**ATTENUATION OF ENDOPLASMIC RETICULUM STRESS BY 4-PHENYLBUTYRIC ACID PROMOTES THE FUNCTIONAL SURVIVAL AND THERAPEUTIC EFFICACY OF BONE MARROW-DERIVED MESENCHYMAL STEM CELLS FOR HEART REPAIR**

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Endoplasmic reticulum stress (ERS) has recently been revealed to be a critical player and therapeutic target in ischemic heart injury. However, whether regulation of ERS in ischemic heart could potentiate stem cell therapy remains equivocal. In this study, we employed a well-known ERS inhibitor, 4-Phenylbutyric acid (PBA), to examine its impact on bone marrow-derived mesenchymal stem cells (BMSCs) survival and efficacy in ischemic heart. Our results depicted that PBA improved the survival of engrafted BMSCs in ischemic myocardium, accompanied by significant ameliorations of myocardial ERS . Moreover, echocardiography revealed that the combined treatment of PBA and BMSCs synergistically improved cardiac function. Furthermore, cardiac inflammatory cytokines, oxidative stress (ROS generation, MDA) and apoptosis also experienced a significant reduction in combined therapy group. In vitro studies revealed that PBA alleviated BMSCs ERS induced by hypoxia/serum deprivation (H/SD) insult and exerted cyto-protective effects on BMSCs via attenuating inflammation, apoptosis and oxidative stress. Intriguingly, up-regulating the CHOP expression by lentivirus significantly antagonized the inhibitory effect of PBA on H/SD-induced inflammation, apoptosis and oxidative stress in BMSCs. Our data support the promise of anti-ERS by PBA in ischemic heart as a promising strategy to facilitate MSC-based therapy for MI.

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