題名:Effect of ATP-sensitive potassium channel agonists on sympathetic hyperinnervation in postinfarcted rat hearts.

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摘要:Although the acute administration of ATP-sensitive potassium (K(ATP)) channel agonists provides a neuroprotection, it is unclear whether similar benefits are found by modulating sympathetic innervation in chronic settings after myocardial infarction. We assessed whether K(ATP) channel agonists can attenuate the sprouting of cardiac sympathetic nerves after infarction. Male Wistar rats after ligating coronary artery were randomized to either saline, nicorandil, pinacidil, glibenclamide, or a combination of 1) nicorandil and glibenclamide or 2) pinacidil and glibenclamide for 4 wk. To elucidate the role of mitochondrial K(ATP) channels in modulating nerve growth factor, 5-hydroxydecanoate was assessed in an in vitro model. The measurement of myocardial norepinephrine levels revealed a significant elevation in saline-treated infarcted rats compared with sham-operated rats, consistent with excessive sympathetic innervation. Excessive sympathetic innervation was blunted after giving the rats either nicorandil or pinacidil, compared with saline, as assessed by the immunohistochemical analysis of tyrosine hydroxylase, growth associated protein-43, and neurofilament and Western blot analysis and real-time quantitative RT-PCR of nerve growth factor. The arrhythmic scores during programmed stimulation in the saline- or glibenclamide-treated infarcted rats were significantly higher than those of rats treated with K(ATP) channel agonists. In contrast, the beneficial effects of nicorandil and pinacidil were abolished by administering either glibenclamide or 5-

hydroxydecanoate. The sympathetic hyperinnervation after infarction is attenuated by the activation of mitochondrial K(ATP) channels. The chronic use of mitochondrial K(ATP) channel agonists after infarction may attenuate the arrhythmogenic response to programmed electrical stimulation.