exposure to high glucose, as evidenced by decreases in the expression of Runx2, activity of ALP(alkaline phosphatase) as well as calcium nodules.

CONCLUSIONS These results suggest that high glucose induces the ER stress response and apoptosis, leading to high glucose-elicited vascular calcification.

GW26-e5405

Establishment of Swine End-Stage Dilated Cardiomyopathy Model by Percutaneous Venous Intervention

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OBJECTIVES To established a model of swine end-stage dilated cardiomyopathy (DCM) model by percutaneoue venous intervention.

METHODS Ten male pigs were randomly divided into 2 groups, namely DCM group and control group. The DCM group underwent rapid right ventricular pacing by a modified Medtronic unipolar pacemaker connected to an apical pacing lead via percutaneous venous intervention, which at the rate of 230 beats per minute for 4 weeks, and 190 beats per minute for another 4 weeks, while the control group received sham operation. The clinical symptoms and hemodynamic parameters were used to evaluate the severity of heart failure.

RESULTS Cardiac output in the DCM group (3.1 +/- 1.1 L.min-1) was significantly less (P less than 0.01) than in control group (5.4 +/- 0.8 L.min-1); Compared with control group(0.67 +/-0.19 cm), thickness of left ventricular posterior wall was significantly less (P less than 0.01) than in control group (0.51 +/-0.18 cm).

CONCLUSIONS We established a model of swine end-stage dilated cardiomyopathy model by percutaneous venous intervention, which demonstrates that 4 weeks of rapid ventricular pacing at 230 beats/min and another 4 weeks of 190 beats per minute produces a realistic model of end-stage dilated cardiomyopathy in the pig.

GW26-e1009

Protective effect of astaxanthin on contrast-induced acute kidney injury in experimental rats

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OBJECTIVES To explore the protective effect and mechanism of astaxanthin(AST) on the acute kidney injury induced by iohexol in rats.

METHODS Thirty rats were randomly divided into five groups: control group (CON), iohexol group (CM), astaxanthin group(AST, 100mg/kg), low astaxanthin dose group (LAST+CM, 50mg/kg) and high astaxanthin dose group (HAST+CM, 100mg/kg)(6 in each group). The rats in AST, LAST+CM, HAST+CM groups were administrated with AST by oral gavage using an intubation needle for 10 consecutive days. The other rats in CON, CM groups were given with dissolvant instead in equal volume. Except for the CON and AST groups, on day 8, rats were given indomethacin, L-NAME and iohexol in their femoral vein under chloral hydrate anesthesia to build a contrast induced-nephropathy (CIN) model. At the end of the experiment (72h after CIN induction), all rats were sacrificed. The serum creatinine (SCr) level, blood urea nitrogen (BUN) level, renal histology, renal tissue activities in superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), Glutathione (GSH) and level of malondialdehyde (MDA) were performed. Apoptosis of renal cells was detected by Bcl-2, Bax and Caspase-3 with Western blot.

RESULTS ① Compared with CON group, renal function of SCr, BUN levels were significantly increased in CM group ($P < 0.01$), while compared with CM group, the indicators were decreased in treatment groups ($P < 0.01$); Renal tubular structure damage, medulla congestion, loss of brush border, vacuolar degeneration, apoptosis and proteinaceous casts were observed the CM group, and the renal injury scores were higher compared with CON group ($P < 0.05$), however, administrated with AST could significantly improve the changes ($P < 0.05$); ③ Oxidative stress indicators show that MDA level were increased while SOD, GPx, GSH activities were significantly decreased at CM group (all $P < 0.05$), and the indicators above were ameliorated in treatment groups ($P < 0.05$). ④ Western blot showed that the expression of Bcl-2 was down-regulated while the Bax, caspase 3 p17 was up-regulated respectively at CM group ($P < 0.05$), while the HAST+CM group could prevent the changes.

CONCLUSIONS Iohexol can results in oxidative stress increased in kidney, which activate caspase-3 p17 signal path, down-regulated Bcl-2 expression, up-regulated Bax expression respectively, and lead to cell apoptosis. AST can ameliorate the changes, especially with high AST dose, which suggest that the possible protection mechanism is by ameliorating oxidative stress and inhibiting apoptosis pathways.

GW26-e1242

Sodium tanshinoneII-A sulfonate Relaxes Human Mesenteric Artery Via large-conductance Ca2+-activated potassium channels

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OBJECTIVES Danshen as a traditional Chinese medicine is widely used to remedy cardiovascular and cerebrovascular diseases partly by its effects of vasodilatation, and sodium tanshinoneII-A sulfonate (DS-201) a water-soluble derivative of its active ingredient. We aimed to explore the vasodilatation mechanism of DS-201 at the molecular level by investigating the effect of DS-201 on large-conductance Ca2+-activated potassium channels (BK_{Ca}) in human mesenteric artery smooth muscle cells.

METHODS Rings of human mesenteric artery were contracted with 60 mM KCl, and changes in isometric tension were recorded. Then we observe the effect of DS-201 on BK_{Ca} by using patch clamp technique.

RESULTS DS-201 (20 to 120 μM) induced a concentration-dependent relaxation with a maximum of 64 ± 3% in human mesenteric artery without endothelium (n=6, P<0.05). These relaxations were inhibited by 300nM iberiotoxin. In cell-attached patch (Vm =+40 mV), 80μM DS-201 stimulates BKCa activity, DS-201 enhanced open probability (NPO) of BKCa from 0.012±0.001 to 0.039±0.009, the mean open time (To) of BKCa is markedly increased from 7.3±1.1 ms to 15.3±1.3 ms and the mean close time (TC) of BKCa is decreased from 1829.3 ± 408.2 ms to 267.5 ±82.3 ms(n=6, P<0.05), but there were no significant changes in amplitude of current. In inside-out patch (Vm =+40 mV), 80μM DS-201 stimulates BKCa activity significantly: DS-201 enhanced NPO of BKCa from 0.027± 0.008 to 0.175 ± 0.084, To is markedly increased from 19.8±3.1 ms to 43.1±3.3 ms and TC is decreased from 708.1 ± 408.2 ms to 85.607 ±32.3 ms (n=6, P<0.05). In the amphotericin-perforated whole-cell patch-clamp configuration, the current density of BKCa at the voltage of -60 to +30 mV had no significant change before and after adding 80 μM DS-201, but the current density of BKCa at the voltage of + 40 mV,+ 50 mV and + 60 mV was increased significantly after adding 80 μM DS-201, from 12.4 ± 3.6 pA/pF, 17.5 ± 3.8 pA/pF and 24.1 ± 4.6 pA/pF to 18.7 ± 3.6 pA/ pF, 25.8 ± 2.5 pA/pF and 34.5 ± 3.8 pA/pF (n=4, P<0.05).

CONCLUSIONS DS-201 relaxes human mesenteric artery via stimulation of BKCa.

GW26-e1386

Mechanism of hERG potassium channel block by tolterodine

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OBJECTIVES The goal of this study was to determine whether two aromatic residues in the S6 region (Y652 and F656) are important for the inhibition effect of tolterodine on hERG channel.

METHODS hERG cRNA solution (wild type, Y652A and F656A) were injected and expressed in Stages IV and V Xenopus laevis oocytes. And the oocytes were incubated at 17 °C in ND96 solution. The currents were recorded using standard two-microelectrode voltage-clamp technique.

RESULTS The data collected from wild type channels indicated that tolterodine blocked I_{hERG} in a concentration-dependent manner ($[IC_{50}]$ =60.73 nmol/L). The steady state activation and inactivation curves moved to the positive and negative, respectively. Further analysis showed that inhibition of the drug was dependent on the open state of the channel. In addition, it was found that the mutants of Y652A and F656A significantly reduced the blocking effect of drug and produced about 345-fold and 124-fold increases in IC_{50}, respectively.