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论文

奎尼丁阻滞心肌钠通道的闸门相关受体分析

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摘要：

根据闸门相关受体假说,应用计算机模拟分析了奎尼丁与心肌钠通道相互作用的动力学特点及其作用的闸门相关受体。模型预测的奎尼丁(15μmol/L)在刺激频率为1.0Hz时,表现阻滞起效速率为0.371AP^{-1},静息阻滞恢复时间常数为4.13s,均与文献报道一致。门控过程依赖性分析表明,其阻滞作用依赖于激活门控过程,奎尼丁15μmol/L对失活曲线无影响,但使激活曲线峰值降低,提示其作用于激活门相关受体。

关键词： 广东医学院药理教研室

A GATE—RELATED RECEPTOR ANALYSIS OF CARDIAC SODIUM CHANNEL BLOKADE BY QUINIDINE

YJ W U

Abstract:

Based on the gate-related receptor hypothesis ,an analysis of the kinetics of interac-tions of quinidine with cardiac sodium channels and the gate- related receptor bound by the drug wasperformed by computer simulation. Medel-predicted apparent rates of onset of quinidine(15μmol/L)blocking were shown to be 0. 613,0.371,0.274,0.226 and 0.201 Ap^{-1} respectively at stimula-tion frequencies of0.5,1.0,1 67,2.5 and 3.3 Hz. The estimated time constant of recovery fromblock by quinidine was 4.13 s.These results are in agreement with documented experimental data.Analysis of gating process dependent block by quinidine showed that the block depends on the activa-tion gating process.No shift of h_∞curve but a significant decrease of m^3_∞ curve was found in thepresence of quinidine(15μmol/L).The results suggest that quinidine binds to the activation gate-related reeeptor ,and might be trapped in the channel by the activation gate. The binding and unbind-ing of quinidine are modulated by the activation process.

Keywords: Antiarrhythmic agents Sodium channel Computer simulation Gate-related receptor Quinidine

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