Blockade of Slow Component of the Delayed Rectifier K^+ Current (I_{Ks}) Prolonged Action Potential Duration (APD) without Increasing Dispersion between Ventricles

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[Aim] Spatial heterogeneity of action potential duration (APD) and the underlying ionic basis is poorly understood. In the present study, we compared APD together with two components of delayed rectifier potassium current, I_{Kr}, I_{Ks}, and expression of channel subunits in rabbit right and left ventricular myocytes. **[Methods]** APD of epicardium was obtained from right ventricle (RV) and left ventricle (LV) by multi-channel optical recording stained with a voltage-sensitive dye. Effects of I_{Kr} blockade (E-4031 10μM) and I_{Ks} blockade (chromanol 293B 10μM) on APD were investigated. I_{Kr} and I_{Ks} were recorded from single ventricular myocytes by using whole-cell patch clamp techniques; and measured as chromanol 293B (30μM) resistant and E-4031 (10μM) resistant current. mRNA levels were measured by qualitative real-time PCR. **[Results]** E-4031 caused a greater APD prolongation in RV than in LV (e.g. 179 ± 15 ms vs. 123 ± 11 ms at 1Hz, n = 10, $P < 0.05$). However, chromanol 293B caused APD prolongation to a similar extent in RV and LV (e.g. 13 ± 5 ms vs. 18 ± 9 ms at 1Hz, n = 10, $P > 0.05$). The amplitude of I_{Kr} were not significantly different in two ventricles (RV: 0.83 ± 0.08 pA/pF; LV: 0.61 ± 0.13 pA/pF, n=14, $P > 0.05$). While I_{Ks} was considerably smaller in RV than in LV (0.86 ± 0.15 pA/pF vs. 1.72 ± 0.32 pA/pF, n=12, $P < 0.05$). mRNA levels were not significantly different between ventricles in *ERG* (RV: 1103 ± 218 molecules/ 10^5 GAPDH molecules, LV: 886 ± 155, n=4), *KVLQT1* (RV: 645 ± 113, LV: 509 ± 170, n=4) and *mink* (RV: 209 ± 33, LV: 185 ± 47, n=4). **[Conclusion]** I_{Ks} blocker produces a favorable APD prolongation without affecting biventricular dispersion and might be more potent to treat arrhythmias than I_{Kr} blocker.

Internalization and Dephosphorylation of Connexin43 Gap Junctions in Hypertrophied Rat Ventricular Myocytes

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[Aim] Altered expression and distribution of gap junctions in hypertrophied hearts may provide a potential substrate for abnormal conduction. We investigated microscopic gap junction localization and phosphorylation state of connexin43 (Cx43) in association with ventricular hypertrophy. **[Methods]** The Cx43 immunolocarization was studied in hypertrophied right ventricular myocytes isolated from rats with monocrotalin-induced pulmonary hypertension with the aid of confocal microscopy. The phosphorylation state of Cx43 was evaluated by Western blot using an antibody that selectively binds to the non-phosphorylated isoform. **[Results]** In hypertrophied ventricular myocytes, there was a significant increase in the Cx43 immunolabeling within the cytoplasm ("internalized" Cx43) compared with controls in addition to a decrease in the Cx43 labering localized to the intercalated disk and an increase in that on the lateral sarcolemma. These changes were associated with a significant increase in the non-phosphorylation isoform of Cx43 without a change in the total amount of Cx43 protein. **[Conclusion]** Gap junction remodeling in ventricular hypertrophy involves in an inhibition of Cx43 protein localization at the intercalated disk area and such gap junction disorganization may be the result of Cx43 dephosphorylation.