Dilong prevents the High-KCL Cardioplegic Solution Administration Induced Fibrosis in H9c2 cardiomyoblast cells

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Abstract

Dilong（earthwarm）has been used as a traditional medicine in China for several thousand years, and extract from the Dilong has been empirically used in Asia for the treatment of vascular disorders (1). Infusion of high KCl cardioplegia solution (High-KCS) is the most common method for inducing asystole before cardiac surgery. However, our previous study showed the High-KCS can cause cardiac fibrosis in cardiomyocytes and patients who were administered High-KCS prior to undergoing coronary artery bypass graft (CABG) to treat coronary artery disease (CAD).

H9c2 cardiomyoblast cells were cultured in serum-free medium for 4 h then treated Dilong (31.25, 62.5, 125 and 250 μg/ml) for 24h , and followed by High-KCS treatment for 3 h to detect the protective mechanisms of Dilong behind cardiac fibrosis. Cells were harvested for JC1 assay and western blot analysis.

The IGF-I/IGF-IR/ERK pathway involved in cardiac fibroblast proliferation, and the expression/activation of uPA,Sp-1 and CTGF, which are implicated in the development of cardiac fibrosis were upregulated in postcardioplegic right atriums and cardiac fibroblasts. However, Akt for cardiomyocyte survival was greatly deactivated in postcardioplegic right atriums and in cultured cardiomyocytes. However, Dilong highly protection and totally reverse cardiac fibrosis effects induced by High-KCS.

High KCl cardioplegia appears to induce mitochondrial injury and Akt deactivation, causing cardiomyocytes apoptosis. The activated IGF-I/IGF-IR/ERK pathway and the upregulation of uPA, Sp-1 and CTGF in cardiac fibroblasts further promote the development of cardiac fibrosis. However, Dilong totally reversed the High-KCS induced H9c2 cardiomyoblast cell fibrosis effects. Dilong could be a potential agent to block the side effects caused by High KCl cardioplegia in CABG surgery patients.

Keyword：earthworm ; Dilong ; high KCl cardioplegia solution (High-KCS); coronary artery bypass graft (CABG) ; coronary artery disease (CAD) ; H9c2 cardiomyoblast cells ; peripheral nerve regeneration.

1.Introduction