Physiological Concentration of 17β-Estradiol on Sympathetic Reinnervation in Ovariectomized Infarcted Rats

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摘要

Abstract

17beta-Estradiol (E2) has been shown to exert antiarrhythmic effect after myocardial infarction; however, the mechanisms remain unclear. This study was performed to determine whether E2 exerts beneficial effects through attenuated sympathetic hyperreinnervation after infarction. Two weeks after ovariectomy, female Wistar rats were assigned to coronary artery ligation or sham operation. Twenty-four hours after coronary ligation, rats underwent one of five treatments: 1) sc vehicle treatment (control), 2) sc E2 treatment, 3) sc E2 treatment + tamoxifen (a potent estrogen receptor antagonist), 4) bosentan (an endothelin receptor blocker), or 5) sc E2 treatment + bosentan and followed for 4 wk. Myocardial endothelin-1 and norepinephrine levels at the remote zone revealed a significant elevation in control infarcted rats, compared with sham-operated rats, which is consistent with sympathetic hyperinnervation after infarction. Sympathetic hyperinnervation was blunted after giving the rats either E2 or bosentan, assessed by immunohistochemical analysis of tyrosine hydroxylase, growth-associated protein 43 and neurofilament, and Western blotting and real-time quantitative RT-PCR of nerve growth factor. Arrhythmic scores during programmed stimulation in E2-treated infarcted rats were significantly lower than in control-infarcted rats. Addition of bosentan did not have additional beneficial effects, compared with rats treated with E2 alone. The beneficial effect of E2 on sympathetic hyperinnervation was abolished by tamoxifen. Our data indicated that E2 has a role for sympathetic hyperinnervation after infarction, probably through an endothelin-1-depedent pathway. Chronic administration of E2 after infarction may attenuate the arrhythmogenic response to programmed electrical stimulation.