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INHIBITION OF THE ACTIVITY OF POLY (ADP-RIBOSE) POLYMERASE REDUCES HEART ISCHAEMIA/ REPERFUSION INJURY VIA SUPPRESSING JNK MEDIATED AIF TRANSLOCATION

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[1]Song Zhao-feng, [2]Chen Dong-yu, [1]Du Bo, [3]Ji Xiao-ping, [1]Song Zhao-feng.
[1]Department of Cardiology, Taian Central Hospital, 271000 Taian, Shandong Province, China; [2]Department of Rheumatology, Taian Central Hospital, 271000 Taian, Shandong Province, China; [3]Department of Cardiology, Shandong University Qilu Hospital, 250012 Jinan, Shandong Province, China

Objectives Poly (ADP-ribose) polymerase (PARP) played an important role in the pathogenesis of heart ischaemia/reperfusion (I/R) injury. The mechanisms are still not thoroughly understood. Here we investigated the effect of PARP inhibition on heart I/R injury and elucidated the underlying mechanisms.

Methods Studies were performed with I/R rats' hearts. 3,4-dihydro-5-[4-(1-piperidinyl) butoxy]-1(2H)- isoquinolinone (DPQ) was used to inhibit the activate of PARP. The myocardial infarction size, cardiac function and cells apoptosis were detected. The activation of PARP, c-Jun NH_2-terminal kinase (JNK) and Apoptosis-inducing factor (AIF) were evaluated during the I/R protocol.

Results Heart I/R caused a significant increase in PARP, JNK and AIF activity. Administration of DPQ decreased myocardial infarction size from 60.97±4.22% to 39.03±3.94% $p<0.05$) and cells apoptosis from 35±5.3% to 20±4.1% $p<0.05$) and simultaneously improved the cardiac function. Administration of DPQ reduced the activation of JNK and attenuated mitochondrial-nuclear translocation of AIF. Administration of SP600125 also attenuated mitochondrial-nuclear translocation of AIF.

Conclusions Our results suggested that the inhibition of PARP was able to reduce heart I/R injury. JNK may be downstream of PARP activation and be required for PARP mediated AIF translocation. Inhibition of the activity of PARP may reduce heart I/R injury via suppressing AIF translocation mediated by JNK.