

中文題目:各種不同降尿酸藥物對心肌梗塞大鼠交感神經再生的影響

英文題目:Differential Effect of Uric Acid Lowering Agents on Sympathetic Hyperinnervation in Post-infarcted Rat Hearts

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前言: The purpose of this study was to determine differential effects of uric acid lowering agents on sympathetic hyperinnervation and the involved mechanisms in infarcted rats.

材料及方法: Male Wistar rats after ligating coronary artery were randomized to either allopurinol, or febuxostat, chemically unrelated inhibitors of xanthine oxidase, benzbromarone or vehicle for 4 weeks.

結果: Post-infarction was associated with increased oxidant release, as measured by myocardial superoxide, isoprostane, xanthine oxidase activity and dihydroethidine fluorescence staining. Measurement of myocardial norepinephrine levels revealed a significant elevation in vehicle-treated infarcted rats compared with sham-operated rats. Sympathetic hyperinnervation was blunted after administering both xanthine oxidase inhibitors, assessed by immunofluorescent analysis of tyrosine hydroxylase, growth associated factor 43 and neurofilament, and Western blotting and real-time quantitative RT-PCR of nerve growth factor. Arrhythmic scores during programmed stimulation in the xanthine oxidase inhibitors-treated infarcted rats were significantly lower than that in those treated with vehicle. For similar levels of urate lowering, the uricosuric agent benzbromarone had no beneficial effects on oxidative stress, sympathetic hyperinnervation and arrhythmia vulnerability.

結論: Xanthine oxidase-related free radicals are implicated in the sympathetic hyperinnervation after infarction. Chronic use of xanthine oxidase inhibitors, but not uricosuric agent, is associated with down-regulation of nerve growth factor proteins probably through a superoxide-dependent pathway and thus plays a critical role in the beneficial effect on arrhythmogenic response to programmed electrical stimulation.