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Propofol and salvianolic acid A synergistically attenuated hypoxia/reoxygenation induced H92 cells injury under high-glucose and high-fat condition via modulating CD36

Jiaqi Zhou,[1] Ronghui Han,[1] Anyuan Zhang,[2] Jiajia Chen,[1] Yuxin Jiang,[1] Dongcheng Zhou,[1] Danyong Liu,[1] Liangqing Zhang,[1] Weiyi Xia,[3] Youhua Xu,[4] and Zhengyuan Xia[5]

[1]Department of Anesthesiology, Affiliated Hospital of Guangdong Medical University, Zhanjiang, China; [2]Department of Anesthesiology, the Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou; [3]Department of Orthopaedics and Traumatology, The University of Hong Kong, Hong Kong, China; [4]Faculty of Chinese Medicine, State Key Laboratory of Quality Research in Chinese Medicine, Macau University of Science and Technology, Taipa, Macao, China; and [5]State Key Laboratory of Pharmaceutical Biotechnology, Department of Medicine, The University of Hong Kong, Hong Kong, China

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Abstract

Subjects with diabetes are more vulnerable to myocardial ischemic-reperfusion injury (MIRI) and less or not sensitive to myocardial protective interventions such as ischemic preconditioning that are otherwise effective in non-diabetic subjects, and the underlying mechanism is unclear. Propofol (PPF), a widely used intravenous anesthetics, has been reported to attenuate MIRI through its reactive oxygen species scavenging property at high doses *in vitro* and *in vivo*, while application of propofol at high doses clinically may cause hemodynamic instability. Salvianolic acid A(SAA) is a potent antioxidant that confers protection against myocardial ischemic injuries. PPF and SAA both bear phenolic moieties in their molecular structure, however, whether or not these two molecules may confer synergistic cardioprotection, in particular in the context of myocardial ischemic injury under diabetic conditions, is unknown. The aim of this study was to investigate the protective effects and its underlying mechanisms of low doses of PPF combined with SAA against hypoxia/reoxygenation(H/R)-induced cardiomyocyte injury in high glucose (HG) and palmitate-treated H9c2 cardiomyocytes. Our data showed that culture H9c2 cells under stimulated diabetic condition with HG and palmitate resulted in significant cellular injury evidenced as decreased cell viability and increased lactate dehydrogenase (LDH) leakage that was concomitant with increased levels of the lipid peroxidation product malondialdehyde(MDA) and significant increase in CD36, while levels of p-AMPK was significantly reduced. These HG and palmitate-induced cell injuries/damages were further significantly exacerbated by H/R (composed of 6 hours of hypoxia followed by 12 hours of reoxygenation) but reversed by PPF or SAA respectively in a concentration dependent manner in the dose ranges of 12.5, 25 and 50 μM. Co-administration of low concentrations of PPF and SAA at 12.5 μM in H9c2 cells cultured under HG and palmitate significantly reduced the production of reactive oxygen species, ferrous ion content and lipid peroxidation and reduced CD36, while significantly increased p-AMPK, as compared to the effects of PPF at the concentration of 25 μM. Moreover, HR-induced cellular injuries and ferroptosis were significantly exacerbated by overexpression of CD36. It is concluded that combinational usage of low doses/concentrations of PPF and SAA confer superior cellular protective effects to the use of high dose of PPF alone, and that inhibition of H/R induced CD36 over-expression may represent a major mechanism by which PPF and SAA combat against cardiomyocyte H/R injuries under HG and high lipid conditions.