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Aerobic exercise activates CHI3L1/PAR2 to promote cardiomyocyte proliferation and protect cardiac function in rats with MI

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Objective Objectives: The aim of this study is to investigate the changes of protein expression of chitinase-3-like protein 1 (CHI3L1) and its receptor PAR2 (protease-activated receptor 2) after exercise, and the possible mechanism to promote the proliferation of cardiomyocytes and protect MI rats heart.
Methods Methods: Using rhCHI3L1 (150 ng/ml), AMPK agonists (AICAR, 50 mM) separately or together administer stimulation for 24 hours.H9C2 cells were divided into control group (H9C2 group), CHI3L1 recombinant protein intervention group (H9C2+rhCHHI3L1), AMPK agonist intervention group (H9C2+AICAR), and CHI3L1 recombinant protein and AMPK agonist combined intervention group (H9C2+rhCHI3L1+AICAR).SD rats were subjected to left anterior descending(LAD) coronary artery ligation to prepare MI models and randomly divided into sham operation group (S), myocardial infarction group (MI), myocardial infarction aerobic exercise group (ME), and injection of PAR-2 blocker agent (FSLLRY-amide) was divided into 7-day PAR2 blocker injection group (7d+FS), MI 7-day saline injection group (7d+SA), MI 14 days PAR2 blocker injection group (14d+FS), MI 14-day saline injection group (14d+SA). One week after surgery, the ME group were subjected to one-week adaptively exercise followed by four weeks aerobic exercise.At the end of the training, the rats were intraperitoneally anesthetized the next day. Hemodynamic measurements of LVEDP, ±dp/dt max, and LVSP were used to evaluate cardiac function.The protein levels of CHI3L1/PAR2, pPI3K/PI3K, pAKT/AKT, pERK/ERK and Cyclin D1 in H9C2 and rat hearts were determined by Western blotting. The proliferation of H9C2 was detected by CCK-8. The proliferation of H9C2 and cardiac tissue was observed by immunofluorescence. Masson staining was used to observe myocardial collagen volume percent (CFV%).
Results Results: Compared with H9C2 control group, the expression of CHI3L1, pPI3K/PI3K, pAKT/AKT, pERK/ERK, and Cyclin D1 protein increased significantly after rhCHI3L1 and AICAR intervention for 24 h, respectively. CCK-8 test and immunofluorescence indicated that H9C2 had significant proliferation effect. In MI rat heart, compared with MI group, the expression of CHI3L1, pPI3K/PI3K, pAKT/AKT, pERK/ERK and Cyclin D1 protein in ME group increased significantly, the number of cell proliferation increased, and LVEDP significantly decreased, ±dp/dt max, LVSP significantly increased, and the CFV% decreased significantly.
Conclusions Conclusion: Exercise may promote cardiomyocyte proliferation and improve cardiac function in MI rats by activating the CHI3L1/PAR2-PI3K-AKT-ERK signaling pathway.