Action Potential Modelling in Isolated Rat Hearts during Hypokalemia

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Introduction: Hypokalemia is the most common electrolyte abnormality encountered in clinical practice and enhances the propensity for ventricular fibrillation. Melatonin is a potential antiarrhythmic, but the mechanisms of action are poorly understood. For a better analysis of hypokalemic electrophysiological effects, we developed an automatic methodology for modeling rats action potential and ECG.

Materials and Methods: Isolated rat hearts underwent low K+ perfusion (1 mEq/L) in 4 groups: 1) Mel, 100 μM melatonin; 2) Luz, luzindole 5 μM a melatonin receptor blocker; 3) Mel+Luz melatonin+luzindole; or 4) Control. The ECG and epicardial action potential (AP) were recorded and automatically analyzed with an ad-hoc algorithm also presented in this conference. The AP was modeled by morphological and temporal features. The activation delay between the start of the QRS complex and the AP was also calculated.

Results: As expected during hypokalemia, QT interval lengthened in all the groups. All heart developed bradycardia and PR lengthening (in ms: Control 53.2 ± 5.6 to 57.4 ± 8.7 *; Mel 51.7 ± 4.8 to 59.4 ± 6.7 *; Mel+Luz 51.0 ± 4.3 to 58.7 ± 6.9 *; and Luz 52.8 ± 5.7 to 56.5 ± 6.4 *). Melatonin was the only treatment that prevented the prolongation in the activation delay induced by hypokalemia (in ms: Control 8.8 ± 1.9 to 14.2 ± 2.0 ***; Mel 7.8 ± 2.4 to 9.4 ± 2.8; Mel+Luz 8.8 ± 1.3 to 15.7 ± 2.2 ***; and Luz 8.8 ± 1.4 to 13.3 ± 2.6 *). On the other hand, hypokalemia increased QRS duration only the control group (in ms: Control 13.2 ± 1.7 to 18.3 ± 1.7***; Mel 12.7 ± 2.6 to 14.4 ± 2.1; Mel+Luz 12.1 ± 2.0 to 15.2 ± 3.2; and Luz 11.2 ± 1.7 to 15.4 ± 1.5). * $P<0.05$, ** $P<0.01$, and *** $P<0.001$ by ANOVA.

Discussion: Hypokalemia increases the incidence of arrhythmic death. Melatonin protects against several cardiovascular diseases and exhibits antiarrhythmic potential. Our results with melatonin could be related to a previously described up-regulation of myocardial connexin-43, the main protein responsible for electrical coupling. The automatic methodology presented in this work allowed a more accurate insight of the differential effects in QRS and activation delay lengthening of melatonin as a therapeutic option against hypokalemia.