OMICS Group Conferences
Accelerating Scientific Discovery

4th World Congress on
Diabetes & Metabolism

August 14-16, 2013 Holiday Inn Chicago-North Shore, IL, USA

N-Acetylcysterine and Allopurinol confer synergy in attenuating myocardial ischemia injury via restoring HIF-1α /HO-1 signaling in diabetic rats

Zhengyuan Xia
The University of Hong Kong, China

Background: The antioxidants N-acetylcysteine (NAC) and allopurinol (ALP) can synergistically reduce myocardial ischemia/reperfusion (MI/R) injury in rats with streptozotocin (STZ) - induced diabetes. We investigated whether or not NAC and ALP confer synergistic cardioprotection by stabilizing hypoxia inducible factor 1-α (HIF-1α)/hemeoxygenase 1 (HO-1) signaling in the diabetic myocardium.

Methods: Control or diabetic Sprague-Dawleyrats received vehicle, NAC, ALP or their combination for four weeks starting one week after STZ injection. The animals were then subjected to 30 minutes of coronary artery occlusion followed by two hours of reperfusion in the absence or presence of tin protoporphyrin-IX (selective HO-1 inhibitor) or 2-Methoxyestradiol (HIF-1α inhibitor). Cardiomyocytes exposed to high glucose were subjected to hypoxia/re-oxygenation in the absence or presence of HIF-1α siRNA or HO-1 siRNA.

Results: Myocardial and plasma levels of 15-F2t-isoprostane, an index of oxidative stress, were increased significantly in diabetic rats while cardiac HO-1 protein and activity were reduced, which was accompanied with decreased cardiac protein levels of HIF-1α and augmented post-ischemic myocardial infarct size and cellular injury. Both NAC and ALP but in particular their combination normalized cardiac levels of HO-1 and HIF-1α protein expression and prevented the increase in 15-F2t-isoprostane, resulting in significantly attenuated post-ischemic myocardial infarction. NAC and ALP also attenuated hyperglycemia-induced post-hypoxic cardiomyocyte death in vitro. However, pharmacological inhibition of HIF-1α or HO-1 or their gene knock-down prevented the protective effects of NAC and ALP.

Conclusion: NAC and ALP confer pharmacological cardioprotection in diabetes via the restoration of cardiac HIF-1α and HO-1.

Biography

Zhengyuan Xia had served as a Cardiovascular Anesthetist for more than 10 years in China before he completed his Ph.D. study at the University of British Columbia (UBC), in Canada in 2004 and postdoctoral studies at UBC and University of Calgary in 2007. He is Assistant Professor and Honorary Associate Professor and Director of Cardiovascular Anesthesiology Research Laboratory of the Department of Anesthesiology at the University of Hong Kong. His major focus of research is cardiac protection during ischemia-reperfusion in diabetes. He has published more than 70 papers in reputed journals and is serving as an Executive Editor of Journal of Diabetes & Metabolism.

zyxia@hkucc.hku.hk