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EFFECTS OF GINSENOSIDES-RBL INHIBITING CARDIOMYOCYTE HYPERTROPHY VIA NHE-1-DEPENDENT CALCINEURIN ACTIVATION EX VIVO

Hongliang Kong, Hongbo Sun, Lijie Song *Cardiology Center, The People's Hospital Of Liaoning Province, Shenyang, China*

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Objectives Ginsenosides-Rbl (Gs-Rbl), a main component of Ginsenosides extracted from Ginseng, is a type of activity element playing a therapeutic role in the cardiovascular system. The present study aimed at determining whether Gs-Rbl exerts a direct antihypertrophic effect and the potential underlying mechanisms on cultured cardiomyocytes ex vivo.

Methods Neonatal rat ventricular cardiomyocytes were randomly divided into control group, simple phenylephrine (PE, 5 $\mu\text{mol/l}$, $\alpha 1$ adrenoceptor agonist) group and Gs-Rbl group (on the basis of PE intervention) for 36 h; The concentration of Gs-Rbl is 50 $\mu\text{mol/l}$, 100 $\mu\text{mol/l}$, 200 $\mu\text{mol/l}$ and 500 $\mu\text{mol/l}$, respectively. Cell surface area, $\text{Na}^+\text{-H}^+$ exchanger 1 (NHE-1), and NFAT3 was analysed.

Results Phenylephrine (PE) led to a marked hypertrophic effect on neonatal cardiomyocytes ($847 \pm 20 \text{ m}^2$ to $1147 \pm 30 \text{ m}^2$, $p=0.000$); Gs-Rbl attenuated hypertrophic effect of PE in a concentration-dependent manner ($p<0.01$), in which $\geq 200 \text{ }\mu\text{mol/l}$ Gs-Rbl exerted a complete inhibition of hypertrophy. PE significantly increased the expression of gene and protein of the NHE-1 (Gene: 1.77 ± 0.08 -fold; protein: 1.51 ± 0.04 -fold), increased NHE-1 activity (1.61 ± 0.11 -fold); Gs-Rbl inhibited or completely abrogated ($\geq 200 \text{ }\mu\text{mol/l}$ Gs-Rbl) the above effect of PE in a concentration-dependent manner ($p<0.01$). NFAT3 was translocated to the nuclei from the cytosol by PE, which was significantly reduced, even similar to control group once the concentration of Gs-Rbl $\geq 100 \text{ }\mu\text{mol/l}$, by Gs-Rbl. The effect of PE on increasing calcineurin activity was significantly reduced in the presence of Gs-Rbl, however, which was significantly greater than in control group.

Conclusions Ginsenosides-Rbl inhibited cardiomyocyte hypertrophy induced by phenylephrine ex vivo, which is at least mediated by inhibition of NHE-1-dependent calcineurin pathway.