

DL 既无  $\alpha_2$ -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<sup>(1)</sup>, 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  $\alpha_1$ -肾上腺素受体有关, 对  $\alpha_2$ -受体和钙通道无阻滞作用. 另外也可能与对  $\beta$ -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)  
 BIBLID: ISSN 0253-9756 中国药理学报 *Acta Pharmacologica Sinica* 1993 Jan; 14 (1) : 49-51

雌二醇对豚鼠卵白蛋白致敏过程的影响<sup>1</sup>

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Effect of estradiol on the course of ovalbumin sensitization in guinea pigs<sup>1</sup>

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Received 1990-12-12 Accepted 1992-07-01

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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 ( $84 \pm 35$ ,  $82 \pm 33$ , 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  $E_2$  ( $56 \pm 9$  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  $84 \pm 35$ ,  $82 \pm 33$  和  $100 \pm 32$  s)比去卵巢组( $140 \pm 29$  s)缩短( $P < 0.05$ )。  $E_2$  50  $\mu\text{g}$  组的离体肺总 His 和 Ova 攻击下释放 His 含量( $56 \pm 9$  和  $47 \pm 11$  ng / g wet weight)比去卵巢组( $44 \pm 10$  和  $36 \pm 11$  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<sup>(1)</sup>、年龄<sup>(1)</sup>、月经周期<sup>(2)</sup>及妊娠<sup>(3)</sup>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  $\beta$  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<sup>(4)</sup>, 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**<sup>(5)</sup> 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**<sup>(5)</sup> 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 $\mu\text{g}$	$84 \pm 35^{**}$	$69 \pm 12^*$	$69 \pm 16^*$
B. Ovariectomized + $E_2$ 50 $\mu\text{g}$	$82 \pm 33^{**}$	$72 \pm 17^*$	$58 \pm 17^*$
C. Ovary intact + tea oil	$100 \pm 32^{**}$	$70 \pm 12^*$	$65 \pm 26^*$
D. Ovariectomized + tea oil	$140 \pm 29$	$81 \pm 21$	$70 \pm 27$

后, 再吸入 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<sup>(6)</sup>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<sup>(7)</sup>. His 收缩作用的  $pD_2$  值分别为  $5.68 \pm 0.23$  和  $5.64 \pm 0.27$  ( $n=7$ ,  $P > 0.05$ ). Iso 松弛作用的  $pD_2$  值分别为  $7.56 \pm 0.20$  和  $7.50 \pm 0.31$  ( $n=8$ ,  $P > 0.05$ ).

**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<sup>(8)</sup>. B 组总 His 含量和释放 His 含量分别为  $56 \pm 9$  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  $44 \pm 10$  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  $\beta$  肾上腺素受体 ( $\beta$  受体) 功能未改变. 因为  $\beta$  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  $\beta$  受体功能改变所致.

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