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Altered Sarcoplasmic Reticulum Ca^{2+} Uptake of H9c2 Cells Cultured in High Glucose Medium

Eun Hee Lee, Young Joo Seo, Jun Whee Lee, Joong Sik Jang, Young-Hoon Kim, and Hae Won Kim
Department of Pharmacology, University of Ulsan College of Medicine, Seoul 138-736, Korea

Altered intracellular Ca^{2+} homeostasis is presumably the primary mechanism of the diastolic impairment in diabetic cardiomyopathy. However, causal relations of numerous environmental changes observed in the diabetic heart have been left unresolved. In the present study, we sought to establish an *in vitro* model of diabetic cardiomyopathy using H9c2 cardiac myocyte cell line. Confluent H9c2 cells cultured for 2 weeks showed the morphology of differentiated cardiomyocytes. High glucose (25 mM) did not affect the proliferation or differentiation during this period. We developed a method to measure sarcoplasmic reticulum (SR) Ca^{2+} uptake in digitonin-permeabilized cells and analysed the SR Ca^{2+} uptake in cell groups exposed to normal and high glucose medium. Cells exposed to high glucose showed markedly suppressed SR Ca^{2+} uptake rate (40 % decrease in V_{max} by exposure to high glucose for 2 weeks), and the suppression of SR Ca^{2+} uptake was dependent on the duration of exposure to high glucose medium. The suppression was reversible by normalizing the medium glucose concentration for 5 days. Protein expression levels of SR Ca^{2+}-ATPase (SERCA) and phospholamban (PLB) were also analysed, which indicate the increased expression of PLB but no changes in SERCA expression in high glucose group. Increased expression of PLB was also reversible by lowering the medium glucose concentration. Changes in SR Ca^{2+} uptake of H9c2 cells by high glucose were compatible with those observed in diabetic animal models. We could conclude that high glucose alone can induce SR dysfunction, and the decreased SR Ca^{2+} uptake was, at least in part, due to the increased expression of PLB.