

**TITLE:** METHYLPREDNISOLONE PREVENTS PROPRANOLOL-INDUCED INCREASES IN AIRWAY RESPONSIVENESS IN BASENJI-GREYHOUND DOGS.

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$\beta$ -adrenergic antagonists increase airway responsiveness in patients with asthma and in basenji-greyhound dogs (BG). Since glucocorticoids potentiate  $\beta$ -adrenergic function it is possible that these agents can reverse the increase in airway responsiveness produced by  $\beta$ -adrenergic antagonists. We studied the ability of  $\beta$ -adrenergic blockade to alter airway responsiveness to methacholine (MCH) challenge in the presence and absence of chronic methylprednisolone (MP).

Five BG dogs were studied on 4 occasions during thiopental-fentanyl anesthesia, in random order. Airway responsiveness to MCH was determined alone and in the presence of propranolol (P) (2 mg/kg) prior to and after 4 weeks of MP treatment. P was administered prior to aerosol challenge intravenously as a bolus. Aerosol challenge consisted of 5 standardized breaths with increasing concentrations of MCH (.03, .075, .15, .3, .75, 3.0, and 10.0 mg/ml). Pulmonary resistance ( $R_L$ ) was calculated from simultaneous pressure and flow measurements at points of zero flow. Transpulmonary pressure was estimated as the difference between the pressure measurements of an

esophageal balloon and a needle in the airway. Maximal changes in  $R_L$  were recorded after each MCH challenge. Data were analyzed by two way ANOVA and expressed as the ratio of the post challenge to the pre challenge  $R_L$ .

Neither P nor MP alone significantly changed baseline  $R_L$ . The combination of P and chronic MP treatment, however, significantly altered airway responsiveness to MCH ( $p < 0.05$ ). Four weeks of chronic MP treatment prevented the increased airway responsiveness associated with beta blockade and MCH in BG dogs. During the 4 study conditions (C, P, MP, P+MP) MCH .15 mg/ml, altered airway responsiveness from baseline: (mean  $\pm$  SEM)  $2.19 \pm 0.17$ ,  $3.48 \pm 0.43$ ,  $2.39 \pm 0.10$ ,  $1.86 \pm 0.17$  fold respectively ( $p < 0.01$ ).

We conclude that chronic MP treatment blocks the increased airway responsiveness caused by P in BG dogs. These findings suggest that chronic corticosteroid therapy may prevent the adverse effects of beta-adrenergic blockade in patients with asthma. Supported by NIH HL 38435.

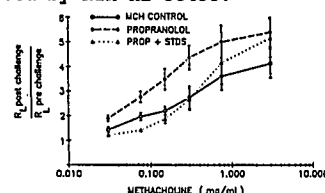


Fig. 1: The effect of propranolol on MCH challenge in steroid treated BG dogs.

A1159

**TITLE:** HIGH RESOLUTION COMPUTER TOMOGRAPHY(HRCT) TO ASSESS CHANGES IN AIRWAY RESISTANCE DURING ANESTHESIA.

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Anesthetic agents alter lung resistance( $R_L$ ). However, recent work has suggested that airway resistance ( $R_{aw}$ ) comprises only a fraction of the traditional  $R_L$ . Direct noninvasive measures of airway caliber such as HRCT may better elucidate the site of this airway constriction. We therefore compared changes in airway size as measured by HRCT and  $R_L$  in 10 dogs challenged with aerosol histamine.

Dogs were anesthetized with thiopental 300mg and fentanyl 25ug and paralyzed with succinylcholine 10mg. Dogs were positioned supine in the CT scanner and ventilated at tidal volume of 400 cc. Airway dimensions were measured in a lung region where at least 10 airways ranging in size from 1-10mm were discernible. Within this region, ten 2mm thick serial HRCT slices were made in each state at FRC. We measured the luminal areas of all airways from a selected slice based on presence of the airway in all the experimental maneuvers. One slice above and below each matched slice was chosen, the airways measured, and the three levels averaged to account for slight displacement in localization. The HRCT scans were imaged from a light box through a video camera to a PC computer. The scans were digitalized and the airway areas were measured by a

computer edging process, and converted to  $R_{aw}$  using  $1/(\text{area})^2$ . On a separate day, we followed the same protocol and calculated  $R_L$  from simultaneous pressure and flow measurements. Data were analyzed by paired t test. Measurements were made in the control state, after histamine aerosol challenge, and following a standardized hyperinflation of three times tidal volume.

Histamine aerosol produced significant increases in  $R_{aw}$  and  $R_L$ .  $R_{aw}$  increased  $458.3 \pm 98.95$  (mean $\pm$ SEM),  $p < 0.001$ , and  $R_L$  increased  $259.0 \pm 24.74$ ,  $p < 0.00001$ . Hyperinflation after aerosol histamine challenge caused a further constriction of  $R_{aw}$  of  $416.8 \pm 157.7$ ,  $p < 0.027$ , but a decrease in  $R_L$  of  $-68.62 \pm 15.45$ ,  $p < 0.002$ .

These data show that HRCT and  $R_L$  measure different airways *in vivo* and may be useful in identifying the site of action of anesthetics on airways. NIH HL 38435

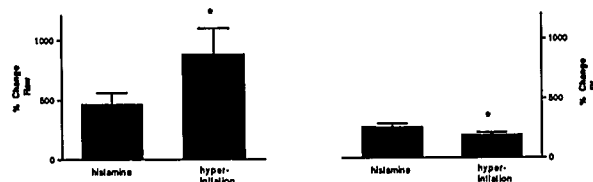


Fig. 1) Change in  $R_{aw}$  as measured by HRCT(left) and change in  $R_L$ (right).