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哇巴因抑制离体蟾蜍心脏收缩作用的时反应量-效关系[1]

汪萌芽，张甫同
(皖南医学院细胞电生理研究室，芜湖241001，中国)

摘要 对离体蟾蜍心脏的收缩张力-心电同步记录，发现哇巴因(Oua) 0.01—30 mmol·L^{-1}抑制收缩作用的张力抑制率，潜伏期，达峰时间，半平衡时间，20%抑制时间及心麻痹时间均呈浓度依赖性($P<0.01$)，且潜伏期和心麻痹时间为双曲线型四参数模型拟合，半平衡时间与对数浓度呈直线关系，表明Oua作用的发生与发展均存在时反应量-效关系。

关键词 哇巴因；心脏；药物剂量-效应关系；心电描记术；时间；回归分析

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Effects of bretylium tosylate on electrophysiologic properties of normal and digitalized papillary muscles of guinea pigs

LIU Yao-Chun[1], ZHU Ping-Jun, LI Zhen-Yuan, YU De-Zhang
(*Department of Physiology, Zhejiang Medical University, Hangzhou 310006, China*)

ABSTRACT The effects of bretylium tosylate (BT) on the electrophysiologic properties of normal and digitalized papillary muscles isolated from guinea pigs were studied with regular glass microelectrode. BT prolonged effective refractory period (ERP) and action potential duration (APD) of normal papillary muscles. The ERP and APD of papillary muscles were shortened by perfusion with ouabain (Oua) 0.2 μmol·L^{-1}. No recovery was seen in perfusion without drug for 30 min. In digitalized papillary muscles with Oua, ERP, APD_{50}, and APD_{90} were prolonged by BT 120 μmol·L^{-1} from 175±20, 187±20, and 146±21 ms to 222±21, 220±19, and 190±19 ms, respectively. The results demonstrated that BT can prolong ERP and APD of papillary muscles digitalized with Oua.

KEY WORDS papillary muscles; electrophysiology; bretylium tosylate; ouabain

Bretylium tosylate (BT) is an anti-arrhythmic agent of class III. BT prolongs the effective refractory period (ERP) and action potential duration (APD) of isolated Purkinje fibers and ventricular myocardium. BT is effective on various arrhythmias, but controversial results have been reported on those induced by digitalis[1,2]. This paper studied the

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[1] *Department of Physiology, Weifang Medical College, Weifang 261042, China.*

effects of BT on the electrophysiologic properties of normal and digitalized papillary muscles of guinea pigs.

MATERIALS AND METHODS

Forty-eight guinea pigs of either sex, weighing 412±s 45 g, were used. The methods and equipments were same as previous reports[3,4].

After ERP and parameters of transmembrane potentials of papillary muscles had been determined, a perfusion of 30 min was made with Tyrode's solution containing different concentrations of BT. ERP and parameters of transmembrane potentials were determined again finally.

The papillary muscles were perfused with solution containing Oua 0.2 μmol·L^{-1} for 30 min. ERP and parameters of transmembrane potentials were recorded before and after Oua perfusion. Then a perfusion of 30 min with drug-free solution was allowed to observe the sustaining action of Oua. In another group, after Oua was washed out, the perfusion was turned to solution containing BT 120 μmol·L^{-1} for 30 min. The effects of BT on the electrophysiologic properties of digitalized papillary muscles were observed. The results were compared with those obtained in the same group after Oua or with those obtained in other group after drug-free perfusion. Only results obtained from the same cell were analyzed. BT and Oua were purchased from Sigma Co.

RESULTS

After perfusion of BT for 30 min, there appeared a prolongation of ERP, APD_{90}, and APD_{50}. The prolongations of ERP and APD were related to the concentration of BT. No significant changes in the resting potential (RP), action potential amplitude (APA), and maximal velocity of phase O depolarization (V_{max}) were detected in 1.2 and 12 μmol·L^{-1}, but a slight lowering in 120 μmol·L^{-1} (Tab 1).

There exist a progressive decrease in all parameters by perfusion of Oua 0.2 μmol·L^{-1} for 30 min. The changed parameters showed a further decrease in perfusion of drug-free solution for 30 min. In the group perfused with BT 120 μmol·L^{-1}, ERP, APD_{90}, and APD_{50} were prolonged, but no significant improvement in other decreased parameters was found (Tab 1).

Tab 1. Effects of bretylium tosylate (BT) on electrophysiologic properties of normal and digitalized papillary muscles with ouabain (Oua) 0.2 μmol·L^{-1}. n=12 guinea pigs. $\bar{x}\pm s$. $^{a}P>0.05$, $^{b}P<0.01$ vs control. $^{d}P>0.05$, $^{e}P<0.05$, $^{f}P<0.01$ vs Oua.

μmol·L^{-1}	ERP/ms	APD_{90}/ms	APD_{50}/ms	APA/mV	RP/mV	V_{max}/V·s^{-1}
Control	200±19	199±20	154±23	110±2	−79±2	185±23
BT 1.2	208±19[c]	208±18[c]	164±21[c]	111±3[a]	−79±2[a]	179±26[a]
Control	207±20	203±16	167±18	111±2	−78±3	186±21
BT 12	223±21[c]	221±17[c]	181±19[c]	111±4[a]	−80±3[a]	201±25[a]
Control	196±21	205±21	166±21	114±3	−84±4	203±24
BT 120	222±22[c]	228±24[c]	189±23[c]	112±4[a]	−81±3[a]	184±23[a]
Control	207±28	221±23	185±20	117±4	−86±4	184±24
Oua 0.2	179±28[c]	195±27[a]	153±29[c]	105±6[c]	−78±4[c]	152±27[c]
Oua-free	170±30[d]	179±28[d]	144±26[d]	104±5[d]	−75±3[d]	142±26[d]
Control	211±18	222±20	182±24	116±4	−84±4	189±30
Oua 0.2	175±20[e]	187±20[e]	146±21[f]	102±5[e]	−77±5[e]	156±27[e]
BT 120	222±21[f]	220±19[f]	190±19[f]	105±5[d]	−77±6[d]	166±29[d]

DISCUSSION

Miura and Biedert[5] demonstrated that the changes of transmembrane potentials of Purkinje fibers induced by a 30 min perfusion of Oua 0.2 μmol·L^{-1} showed no recovery in 60 min perfusion with drug-free solution. The same results were obtained in our study. The results suggested that the prolongations of ERP and APD in the digitalized papillary muscles were related to BT. Oua can selectively inhibit ATPase and induce an increase in intracellular Ca^{2+}. The increase of intracellular Ca^{2+} concentration augmented outward K^+ current so that ERP and APD were shortened. It has been reported that BT may decrease outward K^+ current in ventricular cells of chick embryo[6]. Trón and coworkers demonstrated that BT increased the activity of Na^+-K^+ pump in depolarized lymphocytes and played a role in the repolarization of transmembrane potential[7]. The results suggested that BT may play a improving role on the electrophysiologic properties of the digitalized papillary muscles by prolongations of ERP and APD.

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溴苄铵托西酸盐对正常和洋地黄化豚鼠乳头状肌电生理的影响

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刘耀鑫，朱平军，李震元，俞德章

（浙江医科大学生理教研室，杭州310006，中国）

A 摘要 常规微电极方法观察溴苄铵托西酸盐(BT)对正常和洋地黄化豚鼠乳头状肌电生理特性的影响，BT同步延长正常乳头状肌的ERP和APD. 哇巴因0.2 μmol·L^{-1}缩短ERP和APD. 冲洗30 min无恢复. 换以BT 120 μmol·L^{-1}灌流使ERP，APD_{90}和APD_{50}分别从175±20，187±20和146±21 ms延长到222±21，220±19和190±19 ms. 提示BT对洋地黄化乳头状肌电生理特性有改善作用.

关键词 乳头状肌；电生理学；溴苄铵托西酸盐；哇巴因 BT