ACUTE INDUCTION OF TRACHEO-BRONCHOCONSTRICTION IN MORPHINE/ CHLORALOSE ANESTHETIZED BEAGLE DOGS: PHYSIOLOGICAL APPROACH AND PRINCIPLES OF THERAPY

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The respiratory system serves as a functional gas exchanger which, under neural control, contributes greatly to homeostasis. This study was designed to evoke tracheo-bronchoconstriction by different stimuli and to study the respiratory and hemodynamic effects of three bronchodilators (Canning *et al*., 2001).
Tracheo-bronchoconstriction was induced in morphine/chloralose-anesthetized beagle dogs (n=8) of either sex weighing (mean ± sd) 11.6 ± 2 kg by 5% CO_2, 10% O_2 or intravenous bethanechol (0.5 mg/kg) (Breen *et al*., 1987). Hypercapnia caused no significant ($p>0.01$, ANOVA; paired t-test) respiratory or hemodynamic effects. Hypoxia significantly ($p<0.01$) increased heart rate (HR), pulmonary artery pressure (Pap), cardiac output (CO), and peripheral vascular resistance (PVR) Table 1. No significant changes were observed in left ventricular end-diastolic pressure (LVEDP), tracheal pressure (Tp), airway pressure (Paw), bronchial pressure (Brp), and pulmonary compliance (PC) due to hypoxia. Changes due to gas mixtures were transient and returned to baseline upon normal respiration. In contrast, bethanechol caused significant increases in Pap, LVEDP, PVR, Tp and Paw with no significant changes in HR, CO or Brp. Compared to gas mixtures, bethanechol produced greater respiratory and hemodynamic effects that may resemble asthma and chronic obstructive pulmonary disease.

Stimulus/Recovery	Heart Rate (bpm)	Tp (mmHg)	Paw (mmHg)	Brp (mmHg)	Pap (mmHg)	LVEDP (mmHg)	Cardiac Output (l/min)	Pul. Vascular Ressistance LVEDp-Pap/CO	Pul. Compliance Vt/ΔPaw	Blood Gases PCO_2	Blood Gases PO_2	pH	End Tidal PCO_2	End Tidal O_2%
Baseline	68.4	18.0	1.7	28.4	14.5	13.7	1.7	0.8	159.4	35.2	93.8	7.4	36.0	19.8
	±3.36	±0.57	±0.29	±2.38	±0.75	±0.52	±0.18	±0.20	±32.03	±1.63	±2.13	±0.02	±0.60	±0.16
High CO_2 (5%)	72.5	17.4	1.8	31.4	15.1	15.2	1.7	0.6	154.0	50.7	336.4	7.2	61.1	93.8
	±3.75	±1.08	±0.28	±2.75	±0.77	±0.75	±0.20	±0.21	±30.78	±3.94	±73.04	±0.02	±0.52	±0.37
15 min	72.7	18.4	1.8	34.9	15.8	15.2	1.7	1.2	201.8	36.7	95.0	7.4	39.8	19.5
	±4.96	±0.68	±0.33	±2.67	±1.02	±0.85	±0.20	±0.25	±77.97	±2.65	±2.45	±0.02	±1.51	±0.27
Low O_2 (10%)	141.1	29.3	2.2	34.6	35.7	19.2	3.4	5.5	109.8	33.3	33.8	7.4	39.5	9.0
	±15.07	±5.18	±0.28	±2.81	±1.70	±1.72	±0.51	±0.90	±14.84	±3.79	±3.35	±0.02	±1.54	±0.27
15 min	73.8	18.7	1.7	34.4	17.3	16.8	1.7	0.8	168.3	34.2	86.9	7.4	37.9	19.3
	±4.26	±0.85	±0.31	±2.87	±0.63	±0.52	±0.17	±0.19	±39.66	±2.20	±1.76	±0.02	±1.34	±0.16
0.5 mg/kg	78.1	55.8	3.3	34.7	26.0	24.9	2.2	3.7	73.7	39.6	58.5	7.2	37.6	19.6
Bethanechol	±14.93	±3.05	±0.34	±2.91	±1.31	±2.51	±0.41	±0.85	±13.88	±2.95	±4.90	±0.03	±2.10	±0.18
15 min	94.4	60.8	2.1	34.7	21.3	14.7	2.1	3.4	129.0	35.2	75.5	7.3	38.4	19.4
	±4.40	±4.63	±0.30	±2.92	±0.48	±1.12	±0.22	±0.63	±25.33	±3.45	±3.02	±0.04	±1.53	±0.18
30 min	88.8	55.5	1.9	34.6	20.8	18.3	2.0	3.7	145.2	31.7	81.4	7.3	36.3	19.4
	±5.01	±4.26	±0.33	±3.06	±0.57	±3.06	±0.25	±0.74	±31.68	±2.39	±2.35	±0.03	±1.18	±0.18

Table1: Changes in Respiratory and Hemodynamic Parameters in Response to Different Stimuli Hypercarbia, Hypoxia, and 0.5 mg/kg Bethanechol. Values are Mean ± S.E.M of 8 dogs

Four groups (4 dogs per group) were used to compare the respiratory and hemodynamic effects of intravenous injection of aminophylline, atropine, terbutaline, or saline control on bethanechol-induced bronchoconstriction. Both atropine (0.04 mg/kg) and aminophylline (20 mg/kg) increased HR significantly ($p<0.006$) compared to control. Atropine, starting at 0.02 mg/kg, significantly decreased the bethanechol-elevated Pap, with no changes in the other groups. Atropine (0.02 mg/kg) and aminophylline (20 mg/kg) significantly decreased LVEDP after bethanechol. Atropine decreased 65% of the elevated Tp compared to 47%, and 12.6% for terbutaline, and aminophylline, respectively. Only terbutaline significantly decreased Paw and increased PC. No significant changes were observed in CO, PVR, Brp, or in blood and end-tidal gases after any bronchodilator. With limitations, this model might be of benefit in evaluating the mechanism of other bronchodilators that alter autonomic nervous control, such as M_3-selective antimuscarinics (Morley 1994).

Breen, P. *et al* (1987). *Journal of Applied Physiology*, vol. **63**, pp 262-269.
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