Physiological and Electron-Microscopic Investigations of the Trachea after Pilocarpine

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Summary. Physiological and electron-microscopic investigations were carried out in normal cats before and after treatment with pilocarpine in an attempt to determine its influence on respiratory tract fluid (RTF), ciliary frequency and the ultrastructure of the epithelia.

The quantity of RTF produced during the control period could not be measured; however, after pilocarpine the quantity of RTF collected ranged from 0.1 ml to 0.3 ml. Ciliary frequency showed a dose-dependent increase.

Pilocarpine exerted a marked stimulatory effect on the exocrine secretory mechanism of the trachea and a faster extrusion of the mucus granules.

Key words: Respiratory tract fluid-Ciliated epithelium-Ciliary activity-Pilocarpine.

Since its discovery, the naturally occurring cholinomimetic alkaloid pilocarpine has been used clinically as a diaphoretic agent, to correct mydriasis, to combat xerostomia in atropine poisoning, and as a diagnostic tool in demonstrating peripheral nerve lesions (Goodman and Gilman, 1970). The literature on the effect of this drug on the tracheobronchial is very scant. Brauchhausen et al. (1969) showed that pilocarpine applied into the conjunctival sac caused an increase in airway resistance of asthmatic patients. In the same year Goldenberg et al. (1969) showed an increased activity of the granular pneumocyte after pilocarpine and incriminated them in the elaboration of pulmonary surfactant. Ivemark and Robertson (1970) showed that pilocarpine administration is followed by a rapid increase in surface activity in the alveolar wash. The continued usage of the cholinomimetic alkaloids warrants a study of their effect on the tracheobronchial tree. We undertook such a study with three questions in mind:
a) How does pilocarpine influence respiratory tract fluid production?
b) What effect does this drug have on ciliary frequency?
c) Are ultrastructural changes demonstrable in the tracheal epithelium after pilocarpine?

METHODS

The experiments were carried out in cats of both sexes weighing between 2.5 - 4.5 kg. They were anesthetized with pentobarbital-sodium (40 mg/kg body weight i.p.).

PHYSIOLOGICAL EXPERIMENTS

1. Respiratory Tract Fluid (RTF)

The cats were tracheotomized at the level of the 3-4 tracheal ring and intubated with the T tracheal cannula. The head of the animal was enclosed in a chamber in which the relative humidity was kept at 80%. The room temperature was 25°C. The cat was tilted at a 45° angle and a collecting tube placed at one side of the T. The femoral artery was cannulated to allow a constant monitor of the blood pressure and heart rate. Respiratory tract fluid was collected over 3 hours and measured. Following this, pilocarpine hydrochloride (0.7 mg/kg) was applied and measurements continued for a further 1 hour.

2. Mucociliary Function

Isolated airway preparations were used as previously described by Iravani (1967). Once the dissection was completed, the temperature in the bath was raised in stepwise fashion to 38°C. A period of 1 hour was allowed to elapse before ciliary function was studied. After this time a control measurement of ciliary activity was studied by means of the ultropak system (Leitz 22 x 10-25 magnification) as previously described (Iravani 1967, 1969). Pilocarpine (10^-8 - 10^-3 g/ml) was then added to the incubating Krebs Henseleit solution (1932), through which carbogen (95 O₂ and 5% CO₂) was continuously bubbled, and ciliary activity was determined after 15-20 minutes. A control measurement was taken before every new dose of pilocarpine.

ELECTRON MICROSCOPICAL STUDIES

One group of rats were sacrificed immediately after anesthetization, the other group received pilocarpine (0.7 mg/kg i.p.). The latter group were sacrificed 60 minutes after administration of the drug. In both groups the trachea was extirpated and part of its mucosa removed.