

论著

## MCI-154对心肌肥厚大鼠离体心脏的正性变力作用及其机制

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收稿日期 2003-11-12 修回日期 网络版发布日期 2008-9-26 接受日期 2994-6-14

**摘要** 目的 探讨钙增敏剂MCI-154〔6-〔4-(4-吡啶氨基)苯基〕-4, 5-二氢-3(2H) 吡嗪酮)对心肌肥厚心脏与对正常心脏的作用是否不同及有关的机制。方法 利用离体心脏灌流技术观察MCI-154对心肌肥厚大鼠心功能的影响;应用离子影像学分析系统同步测定心肌细胞钙浓度瞬变和细胞长度。结果 ① MCI-154 100~400  $\mu\text{mol}\cdot\text{L}^{-1}$ 范围内浓度依赖性地提高了心肌肥厚大鼠心功能的各项指标。在400  $\mu\text{mol}\cdot\text{L}^{-1}$ 时,左室主动收缩压(左室收缩峰压与左室舒张末压之差)及左室压最大上升速率( $+dp/dt_{\text{max}}$ )与对照值相比显著增加,左室压最大下降速率( $-dp/dt_{\text{max}}$ )有增高趋势,但无统计学意义;② MCI-154 10~100  $\mu\text{mol}\cdot\text{L}^{-1}$ 在钙瞬变无明显改变情况下,呈浓度依赖性增加肥厚心肌细胞的缩短程度和钙敏感性;③ MCI-154对肥厚心肌细胞钙瞬变的50%和90%恢复时间影响不大。结论 在心肌肥厚大鼠心脏上,和在正常大鼠心脏上一样,MCI-154主要通过钙增敏作用发挥其正性变力作用。

**关键词** 钙增敏剂 MCI-154 心脏肥厚 心脏收缩 钙,细胞内

分类号 R972

## Positive inotropic effect of MCI-154 on hypertrophied heart of rats and its mechanisms

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### Abstract

**AIM** To explore if there is a differential effect of MCI-154〔6-〔4-(4'-pyridylamino) phenyl〕-4,5-dihydro-3(2H)-pyridazinone hydrochloride trihydrate〕, a calcium sensitizer, on hypertrophied hearts compared with normal hearts and the possible mechanisms underlying it. **METHODS** Functions of rat hypertrophied heart were investigated using Langendorff perfusion.  $\text{Ca}^{2+}$  transient and cell shortening in isolated cardiac myocytes were simultaneously measured using ion imaging system. **RESULTS** ① MCI-154 100-400  $\mu\text{mol}\cdot\text{L}^{-1}$  improved cardiac performance assessed by active systolic pressure (left ventricular systolic pressure minus left ventricular diastolic pressure) and  $+dp/dt_{\text{max}}$  in hypertrophied hearts as well as in normal ones, and  $-dp/dt_{\text{max}}$  tended to increase slightly with no statistical significance; ② MCI-154 concentration-dependently increased cell shortening in hypertrophied myocytes from (4.8±1.7) $\mu\text{m}$  of control to (5.6±1.5), (7.6±1.7) and (10.9±1.7) $\mu\text{m}$  at 1, 10 and 100  $\mu\text{mol}\cdot\text{L}^{-1}$ , respectively, with unaltered  $\text{Ca}^{2+}$  transient amplitude and  $\text{Ca}^{2+}$  transient decline assessed by time at 50% and 90% restoring. **CONCLUSION** MCI-154 exerted positive inotropic effect concentration dependently *via* calcium sensitizing on hypertrophied rat heart as on normal rat heart.

**Key words** calcium sensitizer MCI-154 heart hypertrophy myocardial contraction calcium cytosolic

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