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Antiarrhythmic action of melatonin is associated with its effects on ventricular spatiotemporal depolarization pattern

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Topic(s):
Basic Science - Cardiac Diseases: Arrhythmias

Citation:
The study was supported by Russian Science Foundation (RSF 18-15-00309).

Introduction: Melatonin was proposed as a versatile cardioprotective agent in ischemia/reperfusion conditions with probable antiarrhythmic effects, whose mechanisms remain to be established. This study aimed to assess an association between chronic melatonin effects on spatiotemporal ventricular electrophysiological parameters and incidence of ventricular tachycardia and/or ventricular fibrillation (VT/VF) in experimental model of acute ischemia/reperfusion in rats.

Methods: Melatonin (2.5-10 mg/kg, orally) was administrated for 7 days to adult male rats (n=28), whereas control animals (n=13) received placebo. Myocardial ischemia was induced in anesthetized rats by 5-min ligation of left anterior descending artery followed by reperfusion. Unipolar epicardial electrograms were recorded from ischemic and nonischemic regions (64-lead arrays) with a custom-designed high-resolution system (4 kHz). Activation time (AT), repolarization time (RT) and activation-repolarization interval (ARI) were measured in each lead.

Results. As expected, ischemia resulted in AT prolongation and RT shortening, whereas reperfusion led to partial recovery of the ATs and RTs. During the first 5 min of reperfusion, 17 out of 41 animals experienced VT/VF episodes. Dose-independently, melatonin treatment decreased VT/VF incidence as compared to placebo (8/20 vs 9/4, p=0.014). The treated animals differed from controls in preischemic (9.39±0.26 vs 10.58±0.33 ms, p=0.012) and reperfusion (11.11±0.50 vs 13.46±0.84 ms, p=0.025) ATs, baseline-reperfusion difference in RTs (2.75±0.66 vs 6.38±1.58 ms, p=0.049) and baseline-reperfusion difference in ARIs (5.46±0.77 vs 9.00±1.69 ms, p=0.033). Among the above parameters, only the preischemic ATs were different in VT/VF-positive and negative animals (10.41±0.35 vs 9.31±0.25 ms, p=0.012) and predicted VT/VF occurrence in a multivariate logistic regression analysis (B=1.872, 95% CI 1.106-3.169, p=0.020).

Conclusion. 7-day melatonin treatment enhanced normal myocardial propagation of depolarization associated with the better arrhythmic outcome in the rat acute ischemia/reperfusion model.