Title: ATTENUATION OF BRONCHOCONSTRICTION BY NIFEDIPINE - A CALCIUM CHANNEL BLOCKER

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Introduction. The treatment of angina or supraventricular tachycardia in patients with bronchospastic disease has been difficult, since administration of beta adrenergic blockers produces undesirable increases in airway tone. Calcium channel blockers are effective at treating tachycardia and angina but their effects on airways are not known. They could have beneficial effects on airways by relaxing airway smooth muscle or by inhibiting mediator release, since both of these processes are calcium dependent. To assess the effect of calcium channel blockers on airway tone, we compared the ability of nifedipine to attenuate bronchospasm induced by an allergic stimulus (Ascaris antigen), an irritant stimulus (citric acid 10%) and a cholinergic stimulus (methacholine) in an animal model of asthma.

Methods. Five Ascaris sensitive Basenji-Greyhound dogs were challenged (in separate experiments) with Ascaris antigen (3 µg/ml) or citric acid (10%) administered for 5 min., or methacholine (0.075, 0.15, and 0.3 mg/ml) given for 5 breaths. Challenges were delivered after pretreatment with aerosolyzed nifedipine (12.5 mg in 40% ethanol) or after a control aerosol (40% ethanol). Pulmonary resistance (R_L) was calculated by the method of Von Neergaard and Wirz and dynamic compliance (C_{dyn}) by dividing the tidal volume by the pressure difference between points of zero flow.

Results. Neither ethanol alone nor nifedipine in ethanol altered resting airway tone. R_L was 2.2 ± 0.17 (mean ± SE) cm H_2O/L/sec, 2.0 ± 0.17 and 2.1 ± 0.20 in untreated, ethanol treated, and nifedipine treated dogs; the respective values for C_{dyn} were 92 ± 8 ml/cm H_2O, 98 ± 10, and 94 ± 12. Nifedipine attenuated citric-acid-induced (Fig. 1) and methacholine-induced (Fig. 2) airway constriction. Nifedipine also attenuated antigen-induced airway constriction. After antigen challenge, R_L increased 5.1 ± 0.83 fold and 3.0 ± 0.48 fold in untreated and nifedipine-treated dogs ($p < .05$) respectively, and C_{dyn} decreased to 0.33 ± 0.04 and 0.48 ± 0.03 times the prechallenge value in untreated and nifedipine-treated dogs, respectively.

Discussion. Nifedipine antagonism of methacholine-induced bronchoconstriction demonstrates a direct effect on smooth muscle. However, since citric acid challenge and antigen challenge release bronchoactive mediators, nifedipine antagonism of the responses to these challenges could be partly due to inhibition of mediator release. Since nifedipine did not increase resting airway tone and effectively attenuated the increases in R_L provoked by antigenic, irritant, and cholinergic challenges, nifedipine may be particularly useful in treating supraventricular tachycardias and angina in patients with bronchospastic disease.

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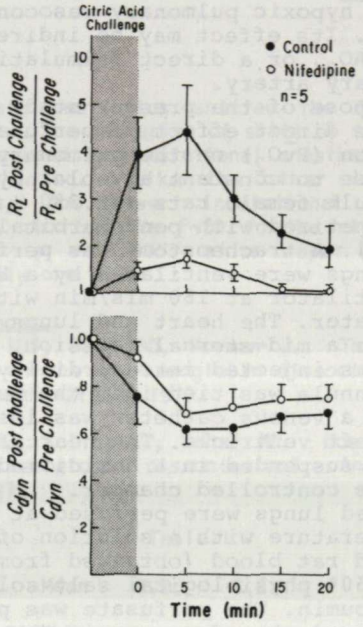

Figure 1 - R_L and C_{dyn} in control and in nifedipine-treated dogs prior to and after citric acid (10%) aerosol challenge. Abscissa represents elapsed time from end of challenge.

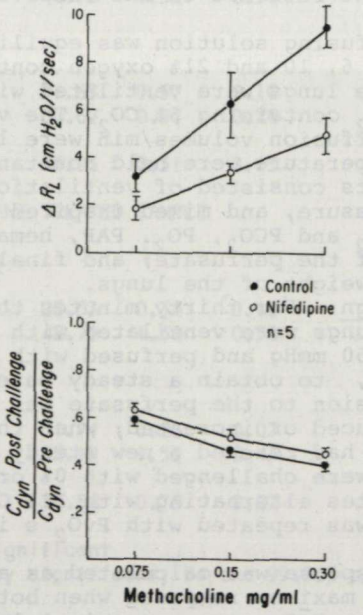

Figure 2 - R_L and C_{dyn} in control and nifedipine-treated dogs challenged with methacholine (0.075, 0.15, and 0.30 mg/ml).