Melatonin as an antiarrhythmic agent – electrophysiological targets in the ischemic myocardium

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Ventricular tachyarrhythmias, especially fibrillation, are frequent and often fatal complications of acute myocardial infarction. Development of cardioprotective drugs with antiarrhythmic properties presents an important research challenge. Melatonin is positioned as a promising cardioprotective medication, whose effects are thought to be largely mediated by its antioxidative properties. On the other hand, a role of signaling pathways via melatonin receptors in the cardioprotective and specifically antiarrhythmic effects of melatonin still need to be determined. As ventricular fibrillation is primarily an electrophysiological phenomenon, it is reasonable to attempt managing this arrhythmia on the basis of electrocardiographic predictions and targeting at specific electrophysiological substrates. Melatonin and some other antioxidants provide pronounced myocardial electrophysiological effects in the ischemic conditions. Dispersion of repolarization, a prerequisite of reentrant arrhythmias, was significantly reduced by several antioxidants. However, few of them had documented antiarrhythmic effects. On the other hand, melatonin not only modified the repolarization parameters but also improved activation spread acting on cellular and tissue levels. The melatonin effect on activation was associated with reduction of ventricular fibrillation incidence, did not relate to oxidative stress but was abolished by the block of MT1/MT2 receptor. These data suggest involvement of MT1/MT2 signaling pathway in the antiarrhythmic action of melatonin.