mESC-derived cardiomyocytes (nt-mESC-CMs) were enriched by Percoll density gradient separation to generate nt-mESCs-PE-CMs. Ischemia was induced by ligating the left anterior descending coronary artery in female Sprague-Dawley rats. Immunosuppressed rats were randomly assigned to receive an intragastric medication of saline or 500 mg/kg of Salvia miltiorrhiza (SAB) intragastrically for 14 days. Low-dose SAL and exhausted exercise groups and high-dose SAL and exhausted exercise groups were administrated saline (100mg/Kg) or high-dose SAL (300mg/Kg) intragastrically for 14 days. Then exhausted exercise model was established. Exhaustive exercise model is a single bout of exhausted swimming model, according to Thomas standards. (2) By ELISA kit to detect lactate dehydrogenase (LDH), creatine kinase isoenzyme (CK-MB), troponin (TNT-1), cardiac troponin I (CTNI) in serum, to verify the existence of myocardial damage. (3) Using fluorescence quantitative polymerase chain reaction (PCR) to detect the gene expression of PGC-1α, NRF-1 and NRF-2 in each group. (4) Western blot was used to detect the protein expression of PGC-1α, NRF-1 and NRF-2.

Results: Analysis performed 8 weeks after transplantation revealed teratoma formation in 80%, 87%, and 33% of rats administered nt-mESCs, nt-mESCs, and nt-mESC-CMs, respectively. (P<0.05 nt-mESC-CMs vs. nt-mESCs). Mean tumor volumes were 82.72±6.52, 83.17±3.58, and 50.50±5.98* mm³, respectively. (P<0.05 nt-mESC-CMs vs. nt-mESCs). In contrast, no teratoma was detected in rats that received nt-mESC-PE-CMs. Octamer-binding transcription factor 4, a specific marker of undifferentiated ES cells, was detected by polymerase chain reaction in rats that received nt-mESCs and nt-mESC-CMs, but not in rats that received nt-mESC-PE-CMs.

Conclusions: nt-mESCs have the same pluripotency as mESCs and teratoma formation with nt-mESC transplantation could be induced by cell differentiation and enrichment.

GW25-e2195
Effect of Regulatory Factors of the Myocardial Mitochondrial Biogenesis of Rats after Acute Exhaustive Exercise at Different Time
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Objectives: Peroxisome proliferator-activated receptor γ, coactivator 1 (PGC-1α), Nuclear respiratory factors NRF-1 and NRF-2 are the key factors of the regulatory of mitochondrial biogenesis. Our study points to the establishment of single bout of exhausted swimming model, our work is to research the protein and gene expression of mitochondrial biogenesis related factors, PGC-1α, NRF-1 and NRF-2 at different time after exhaustive exercise. In order to investigate the effects of exhaustive exercise on mitochondrial biogenesis of rats after acute exhaustive at different time.

Methods: 1 A total of 40 health male Sprague-Dawley rats (average weight (150 ± 20g)) were randomly divided into 5 groups (n=8 in each group), including sedentary control group, low-dose SAL groups (0, 6, 12 and 24h after exhaustive exercise). Exhaustive exercise model is a single bout of exhausted swimming model, according to Thomas standards. 2 By ELISA kit to detect lactate dehydrogenase (LDH), creatine kinase isoenzyme (CK-MB), troponin (TNT-1) in serum, to verify the extent of myocardial damage by Exhaustive exercise. 3 Using fluorescence quantitative polymerase chain reaction (PCR) to detect the gene expression of PGC-1α, NRF-1 and NRF2 each group rats myocardial.4 Western blot was used to detect the protein expression of PGC-1α, NRF-1 and NRF-2.

Results: (1) Compared with control group, level of LDH (U/L), CK-MB (ng/ml), CTN-I (g/ml) in the blood serum of the 0h, 6h, 12h and 24h after exhausted exercise are Significantly higher (P<0.05). And level of the protein expression of NRF-2 in rats myocardial of 0h and 24h after exhausted exercise, low-dose SAL and 0h after exhausted exercise, high-dose SAL and 0h after exhausted exercise are Significantly lower (P<0.05).

Conclusions: (1) Acute exhaustive exercise cause myocardial damage. High doses of Salsola can prevent myocardial damage. (2) High doses Salisola can promote the protein and gene expression of mitochondrial biogenesis regulatory factors, PGC-1α, NRF-1 and NRF-2 of rats after exhaustive exercise.

GW25-e3110
Salvianolic acid B Suppresses Activated Platelets Induced Inflammatory Cytokines mRNA Expression in Endothelial Cells
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Objectives: Salvianolic acid B (SAB) is a hydrophilic component isolated from the Chinese herb Salvia miltiorrhiza (Danshen), which has been clinically used for the treatment of ischemic cardiovascular and cerebrovascular diseases. In this paper, we focus on the modulating effects of SAB on inflammatory reaction in endothelial cells triggered by activated platelets.

Methods: Human umbilical vein endothelial cells (EA.hy926) were pretreated with SAB (final concentration1, 5, 10μg/ml respectively) for 24h followed by co-cultured with ADP-activated platelets for another 24h. The adhesion of platelets to EA.hy926 were observed by Wright’s-Giemsa staining. The NF-kB activation in EA.hy926 cells was detected by immunocytochemistry and a quantitative analysis of phospho-NF-kBp65. The inflammatory cytokines mRNA (ICAM-1, IL-1β, IL-6, IL-8, MCP-1) mRNA expression in cells was monitored. The level of soluble P-selectin released from ADP or z-thrombin stimulated platelets aggregation were monitored. The level of soluble P-selectin released from ADP or z-thrombin stimulated platelets were also detected.

Results: Pretreatment with 10μg/ml SAB could visibly reduce platelets adhesion on cell and a significant decline in NF-kB p65 nuclear-positive cell percentage and, quantitative analysis showed a dose-dependent inhibitory effect of SAB on NF-kB activity. Pretreatment with SAB also decrease the level of inflammatory cytokines mRNA expression in endothelial cells in varying degrees. Specifically, pretreatment with 10μg/ml SAB significantly down-regulated activated platelets-induced ICAM-1 mRNA expression from 12.07 to 5.27 folds, and IL-6 mRNA expression from 5.21 to 3.37 folds. The IL-6 mRNA expression was significantly down-regulated from 10.82 to 8.11 folds at 5μg/ml and to 1.86 at 10μg/ml SAB pretreatment; IL-8 mRNA expression from 7.12 to 4.91 folds at 5μg/ml and to 3.33 at 10μg/ml; MCP-1 mRNA expression from 4.14 to 3.27 folds at 5μg/ml and to 1.49 at 10μg/ml. Additionally, SAB could dose-dependently inhibit ADP or z-thrombin induced platelet aggregation in vitro, the IC50 value was 312.64μg/ml in ADP induced aggregation and 379.74μg/ml in z-thrombin. Significant decline of soluble P-selectin release from both agonists stimulated washed platelets were also observed after pretreatment with SAB at approximate IC50 value and 2-folds of IC50 values.

Conclusions: In addition to the inhibiting effects on platelets activation, SAB was able to attenuate platelets-mediated inflammatory responses in endothelial cells even if the platelets aggregation was induced by real-time SAB activity was related to inhibition of NF-kB-regulated inflammatory factors expression. Our work may help explain the efficacy of Salvia miltiorrhiza in the treatment of ischemic cardiovascular and cerebrovascular diseases.