腺素系统与 LA 镇痛也有关联。

LA 镇痛作用不被纳络酮所拮抗，表明其并非作用于中枢阿片受体，是不同于阿片类的镇痛剂，此结果与文献报道[1]相符。LA 代谢研究表明，LA 在体内主要代谢为 DLA（未发表资料），LA 外周和中枢给药分别表现为镇痛和无镇痛作用，推测 LA 可能通过其外周代谢产物 DLA 在中枢发挥镇痛作用。LA 或 DLA 与吗啡外周和中枢合用的结果也提示 LA 通过 DLA 在中枢与吗啡发挥协同镇痛作用。这种协同作用为临床在两药合用时减少吗啡用量提供了部分依据。

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动脉粥样硬化兔心、脑肾上腺素受体密度的改变及离体肺动脉环的反应性

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Changes of adrenoceptor density in heart and brain and the reactivity of isolated pulmonary artery ring in atherosclerotic rabbit

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ABSTRACT The α-adrenoceptor density in cerebral cortex and brain stem as well as the β-adrenoceptor density in heart were measured by radioligand binding assay in normal rabbits (group 1), atherosclerotic rabbits (group 2) and atherosclerotic rabbits treated orally with aspirin

20 mg/kg daily for 16 wk (group 3).

The results showed that the β-receptor density and the K_D values of the hearts among the 3 groups and the α-receptor density and K_D of brain stem between groups 1 and 2 were not significantly different except that the α-receptor density in group 3 was decreased slightly. The number of α_1-receptor of cerebral cortex was decreased more in group 2 than that in group 3. The contractile responses of isolated pulmonary artery ring by NE were similar among the 3 groups but the reactivity to 5-HT in group 3 was increased significantly.

KEY WORDS atherosclerosis; *alpha* adrenergic receptors; *beta* adrenergic receptors; pulmonary artery; brain; heart

提要 测定了正常、高脂饮食和高脂加阿司匹林兔心脏β受体及脑α_1受体密度及K_D值和肺动脉环反应性。结果表明三组兔的心脏β受体数及K_D值无差异。对照组和高脂组的脑干α_1受体数和K_D值也无差别，阿司匹林组则有下降倾向。高脂组脑皮层α_1受体数减少，阿司匹林组下降更明显。3组兔的肺动脉对NE的反应相同，阿司匹林组对5-HT反应加强。

关键词 动脉粥样硬化；肾上腺素α受体；肾上腺素β受体；肺动脉；脑；心脏

肾上腺素能神经及其受体在调节和维持心血管系统功能方面起重要作用。在高血压[1-3]心力衰竭[4]及药物作用[5-7]下肾上腺素受体密度发生改变。在形成动脉粥样硬化过程中，该受体有无变化，尚未见报道。本工作比较了正常和动脉粥样硬化兔心脏的β受体和脑组织的α受体密度及阿司匹林对动脉粥样硬化兔肾上腺素受体的影响。

MATERIALS AND METHODS

[^{3}H]dihydroalprenolol (1702 GBq/mmol 中国科学院原子能研究所)，[^{3}H]prazosin (962 GBq/mmol, Amersham)，普萘洛尔(propranolol)和哌唑嗪(prazosin)(北京制药厂)，胆固醇(南京生物化学制药厂)，阿司匹林(北京医药公司五七药厂)，去甲肾上腺素(北京和平制药厂)，5-羟色胺(serotonin, 5-HT, 瑞士 Fluka, Buchs)，玻璃纤维纸(上海虹光纸厂49号)。

大耳兔，♂，中国医学科学院动物中心供应。体重2.5±SD 0.7 kg，在实验室饲养2 wk后，检测血清总胆固醇(total cholesterol, TC)含量，TC在0.1 g/L以下者，随机分为3组，每组10只：(1) 正常对照组，仅喂基础食料；(2) 高脂组，基础食料每兔加胆固醇0.5 g/d；(3) 阿司匹林组，除基础饲料和胆固醇外，再喂阿司匹林粉剂20 mg/(kg·d)。实验共16 wk，于给药前及后4，8，12，16 wk取血测定血脂。实验结束后放血处死，立即取心脏和脑，放在冷缓冲液内分别测定心脏β受体和脑的α_1受体。取肺动脉环观察血管反应性。

血清TC用高铁-硫酸显色法测定。受体测定方法如下：心肌细胞膜的制备：将心室肌剪碎，用polytron (set 7, 1.5 s)打成匀浆，冷缓冲液(Tris-HCl 50 mmol/L, $MgCl_2$ 10 mmol/L, pH 7.5)稀释至50 mg湿组织/ml，于4℃，1000×g离心10 min，弃去沉淀取上清于4℃，80 000×g离心10 min，弃去上清，沉淀用缓冲液悬浮，50 000 ×g再次离心10 min，所得沉淀用适量缓冲液悬浮。当天测定β受体密度。脑细胞膜的制备见前文[8]，所得细胞膜用适量缓冲液(Tris-HCl 50 mmol/L, pH 7.5)悬浮，稀释到200 mg湿组织/ml，−20℃保存。

β受体的测定[9] 每管含0.87 ml心肌细胞膜悬液(0.43 mg蛋白)，[^{3}H]DHA 30 μl(终浓度0.25-4.0 nmol/L)，普萘洛尔100 μl(终浓度10 μmol/L，非特异结合管)或缓冲液100 μl(总结合管)，总反应容量1 ml，摇匀后，25℃温孵25 min，用5 ml冰冷缓冲液终止反应，立即经玻璃纤维纸真空抽滤，用缓冲液洗涤4次，每次5 ml。滤纸烘干后，置PPO/POPOP甲苯闪烁液中测定放射性强度。

α受体的测定[8] 每管含脑细胞膜0.87 ml(1.5 mg蛋白)，[^{3}H]哌唑嗪30 μl(终浓度0.1-5 nmol/L)，哌唑嗪100 μl(μmol/L)(非特

异结合管)或缓冲液 100 μl(总结合管),总反应容量 1 ml,摇匀后,25℃温孵 60 min,其它步骤同上。用 Scatchard 法求得受体密度 B_{max} 和受体配体结合平衡解离常数 K_D 值。

肺动脉血管反应性测定 肺动脉环宽 2-3 mm 置于 10 ml K-H 溶液的浴槽内,一端固定在通气钩上,另一端与力位移换能器相连,负荷 1 g,通以 95%O_2+5%CO_2,37℃,平衡 1 h 后,在平衡记录仪上记录累加量的 NE 或 5-HT 的量-效曲线。

RESULTS

高胆固醇饲料兔(高脂组)血清总胆固醇明显高于对照组和阿司匹林组,其值分别为 367±259,72±19,245±192。病理检查证明,高脂组兔有明显动脉粥样硬化病变,与高脂组相比,阿司匹林组的病变明显减轻。每组各取 8 只兔的心脏、脑皮层、脑干和肺动脉进行实验,结果如下:

心脏 β 受体和脑 α_1 受体密度的改变 从 Tab 1 可见正常对照组,高脂组及阿司匹林组心脏 β 受体 B_{max} 和 K_D 无差异,正常组和高脂血组的脑干 α_1 受体 B_{max} 和 K_D 之间也无差异,阿司匹林组的 B_{max} 和 K_D 有下降倾向,但无统计意义。高脂组兔脑皮层的 α_1 受体密度低于对照组,阿司匹林组的这种变化更明显。且 K_D 值也明显降低。

肺动脉的反应性 正常组,高脂血组和阿司匹林组兔肺动脉对 NE 引起的收缩反应(曲线)相似(Fig 1 左),阿司匹林组兔肺动脉对 5-HT 引起的收缩反应,其曲线左移,表明对 5-HT 的敏感性加强(Fig 1 右)。

Tab 1. The α-adrenoceptor in brain and β-adrenoceptor in hearts of rabbits. $n=8$, $\bar{x}\pm SD$. $^*P>0.05$, $^{**}P<0.05$, $^{***}P<0.01$ *vs* 1. $^{\dagger\dagger\dagger}P<0.01$ *vs* 2.

Receptor	Group 1	2	3
	B_{max}(fmol/mg protein)		
Heart β	97±14	98±18*	105±25*
Brain stem α_1	34±4	34±4*	31±6*
Cerebral cortex α_1	98±2	37±9**	27±5***
	K_D(nmol/L)		
Heart β	1.6±0.5	1.6±0.3*	2.0±0.8*
Brain stem α_1	0.76±0.25	0.79±0.4*	0.58±0.28*
Cerebral cortex α_1	0.99±0.2	0.65±0.1*	0.37±0.05†††

1: normal rabbit, 2: atherosclerotic rabbit, 3: atherosclerotic rabbit treated with aspirin.

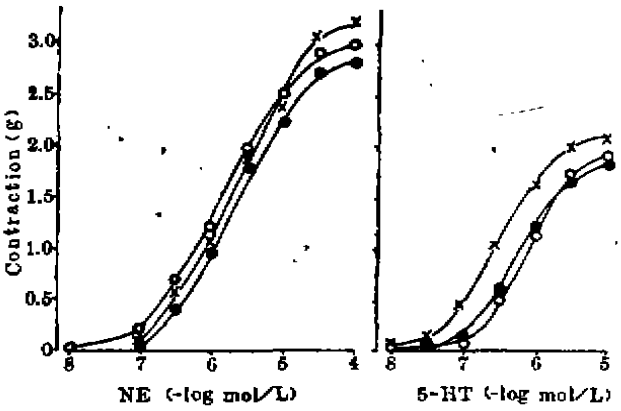

Fig 1. The response of isolated rabbit pulmonary artery ring to norepinephrine (NE) and to 5-hydroxytryptamine (5-HT) in normal rabbits (○), atherosclerotic rabbits (●) and atherosclerotic rabbits treated with aspirin (×). $n=8$.

DISCUSSION

药物和激素对受体数目的调节会影响组织的反应性或敏感性[8,10]。实验性高血压和心力衰竭[9]以及心肌缺血时心脏 β 受体数增加,说明这些病理过程有肾上腺素能神经参与。本工作未观察到动脉粥样硬化兔的心脏 β 受体和调节血压的脑干的 α_1 受体数有何改变,肺动脉环对 NE 的反应也与正常动物相同,说明在动脉粥样硬化的发病过程中,肾上腺素能神经可能未起重要作用。动脉粥样硬化兔大脑皮层 α_1 受体数低于正常兔,K_D 值有下降倾向。阿司匹林使动脉粥样硬化兔的 α_1 受体数进一步减少,亲和力进一步升高,说明高脂血症时皮层

功能有一定改变，阿司匹林使此种改变更加明显。目前尚未见这方面的报告，其意义尚待探讨。

5-HT 是一个强的血管收缩剂，脑血管对 5-HT 更为敏感。本工作观察到阿司匹林组兔肺动脉环对 5-HT 的反应加强，这可能与阿司匹林抑制血小板释放 5-HT，使血中 5-HT 含量减少，5-HT 受体数目增加有关，本工作由于生物样品材料的限制未能进行 5-HT 受体数的测定，也未观察脑血管对 5-HT 的反应。这些都有待研究。

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α 肾上腺素受体激动剂对大鼠心功能及血压的影响[1]

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Effects of *alpha*-adrenoceptor agonists on cardiac function and blood pressure in rats

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ABSTRACT In rat working hearts, α_1-adrenoceptor agonist phenylephrine increased LVP, $\pm dP/dt_{max}$, ABF and HR in the presence of propranolol. But α_2-adrenoceptor agonist B-HT 920 was ineffective. The changes induced by phenylephrine were antagonized by prazosin. In normotensive pithed rats, iv methoxamine dose-dependently increased LVP, $\pm dP/dt_{max}$, LVEDP, SAP and DAP. The changes in haemodynamics elicited by iv methoxamine were also antagonized by pretreatment with prazosin, and were attenuated by nifedipine (1 mg/kg, ia). In these two experiments, the increase in HR developed more slowly. The results suggest that postjunctional α_1-adrenoceptors, which exist in rat myocardium, produce a positive inotropic effect, which is possibly dependent on influx of extra-

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