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CANDESARTAN PROTECTS HEAT SHOCKAGAINST HEAT SHOCK-INDUCED CARDIAC INJURIES IN SPONTANEOUSLY HYPERTENSIVE RATS

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BACKGROUND/AIMS：Angiotensin II plays a role in cardiac dysfunction and injury in hypertension. Blockade of angiotensin II AT1 receptors (ARB) in myocytes protects against cardiac damage and pathologic remodeling. We examined the protective effects of the ARB candesartan on cardiomyocyte injury after heat shock in hypertension

METHODS：Spontaneously hypertensive rats (SHR) and Wistar Kyoto (WKY) controls were treated with ARB (Candesartan, 0.3mg/kg per day) via subcutaneous osmotic minipumps for 4 weeks . Heat shock was induced by exposing the rat to high blanket temperature. Hearts were harvested 1 –to 7 days after heat shock for histopathology, immunof luoresence studies, and quantitative real-time reverse transcriptase-polymerase chain reaction analyses to assess the change in gene expression profiles of α-myosin heavy chain (∂-MHC), atrial natriuretic factor (ANF), and transforming growth factor β_1 (TGF-β_1) .We also investigated the effects of ARB on circulating and cardiac components of the renin-angiotensin system.

RESULTS/CONCLUSIONS：Results were compared with those of age-matched WKY rats and untreated SHR with and without heat shockheat shock . Candesartan in WKY and SHR prevented the changes in α-MHC , AHF, and TGF-β_1 gene expression that are associated with cardiac injury heat shockdue to to heat shock. Candesartan initiated after the heat shock lowered levels of TGF-β_1, mRNA and elevated levels of α-MHC mRNA and AT_2 receptor mRNA in SHR. Circulating levels of renin, angiotensin I , and angiotensin II were elevated after heat shock ,and increased gene expression was higher in SHR. In SHR, AT1 receptor mRNA and protein expression was higher than in WKY with and without evidence of heat shock. After heat shock, candesartan treatment in SHR significantly decreased TGF-β_1 mRNA levels were higher ($P<0.05$), whereas increased AT_2 receptor and α-MHC mRNA levels were higher ($P<0.05$) than WKY. The results suggest that the anti-heat shock cardiac injury benefits of ARB in hypertension may be mediated by effects on the expression of specific genes, including those encoding α-MHC, ANF, TGF-β_1, and local renin-angiotensin system components.

Key word: AT1 receptor blocker, hypertension, rennin-angiotensin system.