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米帕明对兔离体基底动脉的作用

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Effects of imipramine on isolated rabbit basilar artery

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ABSTRACT Imipramine (Imi) inhibited the contractile response to BAY k 8644 (IC_{50} = 2.39 ± 0.33 μmol · L^{-1}), KCl (IC_{50} = 1.00 ± 0.09 μmol · L^{-1}), in rabbit basilar artery rings. Imi was more effective in suppressing the contractile response evoked by KCl, $CaCl_2$, and 5-HT in basilar artery rings than in mesenteric artery rings. The effect of Imi was the same as that of diltiazem (Dil). There was no difference between the inhibitory response of Imi on contraction induced by KCl in basilar artery rings with or without endothelium. The results suggest that Imi may block the calcium channel and inhibit the rabbit basilar artery selectively, and the effect is endothelium-independent.

KEY WORDS imipramine; diltiazem; saponins; basilar artery; mesenteric arteries; vascular endothelium

提要 Imi 抑制 BAY k 8644、KCl 诱发的兔基底动脉收缩，IC_{50} 为 2.39 ± 0.33, 1.00 ± 0.09 μmol · L^{-1}. 非竞争性拮抗 $CaCl_2$、5-HT 所致基底动脉的收缩作用强于肠系膜动脉，其作用特点与 Dil 相似. 在有内皮及去内皮的基底动脉，Imi 拮抗 KCl 量-效反应的 pD_2'值为 5.93，5.94 (P>0.05)，提示内皮细胞不参与此作用.

关键词 米帕明；地尔硫䓬；皂甙类；基底动脉；肠系膜动脉；血管内皮

米帕明(丙咪嗪，imipramine，Imi)为三环类抗抑郁药，抗抑郁药治疗作用的彻底解释应包括对脑血管系统的作用[1]. 本室发现三环类抗抑郁药阿米替林对兔基底动脉有钙拮抗作用[2]. Imi 的抗心律失常机制与阻滞钙内流有关[1]，但其对兔脑血管的作用未见文献报道. 地尔硫䓬 (diltiazem，Dil) 为钙拮抗剂，其对兔脑血管有选择性抑制作用[3]. 本实验以 Dil 为对照，观察了 Imi 对兔离体基底动脉环的作用，并与肠系膜动脉环及去内皮的基底动脉环做初步比较，以研究 Imi 对兔血管平滑肌的直接作用及选择性.

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MATERIALS AND METHODS

Imi 和 Dil 系 Sigma 产品，BAY k 8644 系 CalbioChem 产品，氯化乙酰胆碱 (acetylcholine chloride, ACh) 军事医学科学院提供，肥皂草素 (saponin) 系 Merck 产品，用 Krebs-Henseleit (K-H) 液配制.

兔，♀♂不拘，体重 2.3 ± s 0.2 kg，河南医科大学实验动物中心提供，基底动脉和肠系膜动脉环标本数分别为 50 和 30.

基底动脉和肠系膜动脉环的制备和离体实验方法均见文献[4].

BAY k 8644 引起的动脉环收缩 使浴液中的 BAY k 8644 浓度达到 0.1 μmol · L^{-1}，引起基底动脉环持续收缩[5]，张力稳定后，累积加入 Imi 和 Dil，求 IC_{50}.

高钾引起的动脉环收缩 使浴液中 KCl 终浓度达 45.6 mmol · L^{-1}，引起基底动脉环和肠系膜动脉环的持续收缩[6]，张力稳定后，累积加入 Imi 和 Dil，求 IC_{50}.

$CaCl_2$ 量-效曲线 在高钾等渗无钙液中测基底动脉和肠系膜动脉环的 $CaCl_2$ 量-效曲线，观察 Imi 和 Dil 对其影响，计算 pD_2'值.

5-HT 量-效曲线 测基底动脉和肠系膜动脉环的 5-HT 量-效曲线，观察 Imi 和 Dil 对其影响，计算 pD_2'值.

去内皮细胞实验 基底动脉从脑干部位分离以前，自其一端用 4 号头皮针缓慢推注 1 ml 含 0.1 mg 肥皂草素的 K-H 液，然后用正常 K-H 液 1 ml 推注冲洗，其动脉环制备及张力描记方法同前. 稳定 90 min 后，使浴液中的 5-TH 浓度达 1 μmol · L^{-1}，引起动脉环收缩、达高峰稳定后，累积加入 ACh 1，10，100 μmol · L^{-1}，不引起松弛反应，证明内皮细胞已去除，未去内皮者出现浓度依赖性松弛[7].

KCl 量-效曲线 做完整内皮和去内皮基底动脉环的 KCl 量-效曲线，观察 Imi 对它们的影响，计算 pD_2'值.

RESULTS

Imi 对 BAY k 8644 引起的肌环收缩的抑制作用 BAY k 8644 0.1 μmol · L^{-1} 可引起基底动脉收缩，其作用可维持 2 h 以上，Imi 和 Dil 可导致浓度依赖性松弛，IC_{50} 值分别为 2.39 ± 0.33 及 0.29 ± 0.06 μmol · L^{-1}.

Imi 对高钾引起的动脉环收缩的抑制作用 Imi 和 Dil 对 KCl 引起的基底动脉和肠系膜动脉环的持续收缩产生浓度依赖性松弛，IC_{50} 值分别为 1.00 ± 0.09，3.78 ± 0.09 μmol · L^{-1} ($n=5$，$P<0.01$)及 0.31 ± 0.04，8.82 ± 0.4 μmol · L^{-1} ($n=5$，$P<0.01$).

Imi 对 $CaCl_2$ 的作用 Imi 和 Dil 可非竞争性地拮抗 $CaCl_2$ 对基底动脉和肠系膜动脉环的收缩作用 (Fig 1). Imi 对二动脉作用的 pD_2'值分别为 5.07 ± 0.06 和 4.89 ± 0.17 ($P<0.05$)，Dil 对二动脉作用的 pD_2'值分别为 6.06 ± 0.10 和 5.67 ± 0.17 ($P<0.01$).

Imi 对 5-HT 的作用 Imi 和 Dil 可非竞争性地拮抗 5-HT 对基底动脉和肠系膜动脉环的收缩作用. Imi 对二动脉作用的 pD_2'值分别为 4.59 ± 0.22 和 3.92 ± 0.12 ($n=5$, $P<0.01$)，Dil 对二动脉作用的 pD_2'值分别为 5.47 ± 0.14 和 4.75 ± 0.12 ($n=5$，$P<0.01$).

Imi 对有和去内皮基底动脉环 KCl 的影响 KCl 引起有和去内皮动脉环的最大张力分别为 575 ± 137，568 ± 170 mg ($n=5$, $P>0.05$). Imi 非竞争性拮抗两组动脉的 KCl 量-效反应，pD_2'值分别为 5.93 ± 0.13 和 5.94 ± 0.08 ($n=5$，$P>0.05$).

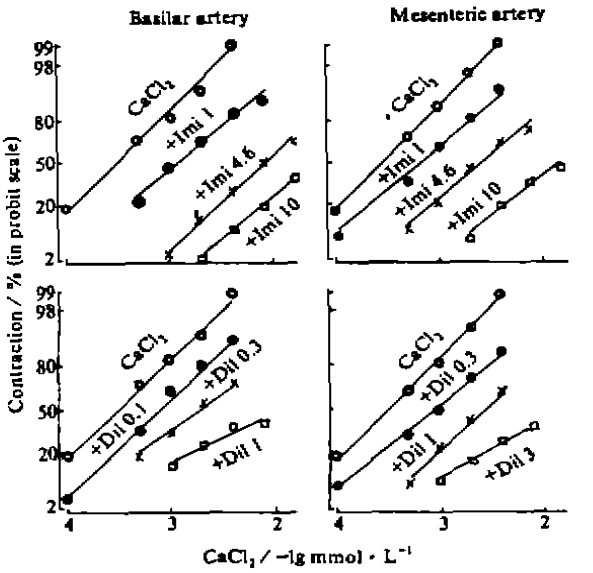

Fig 1. Effects of imipramine (Imi, μmol · L^{-1}) and diltiazem (Dil, μmol · L^{-1}) on $CaCl_2$-induced contraction of rabbit basilar and mesenteric artery rings. $n=5$.

DISCUSSION

尼莫地平对高钾引起的兔基底动脉收缩的抑制作用与外周血管比较无显著性差异[6]，故本实验选用 Dil 做对照.

BAY k 8644 和高钾均可激动电压依赖性钙通道，5-HT 可开放受体操纵性钙通道. Imi 和 Dil 可抑制 BAY k 8644、KCl，5-HT 引起的基底动脉和肠系膜动脉环收缩，对基底动脉的作用显著强于肠系膜动脉，表明 Imi 对兔血管平滑肌有钙拮抗作用、并对脑血管有选择性.

Imi 抗抑郁治疗的最佳血浆浓度为 200-450 ng · ml^{-1} [8]，本实验中，Imi 在 0.42-2.44 μmol · L^{-1} 即 132-755 ng · ml^{-1} 浓度范围，可抑制 KCl 引起的收缩 10-90%.

抗抑郁治疗的最佳血浆浓度在此范围内，Imi的钙拮抗作用与抗抑郁机制之间的关系有待于进一步研究.

用肥皂草素剥脱血管内皮的方法简便易行，本文采用此法观察到内皮细胞的去除不影响 Imi 拮抗兔基底动脉 KCl 量-效反应的 pD_2' 值，提示内皮细胞可能不参与这一作用.

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柳珊瑚酸钠对离体兔回肠的兴奋作用

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Excitant effect of sodium suberogorgin on isolated rabbit ileum

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ABSTRACT Suberogorgin was isolated from *Gorgoniae suberogorgia sp* from South China Sea. The isolated rabbit ileum contracted in a concentration-dependent manner by suberogorgin-Na (Sub) 2.13 $\mu mol \cdot L^{-1}$ or higher. Sub 213 $\mu mol \cdot L^{-1}$ had no effect on the relaxation induced by norepinephrine and isoprenaline 10–100 $\mu mol \cdot L^{-1}$ on ileum. The stimulation of Sub on ileum was antagonized by atropine 56 $\mu mol \cdot L^{-1}$ or indometacin 0.35 $mmol \cdot L^{-1}$ and was partly blocked by indometacin 0.17 $mmol \cdot L^{-1}$, but was not affected by diphenhydramine 10 $\mu mol \cdot L^{-1}$. On the contracted ileum induced by neostigmine 1.7 $\mu mol \cdot L^{-1}$, acetylcholine 0.1 $\mu mol \cdot L^{-1}$ increased the tension but Sub 213 $\mu mol L^{-1}$ did not. Sub obviously inhibited the acetylcholinesterase (AChE) from mouse brain hemogenates *in vitro*. Its pI_{50} (negative logarithm of molar concentration causing 50% inhibition of AChE) was 4.18, while the pI_{50} of neostigmine was 4.75. The results indicated that the ileum-excitant action of Sub was chiefly related to the inhibition of AChE.

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