Pre-conditioning Penehyelidine Hydrochloride Decreases the Myocardial Ischemia-Reperfusion Injury through the Modulation of Mitochondria Pathway

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Background: Recent study found that myocardial ischemia with inadequate oxygen supply followed by successful reperfusion initiates a wide and complex array of inflammatory responses that may both aggravate myocardial injury as well as induce impairment of remote organ function, which is called ischemia-reperfusion injury (IRI). How to attenuate IRI have been becoming the main problems in the treatment of myocardial ischemia.

The mitochondria are the control center of cell life activities. It is not only the center of the cell respiration chain and oxidative phosphorylation, but also the regulation center of cell apoptosis. When promoting apoptosis factor act on the mitochondria, the activity of Voltage-dependentanion channel (VDAC) increase, which results in the mitochondria permeability transition pore excessively open, apoptosis perform factor cytochrome C (cyt-c) released from mitochondria to cytoplasm, then cascade of apoptosis started[1].

Penehyelidine hydrochloride (PHC) is a new selective cholinergic antagonist found by China. Clinical studies have found that it has myocardial protection, anti-inflammatory, cell membrane stability, and improve microcirculation[2], but its mechanism is not clear.

Methods: Male Sprague-Dawley rats weighing 200–300 g were randomly assigned to two groups, IRI group (given saline by introveneous injection at 5 min before IR) and PHC +IRI group (given 1mg/kg of PHC by introveneous injection at 5 min before IR).The IRI was produced in rat heart based on Burke's description with modifications [3]. Myocardial infarct size was expressed as percentage of infarct area (INF) over total area at risk (AAR) (INF/AAR * 100%) [4].The expression of cyt-c and VDAC 1 in mitochondria were determined by western blot.

Results: Myocardial infarct size was 23.96% and 18.85% in IRI group and PHC+IRI group, separately. The cyt-c and VDAC 1 in mitochondria after IRI were shown in figure 1.

Conclusion: Pre-conditioning with 1 mg/kg PHC in IRI rats may decrease the myocardial IRI through the modulation of mitochondria pathway.

References

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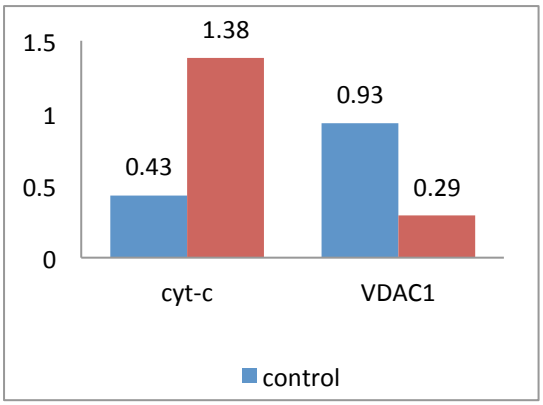

Figure 1. The expression of cyt-c and VDAC 1 in mitochondria.