

Title : A METHYLXANTHINE AEROSOL FOR BRONCHOSPASM DURING ANESTHESIA

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Introduction. Asthmatic patients requiring anesthesia are at higher risk than nonasthmatics. The major problem in these patients is bronchospasm. The theophylline compounds used to treat bronchospasm interact with potent inhalation anesthetics to cause cardiac arrhythmias in a dose-related manner.

Aerosol administration offers two main advantages for bronchodilator therapy. First, for the same level in systemic blood, higher drug concentrations can be achieved in lung. Second, aerosols produce almost as rapid an onset as a direct intravenous injection.

Dyphylline (1,3 dihydroxypropyl theophylline) is 300 times more water soluble than theophylline at a neutral pH, and has been in clinical use for decades as a parenteral and oral preparation for bronchodilator therapy. This study was designed to compare the effectiveness of equivalent blood concentrations of this drug at preventing the development of bronchospasm in experimental canine asthma by the aerosol and intravenous route.

Methods. Asthma was induced in dogs previously sensitized to ascaris antigen by ventilating them with aerosolyzed ascaris antigen for 10 minutes. Pulmonary resistance (R_L) was calculated from simultaneous pressure and flow measurements during fixed volume controlled ventilation at the same peak flow and corrected for elastic recoil pressure. Dynamic compliance (C_L) was calculated by dividing tidal volume by pressure change measured between points of zero flow. The ascaris antigen was dissolved in 10 ml water in the control and dyphylline infusion studies and in 10 ml 25% dyphylline in the aerosol studies. Dyphylline infusion rates were determined from clearance values observed in preliminary experiments with intravenous injection.

Results. Prior to antigen exposure, R_L and C_L were not significantly different in control and dyphylline treated dogs. 15 minutes after the start of antigen administration R_L averaged 27.6 ± 5.12 (mean \pm SEM) in control dogs and only 7.7 ± 1.46 in dyphylline-aerosol treated dogs. This statistically significant difference persisted throughout the experimental period. Dyphylline blood levels averaged $4.1 \mu\text{g/ml}$ at the end of the 10 minute period of aerosol inhalation and remained at that level for 60 minutes. At equivalent blood levels ($4.33 \pm 0.27 \mu\text{g/ml}$) dyphylline infusion produced a much smaller decrease in R_L , not significantly different from control.

Discussion. Dyphylline aerosols are highly effective at preventing antigen induced bronchospasm in experimental canine asthma at low blood drug concentrations. Dyphylline by aerosol route may be a useful drug in the treatment of intraoperative bronchospasm in man.

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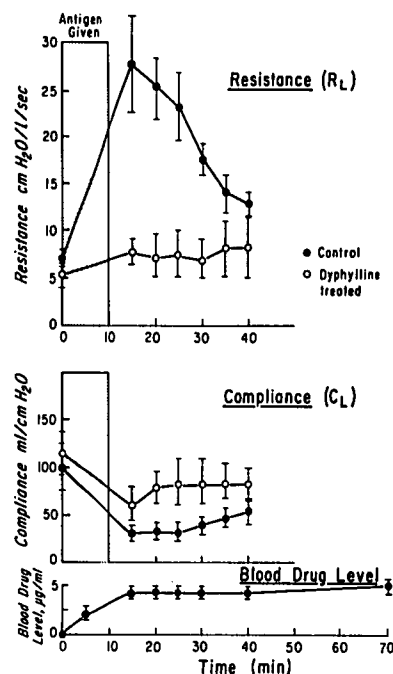


Fig. 1 R_L and C_L changes in control and dyphylline-aerosol treated dogs.

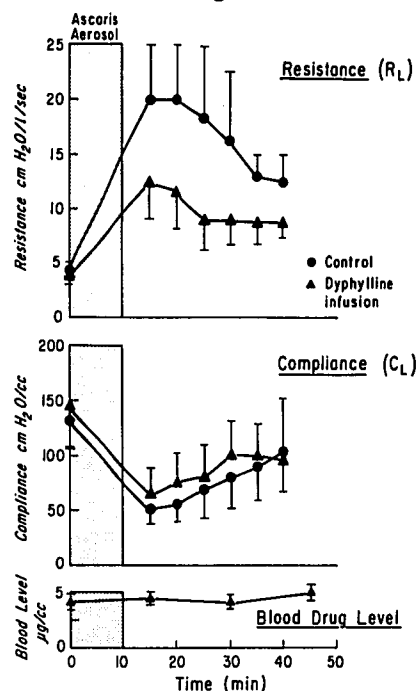


Fig. 2 R_L and C_L changes in control and dyphylline-infusion treated dogs.