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Changes in the Expressional Levels of SR Ca^{2+} Regulatory Proteins of Hypertensive Rats

Miyoung Park*, Eun Hee Lee, Hee Ran Lee[1], and Hae Won Kim
Department of Pharmacology, University of Ulsan College of Medicine; [1]Asan Institute for Life Sciences, Seoul 138-736

We have investigated whether alterations in the expression levels of sarcoplasmic reticulum (SR) Ca^{2+} regulatory proteins in heart and mesenteric arteries from different models of hypertension would occur. Nephrectomied diabetic-hypertensive rats (DM-HT) and spontaneously hypertensive rats (SHR) were used as models of hypertension. Age-matched nephrectomied SD rats and Wistar-Kyoto rats served as normotensive controls for DM-HT and SHR, respectively. The relative expression levels of mRNA encoding the major SR proteins were determined by the competitive RT-PCR using the gene-specific oligonucleotide primers and equal amounts of cDNA synthesized from total RNA extraction. SR Ca^{2+}-ATPase mRNA level was markedly decreased in two models of hypertensive rat heart compared to normotensive control. The expression levels of mRNA for phospholamban (PLB, the regulator of the SR Ca^{2+}-ATPase) were not changed in experimental DM-HT rats heart, whereas they were increased in SHR hearts. The ryanodine receptor mRNA level was not changed in both models. Furthermore, we have determined whether alterations in various SR proteins would occur in small mesenteric arteries from hypertensive rats. Smooth muscle SR from hypertensive mesenteric arteries showed decreases in Ca^{2+}-ATPase, increases in PLB, and no changes in IP_3 receptor (IP_3-R) mRNA levels compared to normotensive smooth muscle SR by RT-PCR in both DM-HT and SHR. These results indicate that the cardiac dysfunction induced by pressure overload is associated with an abnormal calcium-handling defect, which may contribute to a diastolic disorder of the heart by causing intracellular Ca^{2+} overload. The inverse relationship on the changes of expression in SR Ca^{2+}-ATPase and PLB in mesenteric arterial smooth muscle may provide an explanation for the decreased relaxation in these vessels and the elevated total peripheral resistance associated with hypertension. Supported by grant from MOHW (1997.5-1999.4)