

DL 既无 α_2 -肾上腺素受体阻断作用, 也无钙拮抗作用. 高钾去极化时, 细胞外钙内流引起血管平滑肌收缩⁽¹⁾, DL 对这种收缩无松弛作用, 进一步提示 DL 无钙拮抗作用.

综上所述, DL 的降压作用可能与选择性阻断突触后 α_1 -肾上腺素受体有关, 对 α_2 -受体和钙通道无阻滞作用. 另外也可能与对 β -肾上腺素受体和交感神经末梢的影响有关.

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49-51 哮喘 雌二醇 卵白蛋白 组胺 (9)
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雌二醇对豚鼠卵白蛋白致敏过程的影响¹

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Effect of estradiol on the course of ovalbumin sensitization in guinea pigs¹

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ABSTRACT The latent period of ovalbumin (Ova)-induced asthma in Ova-sensitized guinea pigs was shorter in the ovariectomized animals with sc estradiol (E_2) 400 or 50 $\mu\text{g} \cdot \text{d}^{-1} \times 14 \text{ d}$ and in animals with intact ovary (84 ± 35 , 82 ± 33 , and $100 \pm 32 \text{ s}$, respectively) than in the ovariectomized animals ($140 \pm 29 \text{ s}$) ($P < 0.05$). The histamine (His) content of the lungs and His released from lungs under Ova challenge *in vitro* increased in the group of ovariectomy with sc E_2 50 $\mu\text{g} \cdot \text{d}^{-1} \times 14 \text{ d}$ as compared with those without sc E_2 (56 ± 9 and $47 \pm 11 \text{ ng/g wet weight vs } 44$

± 10 and 36 ± 11 ng / g wet weight) ($P < 0.05$). However, the pD_2 values of the contraction of isolated tracheal strips induced by His and those of the relaxation by isoproterenol (Iso) were not affected. These findings suggest that the strengthened effect of E_2 on the sensitization may be related to the content and the release of lung His in guinea pigs.

KEY WORDS asthma; estradiol; ovalbumin; histamine; isoproterenol; ovariectomy

摘要 在 Ova 致敏豚鼠, 去卵巢 sc E_2 400 或 50 $\mu\text{g} \cdot \text{d}^{-1} \times 14$ d 和保留卵巢组的 Ova 引喘潜伏期(分别为 84 ± 35 , 82 ± 33 和 100 ± 32 s)比去卵巢组(140 ± 29 s)缩短($P < 0.05$)。 E_2 50 μg 组的离体肺总 His 和 Ova 攻击下释放 His 含量(56 ± 9 和 47 ± 11 ng / g wet weight)比去卵巢组(44 ± 10 和 36 ± 11 ng / g wet weight)增高($P < 0.05$)。 但 His 收缩和 Iso 舒张气管条的 pD_2 值不改变, 提示 E_2 加强致敏过程与 His 增加有关。

关键词 哮喘; 雌二醇; 卵白蛋白; 组胺; 异丙肾上腺素; 卵巢切除术

支气管哮喘与患者的性别⁽¹⁾、年龄⁽¹⁾、月经周期⁽²⁾及妊娠⁽³⁾密切相关。其中以性激素的变化最令人瞩目。为了探讨性激素在这种联系中的作用, 本文在豚鼠实验性过敏性哮喘的模型上, 观察了苯甲酸雌二醇对致敏过程的影响及其中组胺和 β 肾上腺素受体的可能作用。

MATERIALS

卵白蛋白片(ovalbumin, Ova, Serva 公司), 苯

甲酸雌二醇(estradiol benzoate, E_2 上海第九制药厂), 磷酸组胺(histamine phosphate, His, 中国科学院上海生化研究所), 盐酸异丙肾上腺素(isoproterenol hydrochloride, Iso, 上海天丰制药厂), 邻苯二甲醛(*o*-phthalaldehyde, OPT, Fluka Chemie AG, Switzerland), MPF-4 型荧光分光光度计(Hitachi, Japan), WM-2 型无油气体压缩机(中国天津), XWT-S 小型台式记录仪(上海自动化仪表厂), LVDT-5 型位移传感器(南京虹光仪器厂)。

METHODS AND RESULTS

动物模型与分组 豚鼠 32 只, ♀, 体重 $253 \pm s$ 41 g, 由本校实验动物繁殖中心提供。戊巴比妥钠($33 \text{ mg} \cdot \text{kg}^{-1}$)麻醉后切除双侧卵巢(去势)或保留卵巢(假手术), 恢复 4-6 d 后, 每只豚鼠 ip 10% Ova 生理盐水溶液 1.0 ml 主动致敏⁽⁴⁾, 14 d 后供实验用。其间每只豚鼠每天给予 E_2 或等容量茶油: A) 去势+sc E_2 400 $\mu\text{g} \cdot \text{d}^{-1}$; B) 去势+sc E_2 50 $\mu\text{g} \cdot \text{d}^{-1}$; C) 保留卵巢+sc 茶油; D) 去势+sc 茶油。

Ova 引喘潜伏期⁽⁵⁾ 豚鼠置于密闭钟罩内, 以 53.3 kPa (400 mm Hg) 的恒压雾化吸入 0.5% Ova 生理盐水溶液 30 s。豚鼠逐渐呼吸困难, 以明显腹肌收缩为阳性, 记录引喘潜伏期(Tab 1)。 F 检验和 q 检验表明, A, B, C 组的引喘潜伏期均比 D 组明显缩短($P < 0.05$)。

His 引喘潜伏期及 Iso 的保护作用⁽⁵⁾ 用 Ova 引喘同样的方法, 吸入 0.3% His 15 s, 记录引喘潜伏期。 d 2, 先吸入 0.01% Iso 60 s

Tab 1. Latent period (s) of asthma in guinea pigs inhaled ovalbumin 0.5%, 30 s; histamine 0.3%, 15 s; isoproterenol 0.01%, 60 s; $n = 8$, $\bar{x} \pm s$. * $P > 0.05$, ** $P < 0.05$ vs Group D.

Group	Ova	His	Iso + His
A. Ovariectomized + E_2 400 μg	$84 \pm 35^{**}$	$69 \pm 12^*$	$69 \pm 16^*$
B. Ovariectomized + E_2 50 μg	$82 \pm 33^{**}$	$72 \pm 17^*$	$58 \pm 17^*$
C. Ovary intact + tea oil	$100 \pm 32^{**}$	$70 \pm 12^*$	$65 \pm 26^*$
D. Ovariectomized + tea oil	140 ± 29	81 ± 21	70 ± 27

后,再喷入 0.3% His 15 s,记录引喘潜伏期。Iso 的保护作用以吸入 Iso 后的 His 引喘潜伏期与单用 His 引喘潜伏期之差表示(Tab 1)。可见 E_2 不改变 His 引喘潜伏期及 Iso 对 His 引喘的保护作用($P > 0.05$)。

离体气管条实验 B组和D组豚鼠,参照文献⁽⁶⁾法制成气管螺旋条。每个样本含三节平滑肌。移入 37°C 的 Krebs-Henseleit 液的浴槽内。持续通 O_2 ,前负荷 0.5 g,稳定 2 h。分别描记 His 收缩和 Iso 松弛离体气管条的剂量-效应曲线。量取每一浓度对应的曲线高度,计算 pD_2 值⁽⁷⁾。His 收缩作用的 pD_2 值分别为 5.68 ± 0.23 和 5.64 ± 0.27 ($n=7, P > 0.05$)。Iso 松弛作用的 pD_2 值分别为 7.56 ± 0.20 和 7.50 ± 0.31 ($n=8, P > 0.05$)。

肺 His 含量测定 B组和D组豚鼠肺组织,剪碎,万分之一天平称取 500 mg 两份:煮沸 20 min,滤液所含 His 代表总 His 含量;与 Ova ($1 \text{ mg} \cdot \text{ml}^{-1}$)体外孵育 30 min,滤液所含 His 代表释放 His 含量。采用荧光分光光度法⁽⁸⁾。B组总 His 含量和释放 His 含量分别为 56 ± 9 和 $47 \pm 11 \text{ ng/g wet weight}$ ($n=9$),均比 D 组的总 His 含量和释放 His 含量显著增高($P < 0.05$),分别为 44 ± 10 和 $36 \pm 11 \text{ ng/g wet weight}$ ($n=8$)。

DISCUSSION

本文在 Ova 致敏豚鼠的模型上,观察到体内有 E_2 的 A、B、C 组的 Ova 引喘潜伏期比体内无 E_2 的 D 组均明显缩短,即 E_2 可以加强豚鼠 Ova 致敏过程。

E_2 处理组对吸入外源性 His 的引喘潜伏期不改变;His 收缩离体气管条的 pD_2 值也不

改变,表明气管平滑肌对 His 的反应性未改变;相应肺组织的总 His 含量及在体外 Ova 攻击下释放 His 含量却增加。推测整体吸入 Ova 后, E_2 处理组释放较多的 His,引起气管平滑肌较强的收缩,从而出现整体 Ova 引喘潜伏期的缩短。

实验发现,在 E_2 处理组和非处理组,Iso 对 His 引喘的保护作用和 Iso 舒张离体气管条的 pD_2 值没有差异,表明气道 β 肾上腺素受体(β 受体)功能未改变。因为 β 受体功能的降低或提高可以相应地加重或改善哮喘。由此认为,Ova 引喘潜伏期的缩短并非由于 β 受体功能改变所致。

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