Protective effects of melatonin on myocardial ischemia/reperfusion injury in vivo.

許準榕
Lee YM;Chen HR;Hsiao G;Sheu JR;Wang JJ;Yen MH

Abstract

The production of oxygen free radicals has been strongly implicated as an important pathophysiological mechanism mediating myocardial ischemia/reperfusion (I/R) injury. Various antioxidants have cardioprotective effects. Melatonin, an indoleamine synthesized by the pineal gland, is a potent antioxidant and a direct free radical scavenger. This is the first in vivo study to evaluate the effect of melatonin (0.5, 1.0, and 5.0 mg/kg, i.v. bolus) on myocardial I/R injury in anesthetized Sprague-Dawley rats. Results demonstrate that pretreatment with intermediate or high doses of melatonin (1.0 and 5.0 mg/kg) at 10 min before left coronary artery occlusion markedly suppressed ventricular tachycardia (VT) and ventricular fibrillation (VF), while reducing the total number of premature ventricular contractions and total duration of VT and VF that occurred during the 45-min ischemic period. Pretreatment with melatonin dramatically improved survival rate of rats when compared with the I/R-only group. After 1-hr reperfusion, melatonin caused a significant reduction in infarct size when compared with I/R-only group. Meanwhile, pretreatment with melatonin (1.0 mg/kg) significantly reduced superoxide anion production and myeloperoxidase activity; the latter is an index of neutrophil infiltration in the ischemic myocardium. Additionally, pretreatment with melatonin (1.0 and 5.0 mg/kg) significantly attenuated ventricular arrhythmias and mortality elicited by reperfusion following 5-min ischemia. In conclusion, melatonin suppresses ischemia- and reperfusion-induced ventricular arrhythmias and reduces infarct size resulting from I/R injury. The pronounced cardioprotective activity of melatonin may be mediated by its antioxidant activity and by its capacity for neutrophil inhibition in myocardial I/R.