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Restoration of myocardial brg1 protein expression by antioxidant N-Acetylcysteine attenuates cardiac dysfunction in type1 diabetic rats

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Abstract

Background: Hyperglycemia-induced oxidative stress contributes to the development and progression of diabetic cardiac complications. Brahma-related gene 1(Brg1) is a key gene in inducing the expression of important endogenous antioxidant enzymes, including heme oxygenase-1(HO-1) which is central to cardioprotection, while cardiac HO-1 expression is reduced in diabetes. It is unknown whether or not Brg1 expression is reduced in the myocardium of diabetes. We hypothesize that cardiac Brg1 expression is reduced in diabetes which can be restored by antioxidant treatment with N-acetylcysteine(NAC).

Methods: Control(C) and streptozotocin-induced diabetic(D) rats were treated with NAC in drinking water or placebo for 4 weeks. Upon completion of treatment, cardiac structure and function were assessed by echocardiography, and plasma and heart tissue free 15-F_{2t}-isoprostane, an index of oxidative stress, was assessed by enzyme immunoassay. Myocardial Brg1, STAT3 and HO-1 protein expression were assessed by Western blotting.

Results: Plasma and cardiac free15-F_{2t}-isoprostane in diabetic rats were increased, accompanied with increased plasma levels of tumor necrosis factor-alpha(TNF)-alpha and interleukin(IL)-6,while cardiac Brg1, p-STAT3 and HO-1 protein expression were significantly decreased(all $P<0.05$ vs. control). Left ventricle weight/body weight ratio was higher, while the peak velocities of early (E) and late (A) flow ratio was lower in diabetic than in control rats($P<0.05$). NAC normalized tissue and plasma levels of 15-F_{2t}-isoprostane, significantly increased cardiac Brg1, HO-1 and p-STAT3 protein expression and reduced TNF-alpha and IL-6, resulting in improved cardiac function.

Conclusion: MyocardialBrg1 is reduced in diabetes and enhancement of cardiac Brg1 expression may represent a novel mechanism whereby NAC confers cardioprotecion.

Biography

ZiqingHei has completed his Ph.D from Sun Yat-sen University in China in 2003 and was invited as a visiting scholar in University of Florida in 2009 for 1 year. He serves as a doctor in liver transplantation for more than 20 years. Now, He is a Professor and Head of the Department of Anesthesiology, Third Affiliated Hospital, Sun Yat-sen University, Guangzhou, China. His major focus of research is mechanism of graft injury and therapeutic strategies in liver transplantation. He has published more than 100 papers in reputed journals and services as a reviewer for more than 6 reputed journals.