CONCLUSIONS DQP can effectively regulate lipid metabolism in CHD. The pharmacological effect is achieved by regulating factors in ApoA1-FABP-CPT1A pathway. DQP can also activate the expression of PPARα. In addition, DQP shows anti-inflammatory effects by inhibiting PLA2-COXs pathway mediated by NF-κB. This investigation lays foundation for clinical application of DQP and provides insights into improving the efficacy in the treatment of CHD.

GW26-e2436

Eliminating Sputum and Removing Stasis Formulation improves Atherosclerotic Plaque via regulating Mast Cell function and related mechanism

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OBJECTIVES Study the mechanism of Eliminating Sputum and Removing Stasis Formulation improves Atherosclerotic Plaque via regulating Mast Cell function on the ApoE$^{-/-}$ mice atherosclerotic plaque model.

METHODS

1. Establishment and evaluation of artery atherosclerotic plaque model on ApoE$^{-/-}$ mice.
2. We divided mouse into four groups randomly : control (CON), model (MOD), atorvastain (ATO) and Traditional Chinese Medicine (TCM), n=10. After twelve weeks the difference of plaques proportion and the leves of mast cell degranulation among all groups were compared through HE, oil red O, and toluidine blue staining on the aortic root slicing. We test the level of total cholesterol and total triglyceride by related reagent kit (enzymic method). Mice plasma lipoprotein content was tested by Fast Protein Liquid Chromatography. The Serum tryptase activity was tested by Colorimetric method. Finally Comparing all groups' mast cells genes expression via Quantitative PCR and Western blot.

RESULTS We observe from the Aortic vascular root section staining finding that the model can accelerate the artery plaques formation. Eliminating Sputum and Removing Stasis Formulation can improves atherosclerotic plaques via reducing lipid load level in the plaques (56%), weaken the degree of mast cell aggregation and degranulation(35%).

Among all groups TCM is the most significance on lower the level of mice plasma TC (24%) and the activity of Tryptase (43%) compared with MOD ($P < 0.05$). The level of Low Density Lipoprotein (LDL) are all descend on ATO and TCM ($P > 0.05$).

The mast cell secretion related genes and proteins in aortic vascular tissue such as LeukotrieneC4 synthase (34%), Histidine decarboxylase (25%), Mast cell chymase1 (53%), Mast Cell Tryptase 6 (40%) decline dramatically on TCM groups compared others ($P < 0.05$). Meanwhile the inflammatory factor in plasma such as the level of Tumor Necrosis Factor α decreases 23% compared ATO ($P < 0.05$) and the level of transforming growth factor β1 rises 65% compared ATO ($P < 0.05$).

CONCLUSIONS

1. Combine partial left carotid ligation with left kidney artery stenosis operation and high-fat diet ApoE$^{-/-}$ mice can successfully be induced atherosclerotic plaque formation.
2. The Traditional Chinese Medicine Eliminating Sputum and Removing Stasis Formulation have the similar effect with atorvastatin on the aspects of reducing lipid load in the plaques and lowering plasma LDL levels.
3. Compared with atorvastatin, the mechanism of Eliminating Sputum and Removing Stasis Formulation improves Atherosclerotic Plaque may have extra effects on reducing the content of TC, weakening mast cells aggregation and degranulation and adjusting the level of TNF-α and TGF-β_1 in the plasma.

GW26-e3826

Pharmacological preconditioning and postconditioning with nicorandil attenuates ischemia/reperfusion-induced myocardial necrosis and apoptosis in hypercholesterolemic rats

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OBJECTIVES Pharmacological preconditioning and postconditioning may reduce myocardial necrosis and apoptosis during ischemia/reperfusion (I/R). However, hypercholesterolemia interferes with their cardioprotective mechanisms. In the present study, we investigated whether pharmacological preconditioning and postconditioning with nicorandil could attenuate myocardial necrosis and apoptosis induced by I/R in hypercholesterolemic rats and explored the possible mechanisms involved.

METHODS 160 male Wistar rats were fed normal (normocholesterolemic group, n=10) or high-cholesterol (hypercholesterolemic group, n=150) diets for 8 weeks. Hearts isolated from normal and hypercholesterolemic rats were placed on modified Langendorff perfusion apparatus and subjected to 30-min global ischemia followed by 120-min reperfusion. Nicorandil (1, 3, 10, 30, 100 μmol/l), mitochondrial adenosine triphosphate sensitive potassium (mitoKATP) blocker 5-Hydroxydecanoic acid sodium salt (5-HD) (100 μmol/l), soluble guanylyl cyclase (sGC) blocker 1H-[1,2,4]Oxadiazolo[4,3-a]quinoxalin-1-one (ODQ) (10 μmol/l) were perfused for 10 min prior to ischemia or at the onset of reperfusion. The myocardial infarct size was determined by triphenyltetrazolium chloride (TTC) staining, cardiomyocyte apoptosis was detected by TUNEL staining. Expression of caspase-3, Bax and Bcl-2 proteins were measured by Western blot analysis to investigate the potential mechanisms.

RESULTS We found that pharmacological preconditioning and postconditioning with nicorandil reduced myocardial necrosis and apoptosis induced by I/R in a concentration-dependent manner in hypercholesterolemic rats. The optimal concentration of nicorandil preconditioning and postconditioning in anti-infarct and anti-apoptosis was 30μmol/l. 30μmol/l nicorandil preconditioning and postconditioning reduced the infarct size to 14.88±3.25% and 15.96±3.29%, attenuated the percentage of cardiomyocyte apoptosis to 25.20±3.93% and 26.18±4.82%, respectively. While, the cardioprotection of nicorandil were partly suppressed by cotreatment with 5-HD or ODQ. Western blot analysis showed that pharmacological preconditioning and postconditioning with nicorandil downregulated caspase-3 and Bax expression, and upregulated Bcl-2 expression compared with the I/R group ($P<0.05$).

CONCLUSIONS Taken together, these data suggested that pharmacological preconditioning and postconditioning with nicorandil protected hypercholesterolemic hearts against necrosis and apoptosis induced by I/R, and this cardioprotective effects of nicorandil was due to its dual pharmacological mechanisms of opening the mitoKATP channels and nitric oxide (NO)/sGC dependent mechanism, and the regulation of the expression of caspase-3, Bax and Bcl-2.

GW26-e4697

Improved myocardial fractional flow reserve in pigs with by Cx37 gene silence

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OBJECTIVES This work aims to test the hypothesis that effect of Cx37 gene decreased myocardial fractional flow reserve.

METHODS Lentiviruses carrying small interfering RNA (siRNA) of Cx37 gene were constructed, which significantly knocked down mRNA and protein expression of Cx37 gene in vitro. Sixty pigs with high-fat diet were randomly divided into saline, mock, and different concentrations Cx37 viral suspension to induce coronary plaque formation. Different levels Cx37 viral suspension, saline and mock after performing myocardial fractional flow reserve (FFR) were transfected into the related coronary. After two weeks, four weeks, six weeks and eight weeks, myocardial fractional flow reserve were measured by intravascular ultrasound (IVUS) and After eight weeks plaque characteristics were detected. The expression of Cx37 mRNA was detected by semi-quantitative RT-PCR. The expression of CX37 protein was demonstrated by Western blot.

RESULTS Four weeks, six weeks and eight weeks after lentivirus transfection, FFR in siRNA Cx37 (20 μl) was higher than in siRNA Cx37 (10 μl), in siRNA Cx37 (5 μl) in the mock-siRNA group and in the saline group. Cx37 mRNA levels were lower by 41% in the Cx37 siRNA group (20 μl), by 81% in the Cx37 siRNA group (10 μl), by 84% in the Cx37 siRNA group (5 μl), by 95% in the mock-siRNA group, and by 97% in the saline group ($P < 0.05$). The mock group showed no significant change in Cx37compared with the saline group. Cx37 protein was lower in the siRNA Cx37 group (20 μl) than in other groups (0.21±0.05 vs. 0.78±0.06 vs. 0.72±0.08 ,0.87±0.05 and 0.84±0.06).

CONCLUSIONS SiRNA can be used to efficiently knock down Cx37genes in coronary plaques of pigs. At the same time, FFR in the siRNA Cx37 group (20 ul) was improved.