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槲皮素对大鼠钠钾腺苷三磷酸酶和钙镁腺苷三磷酸酶的影响

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摘要 槲皮素(Que) ig 200 mg·kg^{-1}，qd×14 d 可显著降低大鼠心肌和脑钠钾腺苷三磷酸酶(I)的活力及心肌钙镁腺苷三磷酸酶(II)的活力；槲皮素100 mg·kg^{-1}降低心肌 I 的活力，但对脑 I 无明显影响. 实验结果提示，大鼠心肌 I 对 Que 的反应较脑 I 敏感；槲皮素也能显著抑制心肌 II 的活力.

关键词 槲皮素；钠$^{(+)}$-钾$^{(+)}$-交换腺苷三磷酸酶；钙$^{(2+)}$-镁$^{(2+)}$-腺苷三磷酸酶；心肌；肉膜；脑；细胞膜

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Comparison of dopexamine hydrochloride, fenoldopam, and procaterol on myocardial nutritional flow in rats[1]

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ABSTRACT Myocardial nutritional flow (MNF) was determined using ^{99m}Technetium-methoxy-isobutyl-isonitrile (^{99m}Tc-MIBI) in rats. At 25 nmol·kg^{-1}, dopexamine hydrochloride (DH), fenoldopam, and procaterol increased the uptake rate of ^{99m}Tc-MIBI/g myocardium by 80.8±10.2 % ($P<0.01$), 44.9±6.3 % ($P<0.05$), and 30.2±5.4 % ($P<0.05$) respectively. These findings suggested the potential advantages of DH over other dopaminergic agonists in the treatment of coronary disease.

KEY WORDS dopaminergic agents; myocardium; blood flow velocity; technetium Tc 99m sestamibi

Dopexamine hydrochloride (DH), a novel dopamine receptor agonist at both DA_1 dopamine receptors and β_2-adrenoceptors, unlike dopamine, has little β_1-adrenergic activities and does not stimulate vascular α-adrenoceptors[1]. It can improve the cardiac function by reducing afterload and mild positive inotropism without significant increase in myocardial oxygen consumption[2-4]. DH has an anti-arrhythmic action during myocardial ischemia[5]. In an attempt to verify the anti-ischemic action, we evaluated the effect of DH on myocardial nutritional flow (MNF) and made a comparison with fenoldopam (DA_1 dopamine receptor agonist) and procaterol (β_2-adrenoceptor agonist).

MATERIALS AND METHODS

^{99m}Technetium - methoxy - isobutyl - isonitrile (^{99m}Tc-MIBI), supplied by Jiangsu Institute of Atomic Medicine, Wuxi, China, was used. Preparation of the cationic complex of ^{99m}Tc-MIBI was performed by using radioimmunoassay (RIA) reagent kit. The saline eluent of $^{99m}TcO_4^-$ (370 MBq) was added into the ampule containing 1.0 mg methoxy isonitrile cryo-

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desic catum and heated in boiling water under hermetically sealed condition for 15 min to yield ^{99m}Tc-MIBI solution (pH 7.0). Both radiochemical purity and labeling rate were >95 %[6]. The radioactivity was measured in an automatic radioimmuno-γ-counter (FMJ-87, Shanghai).

Wistar rats (n=32) of either sex weighing 226±s 23 g were anesthetized with pentobarbital sodium 40 mg·kg^{-1} ip. The 3 drugs at the same dosage of 25 nmol·kg^{-1} were injected iv into external jugular vein. The rats were randomly divided into 4 groups: group I — DH (Fisons, UK); group II — fenoldopam (SK&F, USA); group III — procaterol (Sigma, USA); group IV — normal saline. Five minutes after medication, the ^{99m}Tc-MIBI solution 1 ml (79 MBq, radiochemical purity 96.5 %) per kg body weight was given. After 10 minute, the chest was opened and the heart quickly removed, cleared of residual tissues, and washed adequately with saline. After blotting the surface moisture with filter paper, the cardiac muscle was homogenized and a sample of 0.5 g was taken for measuring the radioactivity.

All values were expressed as $\bar{x}\pm s$. Differences between groups were assessed using ANOVA.

RESULTS

At a dose of 25 nmol · kg^{-1}, DH, fenoldopam, and procaterol increased the uptake rate of ^{99m}Tc-MIBI/g myocardium by 80.8±10.2 %, 44.9±6.3 %, and 30.2±5.4%, respectively *vs* control. There were significant differences in the % of increase between DH and fenoldopam ($P<0.05$) or procaterol ($P<0.01$) (Tab 1).

Tab 1. ^{99m}Tc-MIBI uptake by rat myocardium. n=8, $\bar{x}\pm s$. $^{b}P<0.05$, $^{e}P<0.01$ *vs* saline. $^{c}P<0.05$, $^{f}P<0.01$ *vs* dopexamine.

Drug/nmol·kg^{-1}		dpm/g myocardium
Saline		522 125±58 675
Dopexamine	25	935 175±92 882^{c}
Fenoldopam	25	764 723±76 307^{be}
Procaterol	25	688 308±58 065^{bf}

DISCUSSION

Recently, a new cationic complex of technetium, ^{99m}Tc-MIBI, has been developed as a tracer for myocardial perfusion studies. The quantity of ^{99m}Tc-MIBI uptaken depends upon the number and area of opening capillaries thus reflecting the microcirculatory blood flow, ie, MNF[6]. The present results demonstrated that although all 3 drugs can increase the MNF, DH is by far more potent than the other 2 drugs. Its percentage of increase is even greater than the sum of the percentages of increase with fenoldopam and procaterol suggesting the more effectiveness in increasing MNF of combined actions at both DA_1- and β_2-receptors. Our results may help to explain the antiarrhythmic action of DH reported by Parratt *et al*[5].

The relative lack of β_1-adrenoceptor agonism for DH was also considered to be advantageous in the treatment of ischemic heart disease, since β_1 stimulation has been implicated in some other dopamine agonists-induced arrhythmias.

In summary, the present findings coupled with characteristic pharmacologic profile of DH suggested the potential advantages of DH over other dopaminergic agonists in the treatment of ischemic heart disease.

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多培沙明、非诺多泮和丙卡特罗对大鼠心肌营养血流影响的比较

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摘要 用放射核素技术比较了多培沙明、非诺多泮和丙卡特罗对大鼠心肌营养血流的影响. 结果表明，此三种药(25 nmol·kg^{-1})均能增加心肌营养血流，但程度明显不同. 多培沙明使每克心肌^{99m}Tc-MIBI 的摄取量较对照增加 80.8±10.2 % ($P<0.01$)，而非诺多泮和丙卡特罗则分别增加 44.9±6.3 % ($P<0.05$) 和 30.2±5.4 % ($P<0.05$). 提示多培沙明用于缺血性心脏病治疗可能优于其它多巴胺受体激动剂.

关键词 多巴胺剂；心肌；血流速度；锝 Tc 99m 甲氧异晴

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Protection of bradykinin on neonatal rat myocytes subjected to anoxia/reoxygenation injury

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ABSTRACT This study was to investigate the effects of bradykinin (BK) on myocyte cultures. The effects of BK against lipid peroxidation and oxygen free radicals were estimated on an anoxia/reoxygenation injured model. A salicylate hydroxylation product dihydroxybenzoic acids (DHBA) was detected using HPLC with electrochemical detection, a sensitive device for assaying the hydroxyl free radical. BK (10 nmol·L^{-1}) reduced thiobarbituric acid reactive substances (TBARS, from 1.94±s 0.28 to 0.25±0.03 nmol/10^6 cells, $n=5$, $P<0.01$), lactate dehydrogenase (LDH) release (1.28±0.23 to 0.63±0.12 u·ml^{-1}, $n=8$, $P<0.01$) and DHBA (60±5 to 44±12 nmol·L^{-1}, $n=6$, $P<0.01$). These improvements were nullified by pretreatment with $K_{86/4321}$ (1 μmol·L^{-1}), a kind of BK receptor antagonist. Indometacin (Ind, 1 μmol·L^{-1}) had a synergic action with BK to decrease the LDH release, but Ind (30 μmol·L^{-1}) attenuated the protection of BK, while both LDH and TBARS were increased. The mechanism for protection of BK was ascribable to the activation of BK receptor, the inhibition of lipid peroxidation, and the decreased hydroxyl free radical formation.

KEY WORDS bradykinin; myocardium; cultured cells; lactate dehydrogenase; lipid peroxidation; free radicals; indometacin; hydroxybenzoic acids

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