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Mediator difference in contractions between trachea and bronchus of guinea pig induced by stimulation of C-fibers *in vitro*[1]

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ABSTRACT In trachea and bronchus of guinea pig *in vitro*, electric field stimulation (EFS) induced a rapid contraction (phase I) followed by a long-lasting contraction (phase II). The pretreatments of chlorphenamine (Chl) 1 μ mol·L^{-1} and disodium cromoglicate (Cro) 10 μmol·L^{-1} reduced the tracheal contraction of phase II from 49±23 mg and 34±18 mg to 27±21 and 18±12 mg, respectively. The contractile responses of the tracheae to increasing concentrations of substance P (SP) 0.1—3.0 μmol·L^{-1} were reduced by the pretreatment of Cro 10 μmol·L^{-1} ($P<0.01$). On the contrary, the contractile responses of the bronchi were not inhibited by Cro or Chl but were inhibited by pretreatment of atropine 1 μmol·L^{-1} from 61±36 mg to 36±15 mg. These results show that there are different mechanisms in the EFS-induced contractions between the trachea and bronchus; that different mediators amplify the phase II contractions.

KEY WORDS trachea; bronchi; electric stimulation; chlorphenamine; disodium cromoglicate; substance P

The electric field stimulation (EFS) can evoke 2 phasic contractions of smooth muscles in the tracheae or bronchi of guinea pig *in vitro*. The phase II contraction was induced by the release of neuropeptides from the capsaicin-sensitive sensory nerve, ie. C-fibers[1-4]. In the present study, we used the EFS[5] to find whether the neuropeptides from C-fibers are involved in the different mediator releases between the tracheae and bronchi.

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MATERIALS AND METHODS

Hartley guinea pigs of either sex, weighing 0.44 ±0.07 kg, supplied by Experimental Animal Center of Zhejiang Medical University, were stunned and exsanguinated. The isolated tracheae and the main bronchi suspended between 2 platinum ring electrodes in a 10-ml organ bath containing Krebs-Henseleit solution at 37 ℃ and gassed with oxygen[4,5]. The preparations were connected to force-displacement transducers for measurement of isometric tension. The tissues were equlibrated for 60 min and under an initial tension of 0.5 g, and washed with fresh solution every 20 min. Propranolol (3 μmol·L^{-1}) and indometacin (2 μmol·L^{-1}) were present in the physiological solution during the whole experiment.

Rectangular pulses were delivered from a stimulator (model JJC-2, Shanghai). The stimulation of EFS (48 V, 0.8 ms, 15 Hz, 15 s) were applied at an interval of 30 min. The recorders are from Shanghai Dahua Factory (model XWT-264).

Indometacin and substance P (SP) were obtained from Sigma Co., propranolol was purchased from Beijing Pharmaceutical Factory, chlorphenamine (Chl) was from Shanghai 10th Pharmaceutical Factory, disodium cromoglicate (Cro) and atropine were purchased from Shanghai 21th Pharmaceutical Factory and Changzhou Pharmaceutical Factory respectively.

The contractile tension of the airway smooth muscles was expressed as mg ($\bar{x}\pm s$). Differences between means were analysed by paired t test or group t test.

RESULTS

EFS elicited a biphasic contractile re-

sponse of tracheal and bronchial strips. The first phasic contraction (phase I) of all the tracheal and bronchial preparations were not influenced by the pretreatment of Chl ($P>0.05$) or Cro ($P>0.05$). The phase II contraction of the trachea but not bronchus, was reduced by the pretreatments of Chl 1 μmol·L^{-1} and Cro 10 μmol·L^{-1} (Tab 1).

Tab 1. Effects of the pretreatment of Chl, Cro, and atropine on the phase II contraction by electric field stimulation. $\bar{x}\pm s$. $^aP>0.05$, $^bP<0.05$, $^cP<0.01$; *vs* **control.**

	n	Contractile tension of phase II (mg) Control	After pretreatment
Pretreated with chlorphenamine 1 μmol·L^{-1}			
Tracheae	8	49±23	27±21^c
Bronchi	7	24±8	26±9^a
Pretreated with disodium cromoglicate 10 μmol·L^{-1}			
Tracheae	10	34±18	18±12^c
Bronchi	8	58±29	59±22^a
Pretreated with atropine 1 μmol·L^{-1}			
Tracheae	10	35±15	37±19^a
Bronchi	9	61±36	36±15^b

The pretreatment of atropine 1 μmol·L^{-1} abolished the phase I of the tracheal and broncheal preparations ($n=19$, $P<0.01$), which was induced by EFS. The phase II of the bronchus, but not trachea, was reduced by the pretreatment of atropine (Tab 1).

The responses of the preparations to the increasing concentrations SP were not altered with repeated SP challenge (bronchi, $n=4$, $P>0.05$; tracheae, $n=4$, $P>0.05$). The pretreatments of Cro 10 μmol·L^{-1} reduced the contractile responses to SP in the tracheae, but not in the bronchi (Tab 2).

DISCUSSION

As the results and previous reports[1-4], the releases of neuropeptides from C-fibers are responsible for phase II contractions of smooth muscles of the airway. The treatment of Chl and Cro did not influence the resting tension of all preparations of the airway, but they could reduce contractile phase II of the tracheal preparations (Tab 1). SP, a neuropeptide released from C-fibers, is a potent activator of mast cell degranulation in both rat and human skin[3,7] and Cro (1−100 μmol·L^{-1}) did not affect the release of SP-like immunoreactivity content from C-fibers in rat trachea[6], however, the contractile responses of the tracheae to increasing concentrations of SP (0.1−3.0 μmol·L^{-1}) were reduced by the pretreatment of Cro (10 μmol·L^{-1}) (Tab 2). The EFS-induced contractile phase II of the bronchial strips was dissimilar to the responses of tracheae, which were not reduced by the agents. These results suggested that the neuropeptides (SP) released from the C-fibers of guinea pig tracheae (do not include

Tab 2. Contractions (mg) to substance P in the presence of Cro 10 μmol·L^{-1}. $\bar{x}\pm s$. $^aP>0.05$, $^bP<0.05$, $^cP<0.01$ *vs* **control.**

Strip	Group	Contraction (mg)/Substance P (μmol·L^{-1}) 0.1	0.3	1.0	3.0
Trachea ($n=5$)	Control	103±29	169±41	235±42	265±40
	Cro	72±41^c	102±43^c	151±66^c	172±79^b
Bronchus ($n=4$)	Control	52±16	82±22	128±22	154±33
	Cro	50±18^a	81±20^a	126±21^a	157±19^a

bronchi) could stimulate the mast cells to release histamine which amplified the phase II contractile magnitude of the smooth muscles.

Atropine was able to reduce the responses of EFS-induced phase II of the bronchial strips significantly, but did not inhibit EFS-induced phase II of the tracheal preparations (Tab 1). The results suggested that the neuropeptides released by C-fibers in bronchi stimulated the cholinergic nerves to release acetylcholine which increased the contractile magnitude of the phase II. Maybe the neuropeptides from the C-fibers between the trachea and bronchus could have different stimulations to the mast cells and cholinergic endings.

These came to the conclusion that there are different contractile mechanisms of smooth muscles between the tracheae and bronchi of guinea pig when the sensory nervous C-fibers are stimulated by EFS. Except the direct contractile effect of the neuropeptides on smooth muscles, histamine (in tracheae) and acetylcholine (in bronchi) are involved in the contractile responses of phase II to EFS respectively.

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C 神经兴奋体外引起豚鼠气管和支气管收缩的介质差异

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A **摘要** 氯苯那敏和色甘酸钠(Cro)能降低豚鼠气管 C 神经兴奋引起 的平滑肌收缩反应；渐增浓度的 P 物质(0.1—3.0 $\mu mol \cdot L^{-1}$)引起 的气管片收缩效应也可被 Cro 处理降低；然而支气管条的收缩反应 却不受上述药物影响，但能被阿托品处理降低. 提示 C 神经末梢兴奋 平滑肌收缩的介质在豚鼠的气管和支气管部位有明显差异.

关键词 气管；支气管；电刺激；氯苯那敏；色甘酸钠；P 物质