

e0072 **CARDIOPROTECTIVE EFFECT OF β_3 ADRENOCEPTER AGONISM IN PRESSURE OVERLOAD INDUCED HYPERTROPHY**

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Objective β_3 -adrenergic receptors (β_3 -AR) and its downstream signalling are recognised as novel modulators of heart function. We have recently shown impaired cardiac functional compensation in a model of pressure overload. We therefore hypothesised that the selective β_3 -AR agonist, BRL37344 (BRL), would protect the heart from pressure overload induced cardiac remodelling.

Methods and results C57BL/6J mice underwent transverse aortic constriction (TAC) for 3 weeks, resulting in increased cardiac hypertrophy and dysfunction assessed by echocardiography. 3 weeks of BRL treatment (0.1 mg/kg/day via subcutaneous osmotic infusion pump) starting from 1 day post TAC reduced hypertrophy, with lower heart weight normalised to tibia length (100 ± 4 vs 120 ± 7 mg/cm), LV mass (136 ± 7 vs 163 ± 8 mg), wall thickness (1.08 ± 0.02 vs 1.16 ± 0.02 mm) and systolic dimension (1.36 ± 0.09 vs 12.08 ± 0.23 mm; $p < 0.05$ for all), and completely restored systolic function back to normal (58 ± 2 vs $62 \pm 1\%$; $p = \text{NS}$ vs sham, $p < 0.05$ vs TAC). BRL reduced myocyte width by H&E staining, but had no effect on fibrosis scale. These benefits from β_3 -AR stimulation were associated with increased nitric oxide (NO) production (13.73 ± 1.84 vs 5.03 ± 0.52 $\mu\text{M}/\text{mg}$ protein) and suppressed superoxide generation (14017 ± 838 vs 21459 ± 783 CPM/mg tissue; $p < 0.01$ vs TAC for both). Neuronal NO synthase (nNOS) protein expression was up-regulated ~ 3 fold by BRL treatment (1.11 ± 0.22 vs 0.39 ± 0.17 ; $p < 0.05$). More interestingly, the suppressive effect of BRL on superoxide generation was abolished by acute nNOS inhibition by specific nNOS inhibitor N5-(1-imino-3-butenyl)-L-ornithine, monohydrochloride (L-VNIO).

Conclusions These results are the first to show in vivo the cardioprotective effect of β_3 -AR specific agonism in pressure overload hypertrophy and heart failure, and support nNOS as a downstream molecule favouring NO and reactive oxygen species (ROS) balance in this pathologic process in the failing heart.

e0073 **EFFECT OF BONE MARROW MESENCHYMAL STEM CELLS TRANSPLANTATION ON EXPRESSION OF NF- κ B AND PCNA AND VASCULAR STENOSIS AFTER CAROTID ARTERY BALLOON INJURY OF RABBIT**

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Objective To investigate effect of bone marrow mesenchymal stem cells transplantation on expression of nuclear factor κ B (NF- κ B) and proliferating cell nuclear antigen (PCNA) and vascular stenosis after carotid artery balloon injury of rabbit.

Methods 36 carotid artery atherosclerotic stenosis rabbits were randomly divided into the control group (balloon injury+PBS solution) and the MSCs transplantation group (balloon injury +MSCs transplantation). MSCs ($5 \times 10^7/\text{ml}$) were pre-labelled by DAPI and then infused into MSCs transplantation group rabbits by the ear vein, and control group was infused with the same amount of PBS solution. 1 week after MSCs transplantation, DAPI labelled cells were detected under immunofluorescence microscope; The plasma tumour necrosis factor- α (TNF- α) and interleukin-6 (IL-6) levels were detected with ELISA on the 1st, 2nd and 4th week after

MSCs transplantation. After 2 weeks and 4 weeks, the injured vessels were stained by HE and the immunohistochemical analysis of NF- κ B and PCNA.

Results The DAPI-labelled MSCs could be detected on impaired intima 1 week after MSCs transplantation. NF- κ B and PCNA expression was not seen in the normal blood vessels after 2 weeks, the expression of NF- κ B and PCNA in MSCs transplantation group decreased significantly compared with control group. The plasma TNF- α and IL-6 levels in MSCs transplantation group were significantly lower than those in control group. The intimal area, the ratio of the intima/media area and the luminal stenosis ratio were significantly lower in MSCs transplantation group than control group at 4 weeks.

Conclusions MSCs are capable of decreasing the inflammatory reaction of injured vessels and lighten the restenosis of injured vessels.

e0074 **EFFECTS OF TRANSPLANTATION OF PERIPHERAL BLOOD MESENCHYMAL STEM CELLS WITH HYPOXIA PRECONDITIONING ON POSTANGIOPLASTY RESTENOSIS IN RABBITS**

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Objective To investigate the function and the mechanism of transplanting bone marrow derived peripheral blood mesenchymal stem cells (PBMSCs) on restenosis after carotid balloon angioplasty in the model of carotid atherosclerosis rabbits and to determine if the functions of PBMSCs are enhanced after hypoxia preconditioning.

Methods Bone marrow cells were mobilised by granulocyte colony-stimulating factor (G-CSF), and PBMSCs were connected through density gradient centrifugation and adherent culture, labelled with enhancement type green fluorescent protein (EGFP) genes. All animals with carotid atherosclerosis stenosis were randomly divided into three groups: hypoxia preconditioning group ($n=24$, received intravenous transplantation of PBMSCs with hypoxia preconditioning), non-hypoxia preconditioning group ($n=24$, received normal culture of PBMSCs) and control group ($n=24$, only received equal-volume of culture medium). Vascular endothelial growth factor (VEGF) was determined by enzyme linked immunosorbent assay (ELISA) at 7 d, 14 d and 28 d post-angioplasty, respectively. The vessel morphology, the homing of MSCs and the reendothelialization were analysed with Weigert staining and immunohistochemistry.

Results Compared to control group, the level of VEGF significantly increased in both hypoxia preconditioning group and nonhypoxia preconditioning group at all time points ($p < 0.01$). The level of VEGF in hypoxia preconditioning group was higher than that in nonhypoxia preconditioning group ($p < 0.05$) at 7 d and 14 d, but no difference at 28 d postangioplasty was observed. At 7d, GFP-positive cells were found in both hypoxia preconditioning group and nonhypoxia preconditioning group. Neointima thickening and the rate of restenosis were lower in hypoxia preconditioning group than those in non-hypoxia preconditioning group at 28 d ($p < 0.05$), but both hypoxia preconditioning group and nonhypoxia preconditioning group were markedly lower than that in control group ($p < 0.01$). The reendothelialization in hypoxia preconditioning group outweighed that in nonhypoxia preconditioning group ($p < 0.05$), but both two groups were lower than that in control group ($p < 0.01$).

Conclusions Intravenous transplantation of PBMSCs contributes to the reendothelialization, and attenuates neointima thickening after carotid balloon induced injury in the rabbit model. Further, hypoxia