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Title : MECHANISM OF TRACHEAL CONSTRICTION BY SUCCINYLCHOLINE

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Introduction. Transient hypertension and disturbances of cardiac rhythm frequently occur following injection of succinylcholine (SCh). Since both are prevented by ganglionic blockade (1,2), they have been attributed to ganglionic stimulation or to reflex activation secondary to stimulation of peripheral sensory receptors. To our knowledge, similar effects in other visceral systems have not been documented. During studies with endotracheal tube cuff-pressure as a monitor of bronchomotor tone in dogs, we noted consistent, large increases in cuff-pressure after SCh injection. To identify possible causes, the effects of atropine and hexamethonium (C_6) were tested on the in vivo response, and isolated preparations were employed to study the direct action of SCh on tracheal smooth muscle in vitro.

Methods. After induction of anesthesia with thiamylal and paralysis with an initial bolus of SCh, dogs weighing about 20 kg were intubated with an 8 mm endotracheal tube fitted with a high volume, low pressure cuff, which was subsequently filled with water to a pressure of about 40 cm H_2O and connected to a pressure transducer. Respiration was controlled manually or with a ventilator. In some experiments, pulmonary resistance (R_L) was determined along with cuff-pressure using an esophageal balloon and simultaneous measurements of flow and transpulmonary pressure. Trachealis muscle obtained from dogs (single rings) and guinea pigs (chains of 3 rings) was mounted in organ baths containing Krebs-bicarbonate solution aerated with 5% CO_2 and 95% O_2; tension was recorded isotonically using counter weights of 1gm and 300 mg for canine and guinea pig tissues, respectively.

Results. Intravenous injection of SCh 0.5 (5 dogs; 11 trials) and 1.0 mg/kg (3 dogs; 5 trials) produced increases in cuff-pressure of 12 ± 2 and 28 ± 3 cm H_2O (mean ± SE), respectively; cuff-pressures remained elevated for more than 10 min before returning to baseline values (Fig. 1A). Intravenous atropine (1 mg/kg) or C_6 (5 mg/kg), injected at the peak of the SCh-response, produced an immediate drop in cuff-pressure to or below baseline values (Fig. 1B). The increase in cuff-pressure elicited by SCh (1 mg/kg) was accompanied by a slight increase in R_L in 2 of 5 trials (from control values of 0.4 and 1.1 cm H_2O/LPS to 1.1 and 1.9), by no change in R_L in 2 trials and by a slight decrease in 1 trial. In studies with isolated trachealis muscle, SCh did not contract canine preparations, but high concentrations (10^{-4} to 10^{-3} M/L) elicited a slight contraction of guinea pig tracheal chains, which was blocked by atropine (10^{-7} M/L).

Discussion. Fasciculations of skeletal muscle could have contributed to the initial rise in cuff-pressure following SCh, but the increase in pressure was of much longer duration than fasciculations and occurred with repeated doses of SCh that did not cause fasciculations. Furthermore, cuff-pressure was promptly returned to control values by atropine or C_6. Therefore, the sustained rise in cuff-pressure reflects contraction of visceral (trachealis) rather than skeletal muscle. Although SCh had weak muscarinic effects on guinea pig tracheal chains, the increase in cuff-pressure in dog experiments cannot be attributed to direct effects on smooth muscle; thus, SCh did not contract canine trachealis muscle in vitro and the increase in cuff-pressure in vivo was reversed by ganglionic blockade. We conclude that SCh can elicit marked contraction of tracheal smooth muscle by a stimulant action on parasympathetic pathways at, or central to, autonomic ganglia.

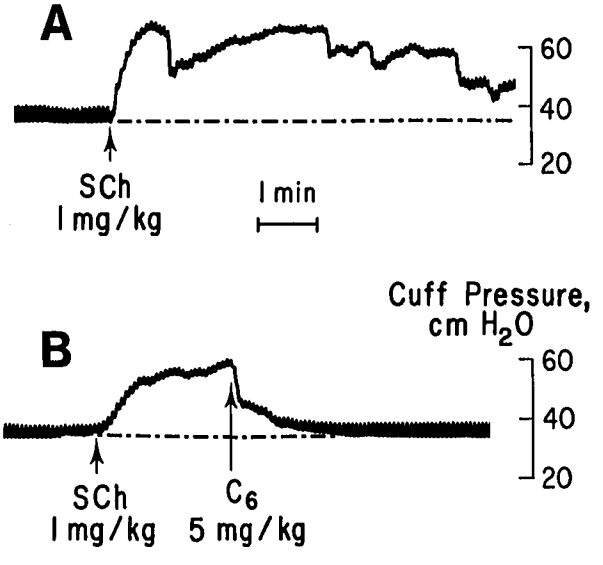

Fig. 1: Increases in cuff-pressure elicited by SCh. The response in trace A persisted for 14 min before returning to control values. Trace B shows a second response to SCh, in the same animal, which was promptly terminated by injection of C_6.

References.
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