(GM-CSF) could enhance the restoration of cells' normal phenotype. However, previous studies suggested GM-CSF might induce hypercoagulability. In this study, we discussed the effect of GM-CSF on coagulation and fibrinolysis after artery deendothelialization.

Methods 24 male New Zealand White rabbits underwent primary iliac artery deendothelialization were randomised to two groups (GM-CSF group and control group). GM-CSF group animals received a subcutaneous injection of GM-CSF, the control group animals were given a subcutaneous injection of equivalent saline. The iliac arteries of all animals were damaged by balloon after 7 days. The plasma levels of tissue-type plasminogen activator (t-PA), plasminogen activator inhibitor-1 (PAI-1) and nitric oxide (NO) were detected before, 1 week, 2 weeks and 4 weeks after angioplasty. The repair and hyperplasia of intima were observed by microscope.

Results The NO levels of the GM-CSF group were higher than that of the control group 2 weeks and 4 weeks after operation [(91.9±11.6) μmol/l vs (81.7±12.2) μmol/l]; [(97.7±10.1) μmol/l vs (83.2±12.6) μmol/l]. Although there was no difference between the two groups in both activities of t-PA and PAI-1 in each specific time point, in 1, 2, 4 weeks after operation, the activities of t-PA became higher than the ones before operation, while the activities of PAI-1 stayed almost the same. Pathological examination showed that the level of intima hyperplasia. VSMC and fibrous tissue of neointima were much lower in GM-CSF group and endothelium was more integrated and smooth.

Conclusion GM-CSF could facilitate the repair of intima, better the function of endothelium without disturbing the balance of coagulation and fibrinolysis.

e0091 POTENTIAL EFFECT OF GRANULOCYTEMACROPHAGE COLONYSTIMULATING FACTOR ON THE ARTERIAL REMODELLING AT THE REFERENCE SITE AFTER ANGIOPLASTY

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Objective Arterial remodelling may also occur at the reference site. Resent studies showed that granulocyte-macrophage colony-stimulating factor (GM-CSF) could facilitate the repair of endothelium and reduce vascular inflammation. To observe the effect of granulocyte-macrophage colony-stimulating factor on arterial remodelling, we evaluated the remodelling at the reference site and the lesion site in rabbit model.

Methods 28 healthy New Zealand White rabbits were randomised to two groups (GM-CSF group and control group). GM-CSF group received a subcutaneous injection of GM-CSF (10 ug/kg/d), the control group were given a subcutaneous injection of equivalent saline. The iliac arteries of all animals were damaged by balloon after 7d. The levels of nitrogen monoxide (NO) were detected before and 4 weeks after angioplasty. Histological sections of iliac from rabbits killed 4 weeks after angioplasty were analysed. Luminal area (LA), external elastic lamina area (EEL), and intimal plus medial areas (I+M) were measured at the lesion ($_L$) and reference ($_R$) sites.

Results The NO level of the GM-CSF group was significantly higher than that of the control group after 4 weeks (97.69±10.21 vs 83.18±12.57 μmol/l). Morphometric analysis showed that the LA ($_L$) of control group was smaller than that of the GM-CSF group (0.87±0.40 vs 1.34±0.52 mm^2, $p<0.05$) and I+M ($_L$) was greater than that of the GM-CSF group (2.62±0.48 vs 2.26±0.43 mm^2, $p<0.05$). There was no difference in EEL ($_L$) between the two groups (3.48±0.80 vs 3.60±0.91, $p>0.05$). Morphometric analysis also showed a smaller LA ($_R$) in the control group (1.60±0.48 vs 1.99±0.54 mm^2, $p<0.05$), whereas there was no difference in I+M ($_R$) between the two groups. EEL ($_R$) significantly correlated with LA ($_R$), EEL ($_L$), and I+M ($_R$) in both groups combined ($r=0.91$, $p<0.0001$; $r=0.909$, $p<0.0001$; and $r=0.685$; $p<0.0001$, respectively). LA ($_R$) also correlated with LA ($_L$) ($r=0.919$; $p<0.0001$).

Conclusion Remodelling can affect both the lesion and the reference sites and appears to occur in parallel and proportionately at both sites. GM-CSF treatment increased reendothelialization of the injured artery and inhibited unfavourable remodelling.

e0092 AVE0991 IMPROVES LEFT VENTRICULAR REMODELLING AND CARDIAC FUNCTION INDUCED BY MYOCARDIAL INFARCTION IN RATS

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Objective To evaluate the effects of 4-week treatment with the nonpeptide angiotensin-(1-7) analogue AVE 0991 on heart function and left ventricular remodelling induced by myocardial infarction (MI).

Methods In this study, we evaluated the cardiac effects of AVE 0991 on normal and infracted male Sprague-Dawley (SD) rats. MI was induced by left coronary artery ligation. After 4 weeks of treatment, transthoracic echocardiography (TTE) was used to evaluate cardiac function. The heart wet weight was recorded, normalised for body weight. Left ventricle serial sections were dyed with triphenyltetrazolium chloride (TTC) stain to quantify the infarct size, with Masson's trichrome stain to quantify collagen volume fraction (CVF), and with haematoxylin-eosin (HE) stain for diameter measurement of cardiomyocytes.

Results Infarct size was slightly reduced in AVE 0991 group compared to control group (42.6±3.6% vs 50.9±4.4%, $p<0.01$). In addition, AVE 0991 treatment attenuated the decrease in LVFS (25.54±7.33% vs 18.41±3.32%, $p<0.05$) and LVEF (54.82±11.63% vs 42.7±6.5%, $p<0.05$) compared to control group. AVE 0991 also reduced MI-induced hypertrophy as quantified by diameter measurements of cardiomyocytes (vs. control group 25.49±4.37 μm vs 32.06±6.85 μm, $p<0.05$).

Conclusion The nonpeptide angiotensin-(1-7) analogue AVE 0991 has a cardioprotective effect on impairment of heart function and ventricular remodelling induced by MI.

e0093 MYOCARDIAL INFARCTION-INDUCED REMODELLING AND INFLAMMATORY CYTOKINES IN RATS ARE ATTENUATED BY AVE0991

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Objective To investigate the effects of 4-week treatment with the nonpeptide angiotensin-(1-7) analogue AVE 0991 on expression of inflammatory cytokines and remodelling induced by myocardial infarction (MI).

Methods In this study, MI was induced by left coronary artery ligation in male Sprague-Dawley (SD) rats. After 4 weeks of treatment, the heart wet weight was recorded, normalised for body weight. Left ventricle serial sections were dyed with triphenyltetrazolium chloride (TTC) stain to quantify the infarct size, with Masson's trichrome stain to quantify collagen volume fraction (CVF), and with haematoxylin-eosin (HE) stain for diameter measurement of cardiomyocytes. RT-PCR was used to investigate the synthesis of TGF-β1, TNF-α, collagen type I and III.

Results Infarct size was slightly reduced in AVE 0991 group compared to control group (42.6±3.6% vs 50.9±4.4%, p<0.01). In addition, AVE 0991 reduced MI-induced hypertrophy as quantified by diameter measurements of cardiomyocytes (vs. control group 25.49±4.37 μm vs 32.06±6.85 μm, p<0.05). The overexpression of TGF-β1 and TNF-α mRNA were inhibited by chronic AVE 0991 treatment alone (vs. control group, TGF-β1: 4.15±1.18 vs 14.23±3.84, p<0.05; TNF-α: 2.21±0.44 vs 3.87±0.55, p<0.05, respectively). AVE 0991 markedly attenuated the increase of the expression of Collagen I (1.79±0.15 vs 4.3±0.75, p<0.001) and III (3.12±0.42 vs 9.55±0.83, p<0.001) mRNA compared to control group.
Conclusion The nonpeptide angiotensin-(1-7) analogue AVE 0991 could attenuate overexpression of inflammatory cytokines and ventricular remodelling induced by myocardial infarction (MI).

e0094 RESEARCH OF TRIPTOLIDE ON ANG II-INDUCED NEONATAL CARDIAC FIBROBLASTS PROLIFERATION AND COLLAGEN SYNTHESIS

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Objectives To observe whether TP can inhibit proliferation and collagen synthesis of cardiac fibroblasts and clarify the possible mechanisms.
Methods Differential attachment technique to obtain and cultivate neonatal SD rat cardiac fibroblasts. Experimental cells were randomly divided into five groups: (1) control (culture medium); (2) Ang II group (10-7 mol/l Ang II); (3) 1 μg/l TP group (1 μg/l TP+10-7 mol/l Ang II); (4) 10 μg/l TP group (10 μg/l TP+10-7 mol/l Ang II); (5) 100 μg/l TP group (100 μg/l TP+10-7 mol/l Ang II). Ang II are simultaneously added into the culture medium. MTT colorimetric determination of cell proliferation. Collagen synthesis, TGFβ1 secretion and phosphorylation of extracellular signal-regulated kinase 1/2 (ERK1/2) by Hydroxyproline, ELISA and Wertern Bloting.
Results 1. The proliferation of CFb is significantly promoted after adding Ang II, compared with the control group (p<0.05 or p<0.01). The 100 μg/l TP showed the effect of inhibiting the proliferation of CFb at the first 24 h (p<0.01), reached a peak within 48 h (p<0.001), started to diminish after 72 h, indicate the best time to exert effects were at 2 to 3 days. 2. With the time increase after adding Ang II, collagen synthesis increased, there is significant difference compared with the control group (p<0.05 or p<0.01). After 24 h, 48 h, 72 h of adding TP, the collagen content of each group compared with the Ang II group were significantly different. The effect of high concentration TP (100 μg/l) reached the peak (p<0.001) at 48 h (p<0.001). 3. After 24 h of adding Ang II, TGF-β_1 expression was significantly increased (p<0.01). After 24 h of adding different concentrations of TP, TGF-β_1 expression were significantly decreased (p<0.05 or p<0.01). 4. After 30min of adding Ang II, ERK1/2 phosphorylation increased compared with the negative control (p<0.05). After 30min of adding 100μg/l TP, p-ERK1/2 expression decreased compared with the Ang II group (p<0.05). And 1 μg/l, 10 μg/l TP did not inhibit ERK1/2 phosphorylation caused by Ang II. Positive control U0126 significantly inhibited the ERK1/2 phosphorylation (p<0.01).
Conclusions Ang II promote neonatal SD rat cardiac fibroblasts proliferation and collagen synthesis, the possible mechanism may be the MAPK signal transduction pathway. Ang II has the effect of promoting cardiac fibroblasts proliferation by increase phosphorylation of ERK1/2 expression; promoting collagen synthesis by increasing the expression of TGF-β_1. Triptolide significantly inhibited the Ang II-induced cardiac fibroblast proliferation and collagen synthesis in a dose-dependent manner, and the mechanism is probably by inhibiting the ERK1/2 phosphorylation and reducing the expression of TGF-β_1.

e0095 THE STUDY ON THE RELATIONS BETWEEN RENNIN-ANGIOTENSIN-ALDOSTERONE SYSTEM AND ATRIAL STRUCTURAL REMODELLING AND ATRIAL FIBRILLATION

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Objective To investigate the effects of perindopril and/or spironolactone on atrial structural and functional remodelling in atrial fibrillation (AF) dogs induced by chronic rapid atrial pacing, and research the relations between rennin-angioensin-aldosterone system (RAAS) and atrial interstitial remodelling and atrial fibrillation.
Methods 24 healthy male hybrid dogs aged 15—18 months were paced for 8 weeks and randomly divided into four groups: control group, perindopril group (P), spironolactone group (S), and combination of perindopril and spironolactone group (P+S). The dogs in P group, S group, and P+S group respectively received perindopril (1 $mg \cdot kg^{-1} \cdot d^{-1}$) and/or spironolactone (10 $mg \cdot kg^{-1} \cdot d^{-1}$). Plasma Angiotensin II (Ang II) and aldosterone (Ald) were measured before and after 4 and 8 weeks pacing. Transthoracic echocardiographic examinations were performed before and after 8 weeks pacing. The number of dogs maintained AF and duration of AF after stopping of pacing were recorded. Atrial collagen volume fraction (CVF) was analysed by Masson staining after 8 weeks pacing.
Results (1) Plasma Ang II and Ald were no significant differences between four groups before pacing. Compared with the control group, plasma Ang II and Ald after 4 and 8 weeks pacing in P group, S group and P+S group were significantly lower. In the control group, plasma Ang II and Ald levels after 4 and 8 weeks pacing was significantly higher than that before pacing; in the other groups, there were no significant differences. (2) Compared with the control group, the diameter, end-systolic volume and end-diastolic volume of the left atrium of P group, S group and P+S group after pacing significantly reduced, but LAEF significantly increased after 8 weeks pacing. (3) Compared with the control group, the rate of dogs maintained atrial fibrillation of three drug treatment groups after stopping of pacing significantly reduced, with a shorter average duration of AF. (4) Compared with the control group, the value of CVF in P group, S group and P+S group was significantly lower.
Conclusion The occurrence and development of atrial fibrillation and atrial structural remodelling is closely related to RAAS activation. The RASS blockers can inhibit atrial fibrosis, improve the changes of atrial structure and function, and reduce the incidence and duration of atrial fibrillation in the atrial fibrillation dogs induced by chronic rapid atrial pacing.

e0096 THE STUDY ON THE RELATIONS BETWEEN ALDOSTERONE AND ATRIAL INTERSTITIAL REMODELLING AND ATRIAL FIBRILLATION

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Objective To investigate the relations between aldosterone (Ald) and atrial interstitial remodelling and atrial fibrillation (AF).