

论著

6- [4-(4'-吡啶)氨基苯] -4, 5-二氢-3(2H)吡嗪酮对大鼠胸主动脉环收缩功能的影响

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摘要

目的 研究新型钙增敏强心剂6- [4-(4'-吡啶)氨基苯] -4, 5-二氢-3(2H)吡嗪酮(MCI-154)的扩血管作用机制。方法 采用生物张力换能器及生理记录仪测定大鼠离体胸主动脉环和蜗膜胸主动脉环的收缩张力。结果 MCI-154可浓度依赖性抑制1 nmol·L⁻¹~10 μmol·L⁻¹去甲肾上腺素(pD₂' 为4.21±0.23)和80 mmol·L⁻¹ KCl(IC₅₀为7 μmol·L⁻¹)引起的血管环收缩, 提示其可通过抑制血管平滑肌细胞膜上受体操纵性和电压依赖性钙通道而减少胞外钙内流。在无Ca²⁺ K-H液中, MCI-154预处理可浓度依赖性降低3 μmol·L⁻¹苯肾上腺素(IC₅₀为5 μmol·L⁻¹)及20 mmol·L⁻¹ 咖啡因(IC₅₀为16 μmol·L⁻¹)引起的血管环收缩张力, 提示其可抑制血管平滑肌细胞胞内钙释放。在1 μmol·L⁻¹ Ca²⁺溶液中, MCI-154可显著降低蜗膜血管环收缩张力(IC₅₀为10 μmol·L⁻¹), 提示其可降低血管平滑肌对Ca²⁺的敏感性。结论 MCI-154可通过抑制血管平滑肌胞外钙内流、胞内钙释放和降低其对Ca²⁺敏感性来降低血管平滑肌收缩张力, 体外具有扩血管效应。

关键词 6- [4-(4'-吡啶)氨基苯] -4,5-二氢-3(2H)吡嗪酮 主动脉, 胸 肌, 平滑, 血管 血管收缩 钙敏感性

分类号

Effects of 6- [4-(4'-pyridyl)amino-phenyl] -4,5-dihydro-3(2H)-pyridazinone on contraction of aorta in rats

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Abstract

AIM To explore the mechanism of vasodilation effect of 6- [4-(4'-pyridyl)-amino-phenyl] -4,5-dihydro-3(2H)-pyridazinone (MCI-154), a novel calcium sensitizer for cardiac contraction protein. METHODS Thoracic aorta rings isolated from rats and tension sensors were used for determining contractile tension *in vitro*. The skinned aortic rings were produced by α -toxin and used for Ca²⁺ sensitivity examination. RESULTS In H-K solution, 0.01-10 μmol·L⁻¹ MCI-154 concentration-dependently decreased contraction of aortic rings induced by 1 nmol·L⁻¹-10 μmol·L⁻¹ norepinephrine (pD₂' 4.21 ± 0.23) and 80 mmol·L⁻¹ KCl (IC₅₀ 7 μmol·L⁻¹), respectively, it suggested that MCI-154 decrease extracellular Ca²⁺ influx by receptor-operate Ca²⁺ channel and potential-dependent Ca²⁺ channel. In Ca²⁺-free H-K solution, 0.01 - 10 μmol·L⁻¹ MCI-154 significantly reduced contraction of aortic rings initiated by 3 μmol·L⁻¹ phenylephrine (IC₅₀ 5 μmol·L⁻¹) and 20 mmol·L⁻¹ caffeine (IC₅₀ 16 μmol·L⁻¹), it was revealed that MCI-154 inhibited intracellular Ca²⁺ release from sarcoplasmic reticulum. In 1 μmol·L⁻¹ Ca²⁺ solution, 0.01-10 μmol·L⁻¹ MCI-154 remarkably decreased the Ca²⁺-activated contraction developed in α -toxin- treated skinned aortic rings (IC₅₀ 10 μmol·L⁻¹), it was indicated that MCI-154 decreased sensitivity of VSM contractile elements by Ca²⁺. CONCLUSION MCI-154 inhibits vascular contraction by decreasing extracellular Ca²⁺ influx, intracellular Ca²⁺ release from sarcoplasmic reticulum and sensitivity of VSM contractile elements by Ca²⁺.

扩展功能

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