

TITLE: BRONCHOMOTOR EFFECTS OF GLYCOPYRROLATE AND ATROPINE AEROSOL INHALATION

AUTHORS: T. J. Gal, M.D., P. M. Suratt, M.D., J. Lu, M.D.

AFFILIATION: Departments of Anesthesiology and Internal Medicine, University of Virginia Medical Center, Charlottesville, VA 22908

Introduction. Atropine aerosols produce significant bronchodilation when inhaled, but the undesirable side effects from systemic absorption have limited their clinical use. Quarternary anticholinergic compounds are poorly absorbed and effects of inhalation are more likely to be confined to the airways. Glycopyrrolate, a quarternary compound, exhibited prolonged bronchodilating activity when given intravenously,¹ but the effects of its inhalation have not been evaluated. This study was conducted to assess the time course and magnitude of any bronchomotor effects of glycopyrrolate aerosols and to compare them with equipotent doses of atropine.

Methods. The study, which received institutional approval, was carried out in six healthy male volunteers (ages 24-26). Each received blindly in random sequence, aerosols of glycopyrrolate (1.0 mg), atropine (2.0 mg), and saline placebo on separate days from a Rosenthal-French Dosimeter. Pulmonary function was tested before aerosol inhalation (control), 30 minutes after each treatment and then hourly for six hours. Airway resistance (R_{aw}) and functional residual capacity (FRC) were measured in a constant volume body plethysmograph. Specific airway conductance (sGaw) was calculated as the reciprocal of R_{aw}/FRC to eliminate changes in airway size arising passively from changes in FRC. Partial expiratory flow volume (PEFV) curves were performed by starting forced expiration at the end of a normal inspiration and then followed by a forced vital capacity (FVC) maneuver. Expiratory flow on PEFV curves was measured at a volume equal to total lung capacity minus 60% of FRC ($\dot{V}_{max} 40$). Forced expiratory volume in 1 sec (FEV_1) was also computed from FVC maneuvers.

Results. A significant decrease in R_{aw} occurred after glycopyrrolate inhalation. Since FRC did not change, sGaw increased significantly (Table 1). The increased sGaw reached 90% at 30 min and was sustained for the remainder of the experiment. Atropine produced an increase in sGaw between 30 min and 2 hrs after inhalation. Increases in $\dot{V}_{max} 40$ with glycopyrrolate followed a pattern similar to sGaw but maximal changes (36%) were considerably less. Atropine also increased $\dot{V}_{max} 40$; the maximal increase (25%) was noted one hour after inhalation. Slight but significant increases in FEV_1 (4-6%) occurred between one and six hours after glycopyrrolate. Atropine produced a similar increase in FEV_1 between 30 min and 2 hrs after inhalation. Subjective sensations after glycopyrrolate did not differ from placebo. Atropine inhalation produced a sensation of dry mouth in all subjects; lightheadedness and drowsiness were noted in four of the six subjects. Heart rate was unchanged after glycopyrrolate but increased 26% during the first 2 hrs after atropine inhalation.

Discussion. The results of this study clearly demonstrate that glycopyrrolate administered by aerosol possessed maximum bronchodilating actions

similar to systemic administration of the drug. The effects of the inhaled drug appeared to be more sustained, lasting more than 6 hrs. Atropine inhalation was associated with much shorter lived airway effects but significantly greater incidence of systemic side effects. We conclude that inhalation of glycopyrrolate aerosol was effective in producing bronchodilation of long duration, free of the undesirable systemic side effects associated with systemic administration of anticholinergic drugs.

Table 1

TIME RELATED CHANGES IN sGAW ($\text{sec}^{-1} \cdot \text{cmH}_2\text{O}^{-1}$) AFTER AEROSOL TREATMENTS

TIME	P	A	G
CONTROL	0.25 (.03)	0.25 (.03)	0.23 (.02)
30 min	0.26 (.03)	0.36* (.05)	0.44* (.04)
1 hr.	0.30 (.03)	0.38* (.06)	0.44* (.05)
2 hr.	0.26 (.02)	0.36* (.04)	0.40* (.04)
3 hr.	0.30 (.02)	0.36 (.06)	0.40* (.04)
4 hr.	0.27 (.03)	0.33 (.04)	0.42* (.03)
5 hr.	0.30 (.03)	0.32 (.04)	0.42* (.03)
6 hr.	0.29 (.03)	0.29 (.03)	0.45* (.04)

Values are Mean \pm SEM for six subjects

*p < 0.01 denotes significant difference from placebo by paired t-test

P = placebo; A = Atropine; G = Glycopyrrolate

References.

- Gal TJ, Suratt PM: Atropine and glycopyrrolate effects on lung mechanics in normal man. *Anesth Analg* 60:85-90, 1981