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神经生长因子在培养的皮质神经细胞中抑制谷氨酸毒性

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关键词 钙; 大脑皮质; 培养的细胞; 谷氨酸; 细胞内液; 神经生长因子; 神经元

目的: 确定 NGF 是否防止原代培养的神经细胞中谷氨酸引起的损伤. **方法**: 采用皮质神经细胞体外培养及形态学观察, 测定神经细胞的生存力和 LDH 的释放来分析 NGF 的作用, 并利用钙指示剂 Fura-2 来检测 $[Ca^{2+}]_i$ 的变化. **结果**: NGF 阻止 $[Ca^{2+}]_i$ 的增加, 并且对谷氨酸引起的皮质细胞的损伤具有拮抗作用, 最大拮抗剂量为 60 μg·L^{-1} **结论**: NGF 通过稳定 $[Ca^{2+}]_i$ 水平, 或阻止 $[Ca^{2+}]_i$ 的升高来保护大脑皮质细胞抗谷氨酸毒性.

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Effect of phencyclidine on dog coronary artery

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KEY WORDS phencyclidine; dextromethorphan; coronary vessels.

AIM: To study the effect of phencyclidine (Phe) on dog coronary artery. **METHODS**: Contraction of spiral strips of dog coronary artery in bioassay and coronary artery blood flow (CBF) using electromagnetic flowmeter on anesthetized dogs were observed. **RESULTS**: Phe 0.1 - 100 μmol·L^{-1} induced contraction of strips in a concentration-dependent manner. Dextromethorphan (Dex) 10 μmol·L^{-1}, an antagonist of Phe receptor, antagonized the action of Phe. *In vivo*, Phe 10 mg·kg^{-1} increased flow of left circumflex coronary artery of anesthetized dogs from 334 ± 35 mL·kg^{-1}·min^{-1} to 510 ± 58 mL·kg^{-1}·min^{-1}, and both left ventrical pressure (LVP) and blood pressure (BP) rose slowly after medication. Dextromethorphan (Dex) 5 mg·kg^{-1} also antagonized the effect of Phe. **CONCLUSION**: The regulation of Phe on coronary artery *in vivo* differs from that *in vitro*, which may result in the contradictory effects.

Phencyclidine (Phe) receptors existed in porcine coronary artery[1]. Phe receptor agonists induced contraction of spiral strips of porcine coronary artery; Phe receptor antagonists, Dextromethorphan (Dex) and haloperidol (Hal), antagonized the effect of Phe[2]. In isolated perfused hearts of guinea pigs, Phe reduced coronary flow which was antagonized by Dex and Hal[3]. The effect of Phe on rat electrocardiogram (ECG) has been observed[4]. Phe induced a rapid elevation of T wave in ECG when injected iv, but no change of ECG when injected intracerebroventricularly. To obtain the direct evidence of Phe on coronary artery blood flow (CBF) *in vivo*, the experiments were proceeded in anesthetized dogs.

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MATERIALS AND METHODS

Phe (white powder, purity >95%) was synthesized by College of Pharmacy, Shanghai Medical University. Dex was produced by Shanghai Meiyou Pharmaceuticals. MFV-2100 electromagnetic flowmeter and RM-6000 polygraph system were produced by Nihon Kohden, Japan. Healthy mongrel dogs of either sex weighing 10.0 ± s 0.5 kg (n = 8), were provided by Department of Animals of Zhongshan Hospital, Shanghai Medical University.

Isolated strips of dog coronary artery The left proximal coronary arteries, isolated from fresh dog heart, were kept at 4 ℃ in Krebs-Ringer solution. Connective tissue was removed and arterial segments were cut into 15 mm × 2 mm helical strips, which were suspended in 5 mL Krebs-Ringer solution at 37.0 ℃ ±0.5 ℃ and gassed with 95 % O_2 + 5 % CO_2. After being equilibrated at a resting tension of 1 g for 2 h, the preparation was exposed to Dex and Phe.

Cardiac hemodynamics in anesthetized dogs Dogs were anesthetized with pentobarbital with artificial respiration. Chest was opened at fourth intercostal space. Left circumflex coronary was isolated for 15 – 25 mm. At apex of heart, a pipe of 7 cm connecting pressure transducer was inserted into left ventricle for left ventrical pressure (LVP). Blood pressure (BP) was measured through femoral vein. The ECG electrodes were inserted under the skin. The CBF, LVP, and BP were measured by electromagnetic flowmeter and polygraph system. Drugs were injected into femoral vein.

RESULTS

Effect of Phe on dog coronary artery strips Phe 0.1 – 100 μmol · L^{-1} induced contraction of strips. Premedication with Dex 10 μmol · L^{-1} abolished the Phe induced contraction (Fig 1).

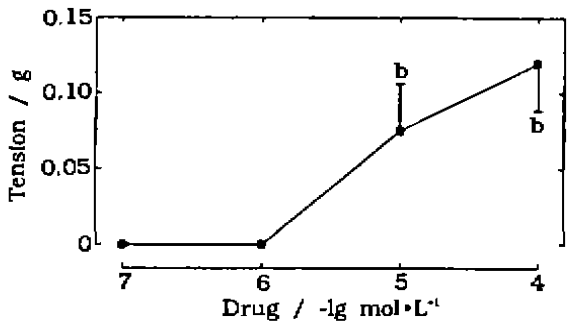

Fig 1. Effect of Phe on contraction of coronary artery in dogs, n = 4, $\bar{x} \pm s$. $^bP < 0.05$ *vs* 0 mg·kg^{-1}.

Effect of Phe on CBF and cardiac hemodynamics in dogs CBF increased 10 s after iv Phe 10 mg·kg^{-1} and reached peak value at 45 s, from basal level 330 ± 40 mL·kg^{-1}·min^{-1} to 510 ± 60 mL·kg^{-1}·min^{-1} (n = 8, $P < 0.01$). It returned to basal level gradually after 45 s. CBF increased slightly 3 min after medication, but no significant change ($P > 0.05$). BP and LVP increased gradually 45 s after iv Phe, from 16.6 ± 1.9 kPa to 20.8 ± 1.9 kPa and 15.4 ± 2.5 kPa to 17.5 ± 1.7 kPa respectively (n = 8, $P < 0.05$). The heart rate (HR) decreased after iv Phe, from 130 ± 17 beats·min^{-1} to 95 ± 16 beats·min^{-1} (n = 8, $P < 0.01$). At the same time of remarkable augment of CBF, the S-T section of ECG rose slightly. The change of ECG disappeared when CBF returned to basal level (Fig 2).

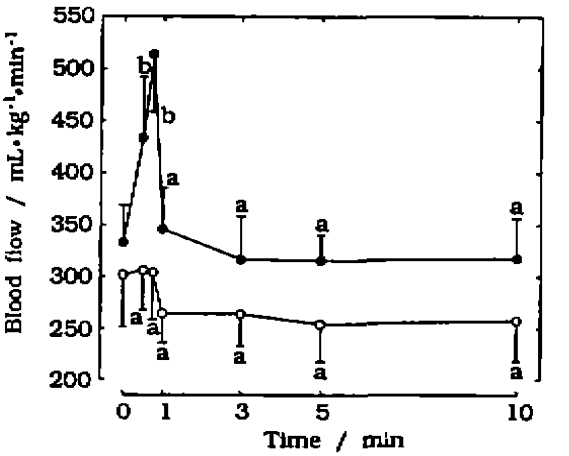

Fig 2. Effect of Phe (n = 8, filled circle) and Phe + DM (n = 5, open circle) on blood flow of coronary artery in anesthetized dogs, n = 8, $\bar{x} \pm s$.
$^aP > 0.05$, $^bP < 0.05$ *vs* 0 mg·kg^{-1}.

Effect of Phe and Dex on CBF and cardiac hemodynamics in dogs When Phe 10 mg·kg^{-1} and Dex 5 mg·kg^{-1} were injected iv simultaneously, the effect of Phe was antagonized, and CBF reduced a little (n = 5, $P > 0.05$). LVP and BP decreased remarkably, from 14.1 ± 0.6 kPa to 6.4 ± 2.8 kPa (n = 5, $P < 0.05$) and 18.6 ± 0.6 kPa to 5.6 ± 0.9 kPa (n = 5, $P < 0.01$), respectively, and HR reduced from 100 ± 14 beats·min^{-1} to 79 ± 7 beats·min^{-1} (n = 5, $P < 0.01$) (Fig 2).

DISCUSSION

Phe induced contraction of strips in porcine and

dog coronary arteries, and reduced CBF in perfused isolated hearts of guinea pigs[3]. Our study showed that the effects of Phe on coronary artery had no race difference *in vitro*, but the effects were contrary to that *in vivo*. Phe dilated the large branches of coronary artery in anesthetized dogs. The difference may be involved in the different regulation of Phe on central and peripheral nervous system. Our previous study[5] showed BP decreased when Phe was injected intracerebroventricularly, but increased when injected from peripheral vein. These results indicated that the effects of Phe on centre nervous were contrary to that on periphery. In our experiment, ischemia change of ECG was simultaneous with the dilation of large branch of coronary artery. Further studies are required to clarify this problem. Hence, when using electromagnetic flowmeter to observe CBF, other cardiac hemodynamics must be considered simultaneously, otherwise, the conclusion would not be comprehensive.

The result showed that the augment of CBF took place before the increase of LVP and BP, so it suggested that the augment of CBF was not induced by the increase of LVP and BP, but the direct action of Phe on coronary artery. Dex, an antagonist of Phe receptor, inhibited cardiac hemodynamics itself slightly *in vivo*, and this phenomenon suggested that Dex may antagonize Phe actions in a non-competitive manner. Although there were some reports about antagonists of Phe receptor[6,7], it was not satisfied with our experiment for its low intrinsic activity, so it is necessary to find higher specific, no intrinsic activity antagonists used in study of Phe receptor.

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苯环利定对犬冠状动脉的作用

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关键词 苯环利定; 右美沙芬; 冠状血管

目的: 研究苯环利定(Phe)对犬冠状动脉的作用. **方法**: 利用冠脉条生物检定, 电磁流量计记录犬血流量等技术分别观察 Phe 对犬冠脉螺旋条和麻醉犬冠状动脉血流量的影响, 同时观察 Phe 受体拮抗剂右美沙芬(Dex)的拮抗效应. **结果**: Phe 0.1 - 100 μmol·L^{-1}量效依赖地使冠脉条收缩, Dex 非竞争性拮抗 Phe 效应. Phe 10 mg·kg^{-1}使麻醉犬冠脉左旋支主干流量增加, 从 334 (35 mL·kg^{-1}·min^{-1}增加到 510 (58 mL·kg^{-1}·min^{-1}. 左室内压和血压缓慢升高, Dex 5 mg·kg^{-1}对整体 Phe 作用有拮抗效应. **结论**: Phe 离体与整体的冠脉调节不同, 提示 Phe 中枢和外周调节效应可能不一致, Phe 整体调节的复杂性.

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