with the sham-operated group, glycoprotein, creatinine, dimethyl glycine, beta-hydroxybutyrate were increased significantly in model group; acetoacetic acid, acetic acid, valine, proline, urea, dimethylamine were reduced. 8 weeks after adminstration, compared with the model group, acetoacetic acid, proline, urea, acetic acid, ethanol, 1-Methylhistidine were significantly increased, dimethyl glycine was significantly reduced.

CONCLUSIONS ^{1}H-NMR metabolomics results suggested Qishen Granule treatment of cardiac functional insufficiency and qi-deficiency and blood stasis syndrome (QDBS) mini pigs main differenced metabolites were concentrated on the major metabolite of amino acid metabolism, glucose metabolism and energy metabolism. That is some certain contribution in pharmacological mechanism for clinical treatment to find new drugs target.

GW26-e2943

Effect of high extracellular calcium on left ventricular monophasic action potentials in Kunming mice

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OBJECTIVES That the calcium ions across the membrane is an important part of the formation of action potential in myocardial cells, and the purpose of this experiment is to observe the effect of high calcium on the left ventricular monophasic action potential(MAP) in open chest model of Kunming mice.

METHODS 10 Kunming mice (9 weeks old, 5 males and 5 females) were suffered thoracic-opening operation, and the epicardial MAP was recorded by using a contact-type MAP electrode placed vertically on the left ventricular epicardium surface. The Tyrode's solution with high concentration of calcium ions was adding to resulting high extracellular calcium, and then extracellular calcium was removed by adding Tyrode's solution free of calcium. Under the three conditions the amplitude of MAP(Am), the maximum upstroke velocity(Vmax), as well as APDs at different repolarization levels(APD30, APD50, APD70, and APD90) of MAP were determined, and these parameters for interpretation of the effect of extracellular calcium on left ventricular monophasic actin potential were analyzed in detail.

RESULTS (1) Depolarization of MAP The maximum amplitude of depolarization(Amax) of the MAP was an average of 8.14+2.448mV, the maximum rate of depolarization(Vmax) was an average of 1.70+0.346V/s, and the time of peak depolarization(T) was an average of 18.00+4.422ms. After adding high calcium Tyrode's solution, the Amax(4.99+1.171mV) and the Vmax (1.14+0.388V/s) were significantly lowered(q value were 4.433 and 4.171, P<0.01), but the depolarization peak time are different, of which 4 cases prolonged, with an average of 22.75+5.965ms,1 cases had no change and 5 cases shortened, with an average of 14.80+3.033ms.

(2) Repolarization of MAP The action potential duration(APD) was 86.10+7.015ms, 80.67+7.036ms and 87.80+7.300ms in the three conditions of the basic, high calcium and the free of calcium respectively, and there were no significant difference between the three cases(F=2.514, p>0.05). Despite the variation existed in every repolarization were phase, namely APD30, APD50, APD70 and APD90, after the addition and removal of high calcium solution, but there no significant different between the three cases(F values were 2.316, 1.641, 1.529 and 2.071respectively, p>0.05).

CONCLUSIONS High extracellular calcium may decrease depolarization velocity and amplification of left ventricular MAP by inhibiting the inward sodium current.

GW26-e3523

miR-31a-5p controls cardiomyocyte proliferation in postnatal hearts

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OBJECTIVES MicroRNAs (miRNAs, miRs) are a class of endogenous non-coding RNAs, participating in a variety of essential biological processes including development, differentiation, proliferation and apoptosis. Rodents have the capacity to regenerate their hearts in response to injury while the capacity would be lost 7 day after birth, suggesting that mammals gradually lose their regenerative potential during postnatal development. The roles of miRNAs in regulating cardiomyocyte proliferation in postnatal hearts are largely unclear.

METHODS Cardiomyocytes were isolated from rat at day 0 and day 10. Agilent rat miRNA arrays were performed to determine the dysregulated miRNAs in cardiomyocytes between day 0 and day 10. A total of 32 miRNAs were found to be dysregulated between day 0 and day 10 (Fold change over 2 and P values less than 0.05).

RESULTS As determined by quantitative reverse transcription polymerase chain reactions and functional assays using EdU staining and Ki-67 staining, miR-31a-5p was found to be able to promote neonatal cardiomyocyte proliferation. Moreover, the expression of proliferation maker- Proliferating Cell Nuclear Antigen (PCNA) was also increased in cardiomyocytes transfected with miR-31a-5p mimics as determined by PCRs and Western blotting analysis. Tumor suppressor RhoBTB1 was found to be negatively regulated by miR-31a-5p in cardiomyocytes and also was responsible for the pro-proliferation effects of miR-31a-5p in neonatal cardiomyocytes.

CONCLUSIONS These studies demonstrate that miR-31a-5p controls cardiomyocyte proliferation in postnatal hearts by targeting RhoBTB1. miR-31a-5p represents a therapeutic target for cardiac repair and regeneration.

GW26-e3945

The Hemodynamics changes in different time after exhausted exercise in rats

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OBJECTIVES To evaluate the hemodynamic changes on the exercise-induced minor myocardial injury in different time after exhausted exercise in rats.

METHODS 30 male SD rats were randomly divided into 5 groups (n=6): control group (Con), exhaustive exercise group (EE), 6h,12h,24h recovery from exhaustive swimming group (EER6 EER12 EER24). The animal models of exercise-induced myocardial injury were established according to Thomas' method. Rats were forced to swim until they were exhausted. Hemodynamics was recorded and analyzed with Millar pressure- volume system in rats.

RESULTS The heart rate (HR), left ventricular end systolic pressure (Pes), left ventricular developed pressure, arterial elasticity (Ea), the maximum rate of left ventricular pressure rise (dP/dt_{max}), peak rate of left ventricular pressure decline ($-dP/dt_{min}$), left ventricular end diastolic pressure volume relationship curve slope (ESPVR) in the EE group decreased the lowest in all, which had significant difference compared with the Con group, while Left ventricular end diastolic volume (Ved), Pes, left ventricular end systolic volume (Ves), stroke volume, and Tau value increased. Besides, Cardiac output, HR, ejection fraction, end diastolic pressure volume relationship curve slope of each group had no statistical significance ($P>0.05$). HR, Pes, dP/dt_{max}, $-dP/dt_{min}$ in recovery groups (EER6, EER12, EER24) were different to EE group, but had no difference compared with the Con group. Ves, Ved and ESPVR had significant difference with the Con group, but no difference compared with the EE group. The Ped of EER24 decreased significantly compared with EE group. The Pdev of EER12, EER24 group compared with the EE group increased significantly. Ea in EER6 group was lower than that of the control group, but EER12, EER24 had no difference with control group and were significantly lower than the EE. Tau value of three recovery groups had significant differences with EE and Con groups.

CONCLUSIONS Exhausted exercise causes that ventricular volume expansion, cardiac systolic and diastolic function were impaired, particularly diastolic dysfunction of rats' heart, however, with the exhausted recovery time prolonged, the function can be recovered partly.

GW26-e4522

Correlation polymorphism of GDF-15 gene with the Coronary Heart Disease formation of collateral circulation

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OBJECTIVES To explore the correlation polymorphism of -3148C/G site of GDF15 (Growth differentiation factor - 15) gene with the

formation of collateral circulation of Coronary Heart Disease in Han people of Taiyuan area.

METHODS The polymerase chain reaction (PCR), gene sequencing and sequence flanking were used to detect and analyze the polymorphism of -3148C/G site of GDF-15 gene for 92 ST-elevation myocardial infarction (STEMI) patients with 68 collateral circulation group,24 non-collateral circulation group and 56 Patients with normal coronary angiography in a control group.

RESULTS The genotype frequencies of CC, GC were 80.43% and 19.57% in the AMI group, which were 60.71% and 39.29% in the control group respectively. P values of the two groups at -3148C/G CC, GC genotype frequencies distribution is < 0.009. The risk genotype GC, OR =2.660, 95% of confident interval is 1.265 - 5.595. And the genotype frequencies of CC, GC were 85.29% and 14.71% in the AMI collateral circulation group and 66.67% and 33.33% in the AMI non-collateral circulation group individually, P values of two groups at -3148C/G CC, GC genotype frequencies distribution is <0.05; The risk genotype was GC, OR =2.900, 95% of confidence interval is 0.983-8.556.

CONCLUSIONS There is a correlation the polymorphism of - 3148C/G site in GDF15 gene and the Coronary Heart Disease patients with collateral circulation in Ham people of Taiyuan area.

GW26-e4625

Inhibitions of Wenxin Keli on ventricular arrhythmias with various underlying mechanisms

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OBJECTIVES The antiarrhythmic effects of Wenxin Keli, the first state-sanctioned traditional Chinese medicine to treat cardiac arrhythmias, has been attributed to the inhibition of late sodium current. The purpose of this study was to determine the effects of Wenxin Keli on ventricular arrhythmias in rabbit intact hearts with augmentation of late sodium current (sea anemone toxin ATX-II), increased intracellular calcium concentration (Bay K 8644) and inhibition of potassium current (E-4031).

METHODS Female rabbit isolated hearts were perfused in Langendorff mode and paced at a rate of 1 Hz after thermo-ablation of AV nodal area. Endo- and epicardial monophasic action potential duration (MAPD) and 12-lead electrocardiogram were recorded and ventricular arrhythmias were analyzed.

RESULTS Wenxin Keli, at a concentration range of 0.1-5 mg/ml, did not alter the epi- and endocardial $MAPD_{90}$ (n =7, p >0.05). Bay K 8644 (300 nmol/L), ATX-II (3 nmol/L) and E-4031 (80 nmol/L) prolonged endocardial $MAPD_{90}$ from 193±7, 199±6, 188±7ms to 266±13 (n =5, P < 0.01), 354±18 (n =7, P < 0.01) and 306±22ms (n =6, P < 0.01), respectively. In the presence of either Bay K 8644 (300 nmol/L) or ATX-II (3 nmol/L) or E-4031 (80 nmol/L), Wenxin Keli (3-5 mg/ml) decreased the $MAPD_{90}$ by 83%, 74% and 72%, from 266±13 to 210±8 (n =5, P < 0.01), 354±18 to 230±20 (n =7, P < 0.01) and 306±22 to 223±14 ms (n =6, P < 0.01), respectively. ATX-II (3 nmol/L) and E-4031 (80 nmol/L), but not Bay K 8644, increased transmural dispersion of repolarization (TDR) from 16±5 to 36±11 (n =7, P < 0.01), and from 19±2 to 59±13 ms (n =6, P < 0.01). The increase of TDR was reversed by Wenxin Keli (3-5 mg/mL) to 18±4 and18±8 ms, respectively (p <0.01). In the presence of either Bay K 8644 (300 nmol/L) or ATX-II (3 nmol/L) or E-4031 (80 nmol/L), spontaneous and/or pause-triggered ventricular arrhythmias were observed in 5 out of 5, 5 out of 7, 6 out of 6 hearts. The incidences of ventricular arrhythmias were decreased by Wenxin Keli (0.3-3 mg/ml) in concentration dependent manner, and were abolished by Wenxin Keli at concentration of 5 mg/mL in all hearts studied. The half-effective dosage (ED50) of Wenxin Keli for Bay K 8644 (300 nmol/L), ATX-II (3 nmol/L) and E-4031 (80 nmol/L) induced ventricular arrhythmias were 0.31[95% confidence intervals (95%CI) (0.11-0.75 mg/mL)], 1.60 [95%CI (0.60-3.31 mg/mL)] and 0.67 [95%CI (0.22-1.60 mg/mL)], respectively.

CONCLUSIONS Wenxin Keli decreases the ventricular repolarization abnormalities and is effective to be antiarrhythmic. The efficacy of Wenxin Keli is greater in cardiac arrhythmias associated with increased intracellular calcium concentration than that with decreased potassium current.

GW26-e4774

β1-adrenoceptor autoantibodies increase susceptibility to ventricular arrhythmias by shortening effective refractory period and prolonging MAPD90-30 in guinea pigs

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OBJECTIVES Malignant ventricular tachyarrhythmias are life-threatening complications and are the main cause of sudden cardiac death (SCD). While the mechanisms of ventricular arrhythmias are complex and are not completely understood. High titers of autoantibodies against the second extracellular loop of β_1-adrenergic receptors (β_1-AAs) can be detected in the sera of patients with ventricular arrhythmias, but a causal relationship between β_1-AAs and ventricular arrhythmias has not yet been finalized. This study is to investigate whether β_1-AAs can induce ventricular arrhythmias directly and to reveal the underlying electrical mechanism.

METHODS Two peptides (HWWRAESDEARRCYNDPKCCDFVTNR, CHWWRAESDEARR) corresponding to the sequence of the second extracellular loop of the β_1-adrenergic receptor respectively were used as immunogen to synthesize monoclone β_1-AAs.β_1-AAs (10 μmol/L) were injected into the hind foot vein of guinea pigs (0.735 ml/Kg) and ECG was recorded. A Langendorff apparatus was used to retro-perfuse the hearts and ECG and monophasic action potential (MAP) were recorded. Ventricular fibrillation (VF) was evoked by programmed electrical stimulation. The in vitro effects of β_1-AAs (0.1 μmol/L) on ECG, the threshold intensity and duration of electrically induced VF, monophasic action potential duration (MAPD) and effective refractory period (ERP) were observed.

RESULTS Both the in-vivo and in-vitro experiments showed that β_1-AAs induced ventricular premature contraction (VPC) in guinea pig hearts. Heart rate, PR interval, QRS interval and the corrected QT interval (QTc) did not change 30 min after intravenous injection of β_1-AAs. While β_1-AAs shortened the QT interval of paced isolated guinea pig hearts from 360.0 ± 11.1 ms to 333.0 ± 14.0 ms ($P < 0.05$; $n = 5$). β_1-AAs enhanced susceptibility to ventricular fibrillation evidenced by decreasing the ventricular fibrillation threshold from 11.0 ± 2.5 V to 8.8 ± 1.5 V ($P < 0.05$; $n = 5$) and prolonging the ventricular fibrillation duration from 833.0 ± 25 ms to 1608.0 ± 135.0 ms ($P < 0.05$; $n = 5$). β_1-AAs shortened ERP from 100 ms to 84 ms ($P < 0.05$, $n = 5$). No changes in $MAPD_{30}$, $MAPD_{50}$, $MAPD_{90}$, and $MAPD_{90\text{-}30}$ were observed in the control group after a 10-min perfusion with normal Tyrode's solutions ($P > 0.05$, $n = 5$). After perfusion with 0.1 μmol/L β_1-AAs, $MAPD_{30}$, $MAPD_{50}$ and $MAPD_{90}$ were not affected, while $MAPD_{90\text{-}30}$ was prolonged from 23.0 ± 4.2 ms to 40.0 ± 5.0 ms ($P < 0.05$; $n = 5$). ERP/$MAPD_{90}$ was significantly decreased by β_1-AAs.

CONCLUSIONS In summary, β_1-AA can induce ventricular premature contraction directly and increase the susceptibility to ventricular fibrillation in guinea pig heart. The reduced QT and ERP, prolonged $MAPD_{90\text{-}30}$ and decreased ERP/$MAPD_{90}$ caused by β_1-AA may contribute to the repolarization abnormality which gave rise to ventricular arrhythmias.

GW26-e5336

Endoplasmic reticulum stress-mediated apoptosis contributing to high glucose induced vascular smooth muscular cell calcification

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OBJECTIVES To investigate whether high blood glucose-induced vascular calcification in diabetes mellitus is caused by the endoplasmic reticulum response and subsequent apoptosis.

METHODS We examined the effects of high glucose on the endoplasmic reticulum (ER) stress response of vascular smooth muscle cells (VSMCs). ALP activity was determined by using the ALP assay kit. Alizarin Red S staining were performed to detect calcium deposition. Runx2 expression in VSMCs was tested using Western blot analysis.

RESULTS High glucose treatment drastically induced the ER stress response in VSMCs. The high glucose-induced osteoblastic differentiation of VSMCs was significantly attenuated by pretreatment with 500 μM 4-PBA (a endoplasmic reticulum stress inhibitor) prior to